Poster Session 1

P001

DNA methylation of toll-like receptors 2 and 4 in Behçet's disease

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Introduction. Altered innate immune function plays an important role in the initiation of inflammatory response in Behçet's disease (BD). Toll-like receptors (TLRs) has a key role in the innate immune system.
Aims. Since the role of TLRs in the pathogenesis of BD and introducing of epigenetic mechanisms role in the pathogenesis of inflammatory diseases, this study was aimed to evaluate the TLR 2 and 4 expression level and DNA methylation rate in patients with BD.
Methods. In a case-control study, 47 Iranian Azari patients with BD and 61 age, sex and ethnically matched healthy controls recruited to the study. Peripheral blood mononuclear cells were isolated from EDTA blood tubes by Ficoll density-gradient centrifugation. Genomic DNA samples of participants were extracted using the rapid genomic DNA extraction (RGDE) method from the peripheral blood collected in tubes containing EDTA. Total RNA was extracted from the PBMCs according to the TRIzol protocol. TLR2 and TLR4 genes promoter CpG islands were predicted with eukaryotic promoter database (EPD). Methylated DNA immunoprecipitation (MeDIP) was carried out using EpiQuik™ MeDIP Ultra Kit.
Results. Forty-seven patients with diagnosis of BD and 61 healthy control included in this study. TLR4 expression were significantly higher in the BD group compared with control group. TLR4 methylation rates in the BD group was significantly lower. Furthermore, there was no significant difference in the TLR2 expression and methylation rates between patient and control groups. No association was observed between the TLR 2 and 4 methylation rates and clinical manifestations of BD and disease activity.
Conclusion. Our preliminary findings here suggest that the hypomethylation of TLR4 gene and increased expression of TLR4 may play a role in the pathogenesis of BD.

References

1. WU H, ZHANG Y: Reversing DNA Methylation: Mechanisms, Genomics, and Biological Functions. *Cell* 2014 Jan 16; 156(1-2): 45-68.
2. WU X, ZHANG Y: TET-mediated active DNA demethylation: mechanism, function and beyond. *Nat Rev Genet* 2017 Sep; 18(9): 517-534.
3. ZHANG X, FU R, YU J, WU X: DNA demethylation: where genetics meets epigenetics. *Curr Pharm Des* 2014; 20: 1625-31.
4. JEFFRIES MA, SAWALHA AH: Autoimmune disease in the epigenetic era: how has epigenetics changed our understanding of disease and how can we expect the field to evolve. *Expert Rev Clin Immunol* 2015 Jan; 11(1): 45-58.

P002

Histopathological characteristics of central nervous system in chronic progressive neuro-Behçet's disease

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Introduction. Central nervous system (CNS) involvement in Behcet's disease, usually called neuro-Behçet's disease (NB), is one of the most serious complications of the disease. Accumulating evidence has clarified that NB can be classified into acute type (acute NB) and chronic progressive type (CP NB) depending on their clinical courses. CP NB is characterized by the persistent elevation of cerebrospinal fluid (CSF) IL-6. However, the mechanism of the continuing elevation of CSF IL-6 remains to be elucidated.
Aims. The present study was carried out to disclose the histological evidence for the sustained elevation of IL-6 in CP NB.
Methods. Immunohistological features of autopsied brain tissues from a patient with CP NB were compared with those from another patient with NB who had been in a long-term remission of acute NB and died of myocardial infarction. Brain tissues were stained with anti-TMEM119 antibody and anti-CD68 antibody, and analysed under the light microscopy.
Results. Marked proliferation of microglia was observed in the brainstem of CP NB as well as in that of NB in a long-term remission. However, infiltration of CD68+ cells in the brainstem was observed only in CP NB, but not in NB in a long-term remission. Infiltration of CD68+ cells was distributed mainly around small vessels throughout the brainstem (Figure). Double staining of brain tissues confirmed that CD68+ cells were macrophages, but not TMEM119+ microglial cells. In addition, infiltration of CD68+ cells was observed most markedly in pons and medulla, but it could be detected also in cerebellum, cerebrum and hippocampus.

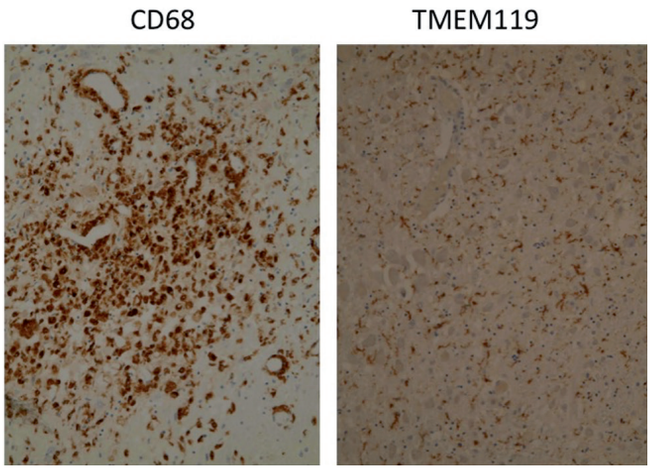

Fig. 1. Infiltration of CD68+ cells in the brainstem of a patient with CPNB.

Conclusion. These results indicate that perivascular infiltration of CD68+ monocyte throughout the whole brain tissue is a pivotal histopathological feature of CP NB. Moreover, it is strongly suggested that infiltration of activated monocytes, but not proliferation of activated microglia, might result in the prolonged elevation of CSF IL-6, thus accounting for the efficacy of methotrexate and infliximab in CP NB.

References

1. HIROHATA S: Neurological and neuropsychological manifestations in Behçet's syndrome. *In*: EMMI L, ed. Behçet's syndrome, Rare diseases of the immune system. Springer Verlag Italia. Milan. pp.83-96, 2014.
2. HIROHATA S: Neurological Involvement. *In*: ISHIGATSYBO Y, ed. Behçet's Disease, From Genetics to Therapies. Springer Japan. Tokyo. pp.101-116, 2015.
3. HIROHATA S, KIKUCHI H: Pathological characteristics. *In*: HIROHATA S, ed. Behçet's Disease- Progress in recent years and unmet needs for the future. Nova Biomedical, New York. pp.59-74, 2015.

P003

Elevated levels of serum immunoglobulin D in active mucocutanous Behçet's disease

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Introduction. Behçet's disease (BD) is an autoinflammatory disorders mainly characterized by recurrent oral aphthosis, genital ulcers, and chronic relapsing bilateral uveitis. Although several mechanisms have been proposed to explain the complex BD physiopathology the etiology is still not understood. Regulators of B-cell survival and immunoglobulin class-switch recombination have been reported to be up-regulated in BD. Even though, increased serum immunoglobulin levels in BD were observed, the involvement of Immunoglobulin D (IgD) in both BD physiopathology and development of the clinical manifestations disease is still unknown.
Aims. This work was conducted to compare the circulating levels of IgD in a cohort of patients with BD and healthy control (HC), and to correlate IgD levels with the status of disease activity, severity and specific clinical parameters.
Methods. Serum amyloid A (SAA) and IgD serum concentration were determined by ELISA assay in ninety-nine serum samples collected from 72 BD patients and 29 HC subjects.
Results. Serum concentration of IgD resulted higher in BD than HC (p=0.029) and in patients with high serum levels of serum amyloid A (SAA)-BD than low SAA-BD subgroup (p=0.035), as well as in active mu-

cocutaneous subset (p=0.036) (Fig. 1). In addition, the analysis of association between a putative risk factor and high IgD levels showed that high SAA-BD as well as active mucocutaneous-BD disease subset were associated with a high risk for higher IgD (odds ratio = 3.978, CI: 1.356 - 11.676 and odds ratio = 4.286, CI: 1.192 - 15.407, respectively).

Conclusion. Although further studies are needed to clarify the role of IgD in BD pathogenesis, our results showed that elevated levels of IgD observed in BD could discriminate subset of patients according to presence / absence of active mucocutaneous manifestations.

References

1. YAZICI H, SEYAHI E, HATEMI G *et al*.: Behçet syndrome: a contemporary view. *Nat Rev Rheumatol* 2018 Jan 24; 14(2): 119.
2. CHEN K, XU W, WILSON M *et al*.: Immunoglobulin D enhances immune surveillance by activating antimicrobial, proinflammatory and B cell-stimulating programs in basophils. *Nat Immunol* 2009 Aug; 10(8): 889-98.
3. VITALE A, RIGANTE D, LOPALCO G *et al*.: Serum amyloid-A in Behçet's disease. *Clin Rheumatol* 2014; 33: 1165-1167.
4. LOPALCO G, LUCHERINI OM, VITALE A *et al*.: Putative Role of Serum Amyloid-A and Proinflammatory Cytokines as Biomarkers for Behçet's Disease. *Medicine* (Baltimore) 2015 Oct; 94(42): e1858.

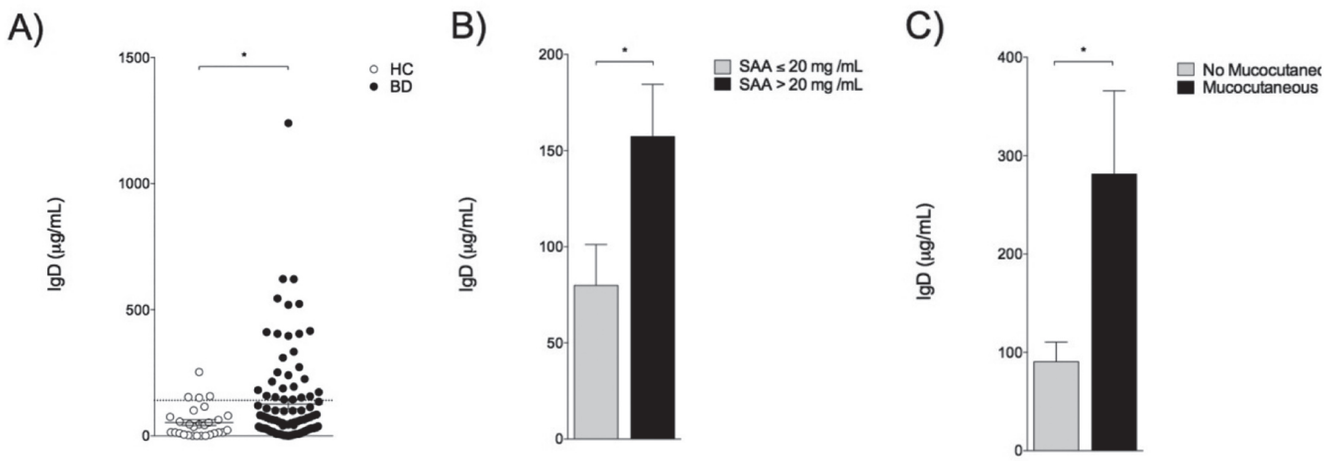

Fig. 1. Serum IgD levels in BD patients and HC.

P004

Hughes-Stovin syndrome in Behçet's disease: 13 cases

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Introduction. Hughes-Stovin Syndrome (HSS) is a very rare clinical disorder characterized by thrombophlebitis and multiple pulmonary and/or bronchial aneurysms or Aneurysms in systemic circulation. HSS has also been considered as a variant of Behçet's disease (BD).
Aims. The aim of this study is to describe the epidemiological, clinical characteristics and therapeutic possibilities in Moroccan patients suffering from BD with HSS
Methods. We analyzed retrospectively the medical records of 1646 patients fulfilling the international diagnostic criteria of Behçet's disease. We included those with Hughes-Stovin syndrome, and determined their demographic, clinical and biological characteristics and outcomes.
Results. Eleven male patients and two women had Hughes-Stovin syndrome associated to Behçet's disease. The mean age was 31 years (19-52 years). BD was revealed by deep vein thrombosis in 7 cases and by aneurysms in 3 cases. the association of these 2 vascular lesions revealed Behçet's disease in 1 case and complicate it in 2 cases. Venous thrombosis was multifocal in 3 cases and involved the inferior vena cava (6 cases), the superior vena cava (1 case), the ilio-femoro-popliteal axis (4 cases), the upper limb (1 case). the hepatic veins (3 cases) and / or the cerebral sinuses (1 case), pulmonary embolism was observed in 1 case. Pulmonary arterial aneurysms were multiple in 4 cases, most often bilateral (6 cases). Treatment was based on steroids and cytotoxic agents (Cyclophosphamide/ Azathioprine) in all our patients. 2 patients received anticoagulants (isocoagulant dose) and 6 received antiplatelet agents under strict surveillance.7 cases have been treated surgically. Three deaths occurred following a major hemoptysis related to rupture of pulmonary aneurysm. The evolution was good in 7 cases and imprecise in 3 cases.
Conclusion. Hughes-Stovin syndrome should be considered in the presence of deep vein thrombosis in a young man with Behçet's disease, especially when hemoptysis occurs.
Medical management includes the use of steroids and cytotoxic agents. Cyclophosphamide, in particular, is a favored therapeutic agent in this regard. Anticoagulants and thrombolytic agents are generally contraindicated due to an increased risk of fatal hemorrhage. However, their use may be considered with great care under special circumstances, for instance, massive pulmonary embolism.

P005

Serum levels of epidermal growth factor receptor ligands in patients with non-infectious uveitis

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Introduction. Human endogenous uveitis is considered as an autoimmune disorder associated with Th1/Th17 immune cells. We previously reported the unique inflammation amplifier mechanism activated by the simultaneous activation of NF-kB and STATs in "non-immune" cells such as vascular endothelial cells. It induces synergistic increase of inflammatory cytokines including IL-6, chemokines, and growth factors to promote local inflammation. DNA microarray and a genome-wide short hairpin RNA screening reported 8 candidate genes. Among them, receptor-ligand complex is only expected in epidermal growth factor receptor (EGFR) and epiregulin. EGFR binds to its ligands: a growth factor family including epiregulin, amphiregulin, betacellulin, transforming growth factor-alpha (TGF-α), heparin-binding EGF (HB-EGF) and EGF. It was reported that these growth factors were increased in rheumatoid arthritis and multiple sclerosis patients.
Aims. To examine the serum levels of EGFR and its ligands in non-infectious uveitis patients.
Methods. Serum samples were collected from 25 Behçet's disease (BD), 30 sarcoidosis, and 30 Vogt-Koyanagi-Harada (VKH) disease patients at Hokkaido University Hospital, Japan. Samples from 25 healthy people were considered as controls. Serum levels of EGFR and its ligands such as epiregulin, amphiregulin, betacellulin, TGF-α, HB-EGF, and EGF were quantified with multiplex assay.
Results. Serum levels of epiregulin, amphiregulin, betacellulin, TGF-α,

HB-EGF, and EGF were significantly higher than controls (p<0.01) in BD and sarcoidosis. Levels of these ligands except for EGF were also significantly elevated (p<0.01) in VKH disease.
Conclusion. Inflammation amplifier mechanism associated with non-immune cells may be involved in the onset and exacerbation of uveitis.
References

1. OGURA H, MURAKAMI M, OKUYAMA Y *et al*.: Interleukin-17 Promotes Autoimmunity by Triggering a Positive-Feedback Loop via Interleukin-6 Induction. *Immunity*, 2008.
2. MURAKAMI M, HARADA M, KAMIMURA D *et al*.: Disease-Association Analysis of an Inflammation-Related Feedback Loop. *Cell Reports*, 2013.
3. HARADA M, KAMIMURA D, ARIMA Y *et al*.: Temporal Expression of Growth Factors Triggered by Epiregulin Regulates Inflammation Development. *J Immunol*, 2015.

P006

Metabolomic profiles of Behçet's disease patients define differences in the metabolic processes supporting inflammation compared to other inflammatory diseases

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Introduction. Inflammation is highly dependent on active metabolism to support the cellular and molecular processes involved. We hypothesised that the metabolic processes in Behçet's disease (BD), an auto-inflammatory condition would differ from those seen in inflammatory conditions driven by autoimmune process, arthritis.
Aims. We compared NMR-based metabolomic profiles of urine and serum from a cohort of BD with those from patients within 3 months of diagnosis of inflammatory arthritis.
Methods. Serum and urine were collected from 315 patients attending the Birmingham, UK early arthritis clinics at the City Hospital and Queen Elizabeth hospital Birmingham, within 3 months of the initiation of their joint inflammation and before disease modifying drugs were administered. Serum and urine were collected from 70 patients at the Behçet's Centre of Excellence, City Hospital Birmingham. Samples were frozen at -80ºC within 2 hours of collection. Samples were prepared and 1D NOESY NMR spectra were acquired using a Bruker Avance 600MHz spectrometer equipped with a 1.7mm cryoprobe. Spectra were phased, aligned, binned and PQN normalised and Glog transformed using the Metabolab NMR software package. OPLSDA analysis was performed using the SIMCA software.
Results. An OPLSDA model identified a clear difference between the 2 groups of patients in their urinary metabolite profiles. The robustness of the model was shown from the ROC curve which identifies a 96% specificity and sensitivity for the model. Furthermore cross validation of multiple models in which data is left out and assessed using ANOVA gave P value of 1.07 e^{-24}.
The same approach to the analysis was undertaken to assess the metabolites profiles in serum from the patients. The serum was first filtered through a filter to remove molecular species greater than 3000MW since these can interfere with the spectra of metabolites.
An OPLSDA model of the data from the sera showed a clear difference between the early arthritis and BD patient metabolites profiles. A ROC curve indicates a robust model with sensitivity and specificity of around >99% and an ANOVA cross validated p<1e^{-30}.
The OPLSDA suggests a greater degree of heterogeneity in the serum profiles from the early arthritis cohort compared to the urine and assessing the reasons for this is a focus of ongoing work. Given the early stage of these patients in their disease it is not surprising that differences are observed, since we and others have shown that the metabolites in serum strongly relate to the disease phenotype.
Conclusion. Behçet's disease is characterised as an auto inflammatory disease because of the absence of autoantibodies. Rheumatoid arthritis, which will be represented strongly within the early arthritis cohort, is a largely autoimmune disease the strong contribution from the adaptive immune response and autoantibodies, The metabolic profiles may well reflect these immune processes directly, but may also reflect the different tissues and organs involved in the pathologies. Further analysis of these data and samples from Qatar will allow us to identify the metabolic pathways altered in these diseases.

P007

Metabolomic alterations associated with Behçet's disease

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Introduction. The diagnosis of Behçet's disease (BD) is mainly based on clinical manifestations and remains a challenge in current clinical practice because of its lack of diagnostic biomarkers. Metabolomics, an emerging "omics" science, uses state-of-the-art quantitative analysis approaches and advanced bioinformatic methods to characterize the metabolome. It reflects both physiological and pathological states, and it may detect the alterations of affected metabolites at the early stages of disease due to its great sensitivity (1). Metabolomic methods have been used for evaluating clinical diagnosis and therapeutic treatment in a variety of diseases, such as cancer, diabetes, multiple sclerosis, primary biliary cirrhosis, and autoimmune hepatitis (2-6). Metabolic abnormalities in BD remain elusive.
Aims. This study aims to identify serum metabolites associated with BD and to search for the metabolites responsive to treatment.
Methods. Medical records and serum samples of 24 pre-treated BD patients, 12 post-treated patients, and age-matched healthy volunteers were collected for metabolomics and lipidomics profiling using UPLC-QTOFMS and UPLC-QTOFMS^E approaches. Additionally, serum samples from 25 pre-treated BD patients and 19 healthy volunteers were collected for further validation of two potential biomarkers using UPLC-QTOFMS analysis.
Results. Unsupervised principal component analysis (PCA) showed a clear separation of metabolomics profiles of BD patients from healthy volunteers. Statistical analysis of the data revealed differential metabolites between BD patients and healthy volunteers. The serum levels of some phosphatidylcholines (PCs) were found to be significantly lower in BD patients, while the levels of several polyunsaturated fatty acids (PUFAs) were increased markedly in the BD group compared to in the healthy control group. It is of interest to note that treatment reversed changes of two omega-6 PUFAs, linoleic acid and arachidonic acid, but not the other differential metabolites. In the validation cohort, the contents of LA and AA in BD patients were significantly higher than they were in healthy volunteers, with p-values of 5.76×10^{-5} and 1.02×10^{-7} by T-test, respectively. Receiver operating characteristic (ROC) analysis indicates good sensitivity and specificity.
Conclusion. Our study shows an altered serum metabolomics profile in BD patients and suggests that levels of PCs and PUFAs may assist in the diagnosis of BD. The two omega-6 PUFAs may provide valuable insights for therapeutic effects.
Reference

1. NICHOLSON JK, LINDON JC: Systems biology: Metabonomics. *Nature* 2008; 455(7216): 1054-1056.

P008

Immunogenicity of infliximab among patients with Behçet's syndrome: a controlled study

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Introduction. Immunogenicity of anti-TNFs has been recognized as an important problem that may cause loss of efficacy and adverse events such as infusion reactions. Anti-TNFs are being increasingly used among patients with Behçet's syndrome (BS).
Aims. We aimed to investigate the prevalence of anti-drug antibodies against infliximab (IFX) in patients with BS together with controls.
Methods. We collected serum samples from 66 consecutive BS patients (51 M, 15 F and mean age 37±9 years) who were treated with IFX. Additionally, 53 ankylosing spondylitis (AS), 25 Crohn's disease (CD) and 27 rheumatoid arthritis (RA) patients, and 31 healthy subjects were included as controls. We included patients who had received at least 4 cycles of IFX. Samples were collected just before an infusion, stored at -80º C until analysis, and serum IFX trough levels and anti-IFX antibodies were measured by ELISA at the same time. We used a cut-off value of 1 μg/mL for serum IFX trough

level, extrapolating from RA studies. After serum sampling, we continued to follow up patients regarding allergic reactions and treatment efficacy.
Results. Anti-IFX antibodies were detected in 4 (6%) BS, 5 (18.5%) RA, 3 (12%) CD, and 1 (%2) AS patient, and in none of the healthy subjects. The mean number of IFX cycles was 19±14 in BS, 21±13 in RA, 19±21 in CD, and 33±18 in AS patients. Allergic reactions had occurred in 9 (14%) BS, 6 (22%) RA, 5 (20%) CD, and 4 (7.5%) AS patients. 3/6 RA patients and 3/5 CD patients who had experienced an allergic reaction had anti-IFX antibodies whereas none of BS and AS patients did.
The median serum IFX trough level was significantly lower in patients with anti-IFX antibodies compared to those without antibodies (2.32 (IQR: 0.6-3.6) vs 3.35 (IQR: 1.63-5.6; p=0.019). The serum IFX trough level was lower than the cut off value in 6/13 patients with anti-IFX antibodies and in 25/158 without anti-IFX antibodies (46% vs 16%; p=0.015).
We were able to get samples before at least 2 consecutive infusions in 27 BS patients and the presence of anti-IFX antibodies was consistent across the samples in all of these patients.
During a median follow up of 1.5 years, 2/4 BS patients with anti-IFX antibodies had flares (Table). Among the 62 patients without anti-IFX antibodies, 49 are still on IFX and IFX was stopped due to remission in 12 and due to infusion reaction in one patient. Overall, 5 infusion reactions occurred during the follow up (4 without anti-IFX antibodies and 1 with anti-IFX antibodies; 6.5% vs 25%).
Conclusion. Immunogenicity does not seem to be an important problem in BS patients treated with IFX. The frequency of anti-IFX antibodies was lower than RA and CD patients. The presence of anti-IFX antibodies may not be associated with efficacy loss in BS. However, longer follow-up is needed to make that statement as BS has a relapsing-remitting course.

Table. Clinical characteristics of BS patients who had anti-IFX antibodies.

BS manifestation requiring IFX use	Concomitant drugs	Serum IFX trough level (µg/mL)	Infusion reaction	Outcome of BS manifestations	Current status
Uveitis	AZA	3.08	No	Active mucocutaneous lesions and arthritis	On ADA
Venous ulcer	AZA, Pred	4.06	No	Remission	On IFX
Uveitis	AZA, Cyc-A	4.22	Yes	Uveitis attack	Stopped due to infusion reaction, switch to ADA
Uveitis	Pred	0.96	No	Remission	On IFX

P009

Neutrophil phenotype and function in ocular inflammatory disorders

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Introduction. Neutrophils are the first line of defence against invading pathogens and have diverse functions such as phagocytosis, neutrophil extracellaur traps and the production of reactive oxygen species (ROS). Mantovani *et al*., (2011) expressed the role of neutrophils in the pathogenesis of many different inflammatory disorders. Neutrophils for many years were considered to be a homogenous population of differentiated cells with a well distinct and conserved function. Recent it has become clear that neutrophils can be separated into different subsets that have different function. Low density neutrophils (LDN) and Normal density neutrophils (NDN) can co-exist in the circulation and contribute towards inflammatory disorders (Scapini *et al*., 2016). The ocular inflammatory disorders are the result of the failure of protective ocular barriers. Behçet's disease (BD) and Ocular Mucus Membrane Pemphigoid (OcMMP) are classical chronic inflammatory eye disorders, in which neutrophils have been implicated in pathogenesis.
Aims. It is hypothesised that constant mucosal ulceration leads to activation of neutrophils, and as a result neutrophils enter immune privileged sites and cause the breakdown of the immune tolerance. The aim of this study is to investigate whether neutrophils contribute towards the pathogenesis of ocular inflammatory disorders (BD and OcMMP).
Methods. Patients with BD (n=32), OcMMP (n=35) and healthy aged matched (n=30) controls were obtained from Birmingham Midland Eye centre under local ethical approval. Phagocytic capacity and production of ROS by total neutrophils LDN, and NDN were assessed using PhagoTest/Burst kits (Glycotope Biotechnology). Ficoll hypaque segmentation was used to quantify the levels of LDN and NDN and heterogeneity was evaluated using flow cytometry.
Results. The results demonstrate a significantly reduced (p=<0.05) phagocytic capacity and ROS production after stimulating all neutrophils with *E.coli* in BD and OcMMP patients in comparison to healthy controls. The results showed a significantly (p=<0.05) elevated levels of LDN and a significantly (p=<0.05) reduced activity in LDN and NDN of Behçet's and OcMMP patients in comparison to healthy controls. Flow cytometry showed a significant (p=<0.05) high percentage of $CD11B^{bright}$ $CD16^{bright}$ $CD66B^{bright}$ $CD15^{bright}$ $CD54^{bright}$, $CD11B^{+}$ $CD16^{bright}$ $CD66b^{bright}$ and $CD66B^{+}$ population in all neutrophils. A significant (p=<0.05) high percentage of $CD66B^{+}$ and $CD33^{+}$ were also observed in LDN and NDN population in BD and OcMMP patients. A significant (p=<0.05) increase was detected in Granulocytic myeloid-derived suppressor cells (G-MDSCs) ($CD66b^{+}$ $CD33^{low}$ $HLA\text{-}DR^{-}$) within the LDN and NDN population in BD and OcMMP patients in comparison to healthy controls.
Conclusion. The results suggest that neutrophils in BD and OcMMP patients have an altered function and phenotype in disease severity. The presence of LDN and NDN population shows that neutrophils display a heterogeneous population within BD and OcMMP patients which may contribute towards a disease state.

References

1. MANTOVANI A, CASSATELLA MA, COSTANTINI C, JAILLON S: 'Neutrophils in the activation and regulation of innate and adaptive immunity', *Nature Reviews Immunology* 2011; 11: 519-531.
2. SCAPINI P, MARIN O, TECCHIO C, CASSATELLA MA: 'Human neutrophils in the saga of cellular heterogeneity: insights and open questions', *Immunological Reviews* 2016; 273 (1): 48-60.

P010

Genetic characteristics of senescent CD8 T cells in the peripheral blood mononuclear cells of Behçet's disease patients

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Introduction. Behçet's disease (BD) is a chronic inflammatory disease characterized by recurrent mucocutaneous ulceration and complications such as blindness and large vessel inflammation. Immunosenescence, aging of the immune system, is related to increased susceptibility to infectious diseases, vaccine failure, and chronic low-grade systemic inflammation. Our previous study showed an increased frequency of immunosenescent cells in the peripheral blood of patients with BD.
Aims. The aim of this study was to investigate the differences in RNA expression in immunosenescent cells in the peripheral blood of BD patients and controls, and to find its role in autoimmune/autoinflammatory pathogenesis of BD.
Methods. Peripheral blood mononuclear cells (PBMCs) were extracted from BD patients (n=18) and healthy controls (HC, n=18). $CD8^{+}$ T cells were isolated through CD8 microbeads, and those were labeled with conjugated monoclonal antibodies as follows: FITC anti-CD8, allophycocyanin (APC)-H7 anti-CD27 and APC anti-CD28. Using fluorescence-activated cell sorting (FACS), senescent $CD8^{+}$ T cells ($CD8^{+}$ CD27- CD28- cells) and non-senescent $CD8^{+}$ T cells ($CD8^{+}$ $CD27^{+}$ $CD28^{+}$ cells) were sorted. After sorting, each group of cells was pooled together and cultured in medium (RPMI 1640). Cells were stimulated with anti-CD3 (500ng/ml, clone OKT3) for 72 hours. Total RNA was extracted from anti-CD3-stimulated cells with the RNA isolation kit. We performed transcriptome analysis on those RNA samples and analyzed the differentially expressed genes from the four different groups (BD patients *vs*. controls, senescent $CD8^{+}$ T cells ($CD8^{+}$ CD27- CD28-) *vs*. non-senescent $CD8^{+}$ T cells ($CD8^{+}$ $CD27^{+}$ $CD28^{+}$)).

Results. A large number of differentially expressed genes of each group were found out through total RNA transcriptome analysis. Gene Ontology (http://geneontology.org/) was used for the significant differentially expressed genes to conduct the gene set enrichment analysis according to gene ontology's functional classifications, biological process (BP), molecular function(MF), and cellular component(CC). As a result of the analysis, it was found that that the gene set list, which showed the significance, appears differently for each categories.
Conclusion. Through next-generation sequencing, we could find that the gene expression of the senescent $CD8^+$ T cells differs from that of non-senescent $CD8^+$ T cells. These differentially expressed genes of senescent immune cells can be thought of as having an effect on the occurrence and activation of the disease.
Therefore, functional changes in cells caused by immunosenescence are likely to be responsible for the pathogenesis of BD.
References

1. JI YOUNG YANG, MI JIN PARK, SUN PARK, EUN-SO LEE: Increased senescent $CD8^+$ T cells in the peripheral blood mononuclear cells of Behçet's disease patients. *Arch Dermatol Res* 2018; 310(2): 127-138.
2. MAYTE SUAREZ-FARINAS, BENJAMIN UNGAR, JOEL CORREA DA ROSA, DAVID A. EWALD, MARIYA ROZENBLIT, JUANA GONZALEZ, HUI XU, XIUZHONG ZHENG, XIANGYU PENG, YERIEL D. ESTRADA, STACEY R. DILLON, JAMES G. KRUEGER, EMMA GUTTMAN-YASSKY: RNA sequencing atopic dermatitis transcriptome profiling provides insights into novel disease mechanisms with potential therapeutic implications. *J Allergy Clin Immunol* 2015; 135: 1218-1227.

P011

Multiple aneurysms of the pulmonary arteries revealing Behçet's disease in a teenager

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Introduction. Behçet's disease is a multisystemic vasculitis of obscure etiology. Arterial damage is rare but may result in aneurysms of the pulmonary artery. They are due to necrosis of the arteries. They are then accompanied by a fibrotic adventitial inflammation resulting from a destruction of the media and the formation of aneurysms. The prognosis depends on the speed of medical care and close supervision. Some patients may benefit from embolization.
Aims. A rare presentation of Behçet disease.
Methods. A case report.
Results. Arterial damage during Behçet's disease is rare and has a poor prognosis. We report a case of bilateral aneurysms of the pulmonary artery during Behçet's disease in a 17-year-old patient. He had consulted for recurrent average haemoptysis, bipolar aphtosis with long-term fever, and profound impairment of general health. The chest x-ray showed bilateral rounded pulmonary opacities. Chest angioscan showed multiple aneurysms of the pulmonary arteries. The evolution under a treatment based on orthostatic therapy, colchicine and immunosuppressors was marked by a stable apyrexia, a weight gain, the stop of the hemoptysis. Aneurysm of the pulmonary artery during Behçet's disease is rare. It must be considered in the presence of signs suggestive of the disease. The prognosis of these locations is fraught with complications that can lead to death by lightning hemoptysis by rupture of aneurism.
Conclusion. Behçet's disease is a vasculitis of unknown cause. It often affects the young adult. The presence of signs suggestive of the disease should raise the diagnosis. This is based on clinical diagnostic criteria such as those developed by the International Criteria for Behçet's Disease. Pulmonary locations should be actively investigated and confirmed by chest imaging especially in the presence of haemoptysis. It can be a circumstance of discovery of the disease. Aneurysmal pulmonary chest involvement is rare. It is life-threatening by the occurrence of cataclysmic haemoptysis. The clinical picture can make the diagnosis err in tuberculosis endemic zone. The management is not codified in the literature. However, medical treatment based on immunosuppressants, corticosteroids and colchicine can be proposed. Regular close monitoring is essential.
References

1. FEIGENBAUM A: Description of Behçet's syndrome in the Hippocartic Third Book of Endemic Diseases. *Br J Ophtalmol* 1956; 40: 355-357.
2. BEHÇET H: Ueber rezidivierende, aphtöse, durch ein Virus verursachte Geschwüre am Mund, am Auge und an den Genitalien. *Dermatol Wochenschr* 1937;105:1152-1157.
3. ADAMANTIADES B: Sur un cas d'iritis à hypopion récidivant. *Ann Oculist* (Paris) 1931; 168: 271-278.
4. ZUBER JP, BART PA, LEIMGRUBER A, SPERTINI F: Maladie de Behçet : d'Hippocrate aux antagonistes du TNF-α. *Rev Med Suisse* 2008; 4: 1045-54.
5. MAHR A, MALDINI C: Epidémiologie de la maladie de Behçet. *Rev med interne* 2014; 35: 81-9.
6. DESBOIS AC, WECHSLER B, CLUZEL P *et al*.: *Rev Med Interne* 2014; 35: 103-11.
7. HOUMAN MH, BEL F: *Rev Med Interne* 2014; 35(2): 90-
8. HILLER N, LIEBERMAN S, CHAJEK-SHAUL T, BAR-ZIV J, SHAHAM D *et al*.: Thoracic manifestations of Behçet's disease at CT. *Radiographics* 2004; 24(3): 801-8.

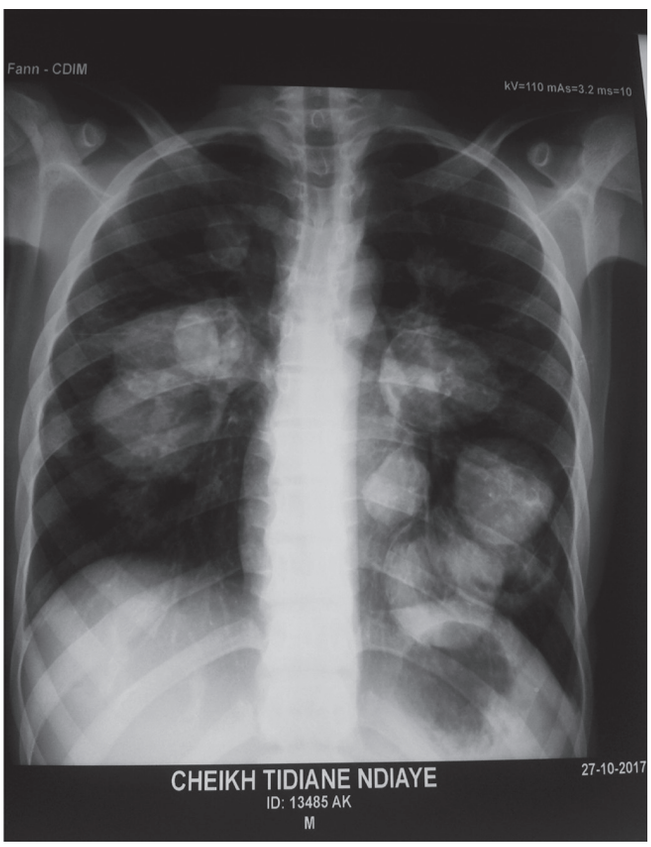

Fig.1. Chest x-ray.

P012

Higher frequencies of lymphocytes expressing the Natural Killer Group 2D receptor and NK cells' cytotoxic potential in Behçet disease patients

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Introduction. The diagnosis of Behçet disease (BD) is based on a combination of clinical symptoms and signs. Currently no laboratory assays or imaging approaches are available to support the clinical diagnosis. The classification criteria, introduced in 1990 and successively reviewed in 2006, are still a matter of discussion (1), however they help the physicians in identifying the patients with this condition.
Aims. This study aimed to identify a specific profile of circulating Natural Killer (NK), NKT and T cells able to discriminate patients with BD and Healthy controls (HC).
Methods. Peripheral blood mononuclear cells (PBMCs) were collected from 38 BD patients and 15 HC. The frequencies of NK, NKT and T cells expressing CD16, CD69, NKG2D, Nkp30, Nkp46 and NKG2A were assessed by flow cytometry. Cytotoxic potential of NK cells was evaluated by flow cytometry as the percentage of cells expressing the degranulation marker CD107a after incubation with K562 cells. The levels of 27 cytokines were determined in plasma with a multiplex bead-based assay.

Results. Higher percentages of NK, NKT and T cells expressing NKG2D were detected in PBMCs of BD patients than HC. ROC curve analysis showed that the evaluation of NKG2D^{pos} NK, NKT and T cell percentages discriminated between BD patients and HC. Moreover, there was a positive correlation between the BD Current Activity form (BDCAF) scores and the frequencies of NKG2D^{pos} NK and NKT cells. A higher frequency of NK cells expressing CD107a was induced in PBMC from BD patients than HC after incubation with K562 cells. Concentrations of IL-5, IL-10, IL-12 (p70), IL-13, IP-10 and MIP-1β were higher in plasma of BD patients than HC.
Conclusion. Monitoring the frequencies of NKG2D^{pos} lymphocytes, and CD107a^{pos} NK cells after the degranulation assay could help the clinicians in BD patients management. The increased expression of NKG2D in BD patients is likely involved in disease pathogenesis.
Reference

1. MURATORE F, PAZZOLA G, SORIANO A *et al*.: Unmet Needs in the Pathogenesis and Treatment of Vasculitides. *Clin Rev Allergy Immunol* 2017.

P013

Factors associated with damage progression in Behçet's syndrome uveitis

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Introduction. Uveitis in Behçet's syndrome (BS) follows a recurrent disease course with inflammatory exacerbations causing damage in the uvea, retina and optic nerve even with treatment. Frequent attacks and posterior involvement are considered as predictors of poor visual outcome.
Aims. The aim of this study is to delineate the predictors of damage in more detail using a standard screening method among a group of BS patients with long-term regular follow-up.
Methods. Patients with uveitis who were registered in our multidisciplinary BS clinic between 1990 and 2008 were screened. Among these, 50 patients who were followed for at least 10 years, who were regularly seen in our clinic at least once in every 4 months, who did not have > Grade 2 damage at baseline, and who represented different levels of damage severity during the last visit (between Grade 0 and 5) were selected. The damage severity was graded according to a validated damage grading instrument (5=worst) specifically developed for BS uveitis (Ozyazgan *et al*. in preparation). One patient was later excluded because it was realized that he did not fulfill these criteria. A standard form was used for retrieving data on demographics, baseline and final visual acuities, number and localization (anterior/posterior / panuveitis) of attacks during follow-up, presence of retinal infiltration, retinal hemorrhage and hypopyon uveitis. Candidate factors for damage progression were compared between patients who had a progression in damage score and those who did not.
Results. 98 eyes of 49 patients (M:F 35:14, mean age at baseline 27±8 years, mean follow-up duration 20.9±5.5 years, mean number of visits 76.5±35.2) were evaluated. The mean visual acuity was 0.02±0.08 at baseline and 0.47±0.52 at the final visit. The mean number of attacks was 13.2±9.4. Damage grades at baseline were Grade 0 in 79, Grade 1 in 16 and Grade 2 in 3 eyes. Damage grades at final visit were Grade 0 in 15, Grade 1 in 21, Grade 2 in 32, Grade 3 in 12, Grade 4 in 10 and Grade 5 in 8 eyes. There was damage progression in 81/98 eyes at the final visit. Isolated anterior uveitis attacks were not associated with progression of damage (2.5±2.9 vs 2.8±5.5, p=0.7). Parameters that were significantly more frequent among patients with damage progression were: number of attacks (14.5±10.8 vs 23.3±12.3; p=0.008), number of posterior attacks (0.4±1.2 vs 6.5±4.9, p<0.001), number of panuveitis attacks (0.8±1.3 vs 6.6±5.0, p<0.001), number of attacks with severe vitrous opacity preventing examination of the retina (0 vs 3.2±3.8, p<0.001), retinal infiltration (0.2±0.4 vs 1.4±1.9, p<0.001) and retinal hemorrhages in the arcuate region (0.1±0.2 vs 0.7±1.4, p<0.001), and the number of hypopyon attacks (0.2±1.0 vs 0.9±1.3, p=0.019).
Conclusion. This study confirmed that the anterior uveitis attacks are not associated with progressive damage in BS, whereas posterior and panuveitis attacks, attacks causing severe vitreous opacity, retinal infiltrates and hemorrhage in the arcuate region and hypopyon attacks are important predictors of damage. Patients showing these features should be treated more aggressively.

P014

Deep immune-profiling of CD4$^+$ T cells in Behçet's disease

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Introduction. Functionality and immune-phenotypes of the human CD4$^+$ T-cell compartment in Behçet's disease (BD) are under-investigated, but several lines of evidence point to its relevance in the pathogenesis and progression of the disease.
Aims. We aimed to apply an unbiased single cell approach to assess protein expression levels of phenotypic and functional markers within the human CD4$^+$ T cell compartment in subjects with prototypical BD in order to identify cell populations of potential pathobiological relevance.
Methods. We determined single cell expression levels of CD3, CD4, CD8, CD127, CD25, CD45RA, CCR7, FoxP3, HELIOS, Ki76, HLA-DR, CD38, CD39 in PBMC by flow cytometry and computed the representation of all mathematically possible cell populations within pre-defined starting populations (*i.e*., CD3$^+$CD4$^+$CD8$^-$; CD3$^+$CD4$^+$CD8$^-$CD127$^-$CD25$^+$). PBMC from BD patients (n=13), healthy donors (HD) (n=25) and diseased subjects with non-BD auto-immune uveitis (n=11, VKH, Sarcoidosis, and HLA-B27 associated uveitis) were used. BD subjects met ISG criteria and were Arab or Chinese. 62% had pan-uveitis, 23% major vascular disease, and 7% parenchymal CNS disease. 46% were HLA-B51 carriers.
Results. Computation of all populations defined by 8 markers (CD127, CD25, CD45RA, CCR7, FoxP3, HELIOS, Ki67, HLA-DR) within the CD3$^+$CD4$^+$CD8$^-$(=CD4$^+$ T cell) compartment yielded a total of 6560 (3^8-1) cell populations per subject out of which 45 populations reached a significance level of p<=0.000001 in ANOVA testing to differentiate 3 groups (BD, non-BD uveitis, and HD). All of these populations comprised sub-types of the human regulatory T (Treg) cell compartment with strong predominance of non-proliferating, non-activated, FoxP3$^+$Helios$^+$ Treg carrying central-memory phenotypes (CD45RA$^-$, CCR7$^+$). 2-group testing of BD vs non-BD revealed 43 distinct cell populations at a significance level of p<=0.002 representing CD25$^+$ non-Treg; comparison of BD vs HD uncovered 58 populations at significance level of p<=0.0001 representing FoxP3$^+$Helios$^+$ subpopulations, and non-BD vs HD identified 61 populations at p<=0.001, comprising CD25$^+$CD127$^{+/-}$ FoxP3$^{+/-}$, but consistently HELIOS$^-$, presumably non-Treg populations. A separate analysis using 6 marker combinations (CD38, CD39, CD226, TIGIT, CD45RA, CCR7) within the CD3$^+$CD4$^+$CD8$^-$CD127$^-$CD25$^+$ compartment which contains most human Treg, showed 48 populations (p<=0.0001) in 3-way comparison (BD, non-BD uveitis, and HD) pointing to high significance of TIGIT and CD226 staining Treg subpopulations, and 18 populations with differential expression of CD39$^+$ between BD and non-BD diseases subjects. TIGIT and CD226 co-expressing Treg (CD127$^-$CD25$^+$) subpopulations also reached significance (p<=0.02) in a longitudinal analysis of 7 BD subjects in active vs inactive disease states, as did 56 out of 6560 populations within total CD4$^+$CD3$^+$ cells, mostly representing non-Treg cells in active disease.
Conclusion. Differential expression of CD4$^+$ Treg and non-Treg cells shapes the immune-phenotype of BD in comparison to healthy and non-BD autoimmune diseases that have phenotypic overlap with BD (uveitis). The populations with the highest significance for differentiating BD from healthy states seem to exist within the HELIOS$^+$FOXP3$^+$compartment of non-activated, non-proliferating Treg, suggesting relevance of a true Treg phenotype. Non-Treg CD25$^+$ cell populations seem more indicative of BD vs non-BD uveitic disease as well as of clinically active BD while populations with high CD39 expression may indicate non-BD states.

P015

A rare association of Behçet's and Crohn's disease

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Introduction. Cases of BD with gastrointestinal tract involvement are difficult to differentiate from CD with extra digestive manifestations, since they share many similar clinical and endoscopic manifestations. Nevertheless, both diseases can coexist in a same patient, raising a nosological problem.
Aims. We report such an exceptional association.
Methods. Case report and literature review of the association of BD and CD.
Results. A 24 year old female with no medical history presented with chronic diarrhea, abdominal pain, oligoarthritis and recurrent oral and genital ulcers. Laboratory studies revealed an iron deficiency anemia and a biological inflammatory syndrome. The colonoscopy showed a diffuse ulcerative colitis. Histological examination of colic biopsies found epithelioid granulomas without vasculitis, compatible with the diagnosis of Crohn's disease. The patient was treated with oral prednisone (1mg/kg/day for 1 month then progressively tapered and stopped after 4 months), achieving both clinical and biological remission without any relapse.
Two years later, she presented with abdominal pain, diarrhea and rectal bleeding. Physical examination revealed pseudofolliculitis lesions, a positive pathergy test and a panuveitis. HLA tissue typing was HLA B-51. The diagnosis of BD was made according to the International Criteria for BD. The colonoscopy showed an extended pseudopolypoid and ulcerative colitis. Histological examination of colic biopsies revealed crypt distortions, epithelioid and gigantocellular granulomas with no signs of vasculitis, once again compatible with CD.
The diagnosis of BD associated with CD was established. She was treated with high doses of prednisone (1mg/kg/day) and 6 monthly intravenous pulses of cyclophosphamide substituted by azathioprine. Skin lesions, diarrhea and uveitis improved within few days, and cleared completely within five months. Currently, the patient remains asymptomatic.
Conclusion. Our case reflects the difficulty of distinguishing BD from CD, especially when they are associated. This is due to the many common clinical and endoscopic features that they share. This could be explained by a strong similar multifactorial etiopathogenesis, involving genetic, infectious and environmental factors leading to abnormal immunological response. Consequently, when a presumed case of CD presented with extra digestive manifestations, BD must be evoked.

Table P015.

Author / Year	Age / Sex	Delay of the diagnosis between the two pathologies	Gastro-intestinal involvement			Other common manifestations
			Clinical signs	Endoscopy	Histology	
Goldstein / 1978	30 / F	3 years	Diarrrhea - abdominal pain - perianal abscess	Stenosis - diffuse ulcerations	Granulomatous colitis	Bipolar aphtosis - erythema nodosum
	37 / F	2 years	Diarrhea - rectovaginal fistula	Stenosis - diffuse ulcerations - colonic perforations	Granulomatous colitis - ulcerations - perforations	Bipolar aphtosis - arthralgia - uveitis
Y'agita / 1978	39 / F	10 years	Abdominal pain	Irregular ileocoecal ulcerations - polyp	Not specific	Bipolar aphtosis
	27 / F	Unspecified	Abdominal pain - right iliac fossa mass	Irregular ulceration of the ascending colon	Not specific	Bipolar aphtosis - arthritis
Mir-Madjlessi / 1972	15 / F	15 years	Diarrhea - abdominal pain - rectovaginal fistula	Diffuse irregular ulcerations stenosis	Non-granulomatous transmural colitis	Bipolar aphtosis - erythema nodosum - thrombophlebitis - neuro-Behçet - arthritis
Tocia / 1989	15 / M	1 month	Abdominal pain - diarrhea	Diffuse linear irregular ulcerations	Microgranulomas	Bipolar aphtosis - panuveitis - erythema nososum - arthralgia
Naganuma / 2002	37 / F	Not specified	Abdominal pain - diarrhea	Longitudinal diffuse ulcerations	Granulomatous colitis	Bipolar aphtosis - erythema nodosum
Kobashigawa / 2014	49 / M	Not specified	Bloody stools - anal fistula	multiple ulcerations	Not specific	Arthralgia - bipolar aphtosis - erythema nodosum
Köksal / 2005	21 / M	3 months	Abdominal pain	Ulcerations	Granulomatous colitis	Bipolar aphtosis - pseudofollicullitis - arthralgia
Berraida / 2017	41 / F	2 years	Diarrhea	Ulcerated ileitis	Not specific	Bipolar aphtosis - anterior uveitis - arthralgia
Our case / 2018	24 / F	2 years	Diarrhea - abdominal pain	Diffuse ulcerative colitis	Crypt distortions - epithelioid granulomas	Bipolar aphtosis - pseudofolliculitis - panuveitis - arthritis

P016

Alterations in the taxanomic and predicted functional profile of gut microbiota in Behçet's disease

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Introduction. Behçet's Disease (BD) is a devastating inflammatory condition of unknown cause. Gut microbiome is important in the modulation of the immune system.
Aims. Therefore, we aim to investigate the phylogenetic and predicted functional compositions of the gut microbiome in patients with BD compared to disease and healthy controls.
Methods. Faecal samples were collected from patients with BD fulfilling the Behçet's Syndrome International Study Group criteria, along with age- and gender-matched disease and healthy controls. Mucous membrane pemphigoid (MMP) was used as disease control as it has similar systemic mucocutaneous involvement to BD. The V4 region of the 16S rRNA gene of bacterial DNA was amplified and sequenced on Illumina MiSeq. Microbial taxa and metagenomic function (KEGG orthologues) was analysed using QIIME and PICRUSt.
Results. A total of 109 participants [BD (n= 47), MMP (n=30), HC (n=32)] were recruited to the study.
The dominant phyla across all three groups were Firmicutes and Bacteroides, followed by Actinobacteria. There was no significant difference in the alpha diversity across the groups. Patients with BD had significantly lower relative abundance of Alphaproteobacteria (p=0.016), and higher relative abundance of Tenericutes (p=0.02) compared to disease and healthy controls. In patients with BD, the family Peptococcaceae had large effect size, whilst in healthy controls, the genus Bacteroides, family Bacteroidaceae, Barnesiellaceae and Lachnospira had large effect sizes. Predicted functional metagenome revealed higher relative abundance of microbial genes related to the RIG-1-like receptor signalling pathway (p=0.018), which is important in RNA viral pathogen sensing and initiation of the innate immunity, and lower relative abundance of genes associated with the NOD-like receptors in patients with BD. Patients who were on immunosuppression had higher relative abundances of microbial genes regulating nucleotide excision repair.
Conclusion. Gut microbiome was altered in patients with BD and was associated with predicted microbial genes regulating the innate immunity.

P018

Primary gastrointestinal lymphoma in a patient with Behçet's disease: a rare association and an exceptional cause of chronic diarrhea!

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Introduction. Primary gastrointestinal lymphoma is a rare entity, representing only 1 to 8% of all gastrointestinal malignancies. The association of Behçet's disease (BD) and malignant lymphoma is very rare. To date only 19 cases have been reported.
Aims. We report the third case of primary gastrointestinal lymphoma with intestinal BD.
Methods. Case report and literature review of the association of BD and lymphoma.
Results. A 35-year-old female with no medical history presented with recurrent oral and genital ulcers and pseudofolliculitis lesions and a positive pathergy test. The diagnosis of BD was made according to the International Criteria for BD. She was treated with colchicine. After two years, she developed uveitis complicated with retinal vasculitis and was treated with prednisone and six monthly intravenous pulses of cyclophosphamide but uveitis persisted so cyclophosphamide was replaced by cyclosprin. Six months later, she presented with abdominal pain and diarrhea which persisted despite stopping colchicine. The colonoscopy showed three ileocoecal ulcerations. Histological examination revealed a high-grade malignant lymphoma, large B-cell-type and vasculitis lesions compatible with intestinal BD. CT of the thorax and abdomen, and bone marrow aspiration were normal. Cyclosporin was stopped and treatment with prednisone was instituted. She underwent right hemicolectomy with ileocolonic anastomosis. The histological examination of surgical biopsies confirmed the diagnosis. At last follow-up 2 years later, she was still in complete remission.
Conclusion. Diarrhea occurring in a patient with BD is often associated with colchicine treatment or with intestinal BD but can reveal a gastrointestinal tumor, such our case. Corticosteroids and immunosupressive drugs, which are often prescribed during BD, may induce sterilization of tumor lesions and provide false negatives at the time of biopsy.

P019

Budd-Chiari syndrome revealing a very vascular juvenile Behçet's disease

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Introduction. Behçet's disease (BD) is a chronic multisystem disease that presents with recurrent oral and genital ulceration and recurrent uveitis. The patients are often diagnosed in the range of 20-30 years of age and BD is more common in men. Although the vascular lesions are frequently observed, the cardiac and hepatic involvement remains rare and is associated with the poor prognosis
Aims. To raise awareness on the importance of thinking about an eventual BD when unusual vascular lesions are involved even in children.
Methods. We report a case of juvenile Behçet's disease revealed by Budd-Chiari syndrome and associating an intracardiac thrombus and massive pulmonary embolism.
Results. Young female patient 15 years old hospitalized in October 2017 at the gastroenterology department for exploration of abundance ascites in a context of deterioration of the general state without other particular symptoms. The abdominal ultrasound objectified an abundant ascites and Doppler showed a thrombosis of the suprahepatic veins and inferior vena cava. The biological assessment was in favor of hepatocellular insufficiency (hypo albuminemia and low prothrombin time). As the heparin and the etiological investigation were started, the patient experienced a NYHA stage 4 dyspnea and hemoptysis; Computed tomography angiogram showed a superior vena cava thrombosis and a massive pulmonary embolism. The patient is transferred to the internal medicine department where the investigations revealed a recurrent oral and genital aphtosis since the age of 12. An exhaustive etiological assessment was carried out and remained negative and the pathergy test was positive. The diagnosis of juvenile Behçet's disease is then retained and the patient received corticosteroids and immunosuppressive therapy, with a good clinical and biological progress.
Conclusion. In childhood pathology, Budd-Chiari syndrome remains a rare entity. In our context as Mediterranean countries, we must think about Behçet's disease even in children, especially since its prognosis has been greatly improved with the use of immunosuppressive therapy in addition to anticoagulation in vascular BD

P020

Molecular characterization of two interleukin-10 gene polymorphisms in a group of Behçet's syndrome patients: a preliminary Italian study

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Introduction. Genome-wide association studies (GWASs) are a significant tool to understand the pathogenesis of complex disease, including Behçet Syndrome (BS), a chronic multisystem inflammatory disorder with unknown pathogenesis. Various risk loci were reported in several previous studies and the interleukin (IL) genes were considered as susceptibility markers due to their critical role in the immune response regulation (1-3). IL-10 is a multifactorial cytokine with both immunosuppressive and anti-angiogenic proprieties. The human *IL-10* gene is located on chromosome 1q21–32 and is formed by 5 exons. The association of *IL-10* gene single nucleotide polymorphisms (SNPs) with BS susceptibility was underlined in a few papers (1, 3, 4).
Aims. The aim of our study was to investigate the mutational state of two *IL10* SNPs in order to describe their frequency in a group of Italian Behçet's syndrome (BS) patients compared with healthy controls.
Methods. Genomic DNA was isolated from whole blood of 77 Italian subjects, including 40 BS patients fulfilling the ISG criteria (mean age ± SD: 46.78±12.76; sex ratio: 24 males/ 16 females) and 42 age- and sex-matched healthy controls. *IL10* rs1518111 and rs1800872 were genotyped after a primer design bioinformatics step using NCBI Primer-Blast tool. SNPs were detected using PCR amplification of genomic DNA and amplicons running on 1.5% agarose gel. Good-quality amplicons were sequenced by the GATC Biotech Sanger sequencing service. A downstream *in silico* step was performed for the variant analysis using bioinformatics tools (BlastN and Mutation Surveyor). The odds ratio (OR) with 95% confidence intervals was calculated to assess the strength of BS association for each genotype.
Results.
Table I shows *IL* polymorphisms distribution between BS patients and control group. *IL* tagSNPs genotypes highlighted a higher frequency of *IL10* rs1800872 mutant CC genotype (62.50%) than wild-type AA genotype (20.00%) within BS group. No statically significant differences were observed when BS patients and controls AA and CC genotypes were compared. The heterozygous genotype (AC) was identified in 7/40 BS patients (17.50% of cases): BS patients showed a significantly lower prevalence of the AC genotype (p-value<0.05). No difference was found between patient and control groups when wild-type AA genotype, heterozygous AG and mutant GG genotype frequencies of *IL10* rs1518111 were compared.

Table I. Genotype frequencies of IL-10 rs1800872 and rs1518111 in BS patients and controls.

Gene	SNP	Genotype	BS patients (n=40) n (%)	Controls (n=42) n (%)	OR (95% CI)	p-value
IL-10	rs1800872	AA	8 (20.00)	4 (9.52)	2.38 (0.65-8.62)	NS
		AC	7 (17.50)	17 (40.48)	0.31 (0.11-0.87)	0.0223*
		CC	25 (62.50)	21 (50.00)	1.67 (0.69-4.02)	NS
IL-10	rs1518111	AA	18 (45.00)	19 (45.24)	0.99 (0.41-2.36)	NS
		AG	7 (17.50)	13 (30.95)	0.47 (0.17-1.35)	NS
		GG	15 (37.50)	10 (23.81)	1.92 (0.74-4.99)	NS

Abbreviations: SNP, single nucleotide polymorphism; BS, Behçet syndrome; n, number of subjects; AS, ankylosing spondylitis; OR, odds ratio; CI, confidence interval
Notes: *statistically significant (p-value<0.05)

Conclusion. Our results demonstrated that the genotypic distributions of *IL10* rs1800872 heterozygous genotype differs between BS patients and the control group. The SNP is a promoter polymorphism that could affect the cytokine-regulating auto-inflammatory response. Going forward, analyses of a larger cohort of patients and matched controls are need to confirm this preliminary data and to explain the SNP role in BS pathogenesis.

References

1. GUL A: *Current Opinion in Rheumatology* 2015; 26: 56-63.
2. TAKEUCHI M *et al*.: *Ann Rheum Dis* 2016; 75(12): 2208-2211.
3. AFKARI B *et al*.: *Immunol Lett* 2018; 194: 56-61.
4. HU J *et al*.: *Mol Vis* 2015; 21: 589-603.

P021

Susceptibility of single nucleotide polymorphism of interleukin 17A concerned with intestinal symptoms in Behçet's disease

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Introduction. Behçet's disease (BD) is a chronic inflammatory disease characterized by the recurrent involvement of oral and genital ulceration, ocular, vascular lesion, and skin lesions such as erythema nodosum, acne-like eruption, and folliculitis. The dysregulation cytokines such as TNF-α, IL-8, IL-12 and IL-17, participates in the pathogenesis of BD. IL-17 is thought to play a central role in Th17 responses in the pathogenesis of BD.
Aims. The polymorphims of IL-8 and IL-17 A gene has been examined.
Methods. The frequency of IL-17 gene SNP (dbSNP ID: rs2275913) was assessed among BD patients (n=95) and healthy controls (n=96).
Results. There were no significant difference in the genotype and allele frequency of IL-17A gene SNP between BD patients and controls. No significant differences in the genotype frequency of IL-17 gene SNP were identified between populations with or without clinical signs, such as skin involvement, ocular involvement, vascular involvement, arthropathy, epididitimitis and central nervous involvement. However there were a higher tendency of IL-17 A genotype A frequency in BD group.
Conclusion. Thus, these results suggest the possibility that there may be some association between IL-17A gene mutaion and gastrointestinal tract formation in Behçet's diseases.
The biological function of IL-17 towards ulcer formation in the gastrointestinal tract will be required in the future experiments.

P022

Interlukin-10 gene methylation in patients with Behçet's disease

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Introduction. Interleukin-10 (IL-10) is mainly produced by monocytes, T helper type 2 (Th2) and regulatory T cells (Treg). IL-10 plays a crucial role in controlling inflammation and regulating the immune response. IL-10 mRNA expression is significantly low in many inflammatory diseases such as Behçet's disease (BD). This often comes with more aggressive phenotypes. The essential molecular process for IL-10 low expression has not been completely realized.
Aims. This study was undertaken to estimate the IL-10 gene copy number variation, promoter methylation and serum levels in patients with BD.
Methods. In this study, blood samples from 47 BD patients and 61 healthy control were taken, with the mononuclear cells isolated with ficoll protocol. The DNA and RNA were then subsequently extracted. Promoter methylation levels were evaluated by MeDIP-qPCR. Following this, the extracted RNA was converted to cDNA using the RT-PCR method. Then, IL-10 expression evaluated by Real-time PCR. After that, serum levels of IL-10 were measured using Enzyme-linked immunosorbent assay (ELISA).
Results. The BD group consisted of 29 males and 18 females, with a mean age of 38.1±10.3 years. The control subjects included 37 males and 24 females with a mean age of 37.4±8.5 years. The serum level of IL-10 in patients with BD (28.6 ± 8.7 pg/ml) was significantly lower than control group (73.3±9.2 pg/ml). IL-10 gene expression in BD group was significantly lower than control group. The relative promoter methylation level of IL-10 gene was significantly higher in the BD group compared with control group

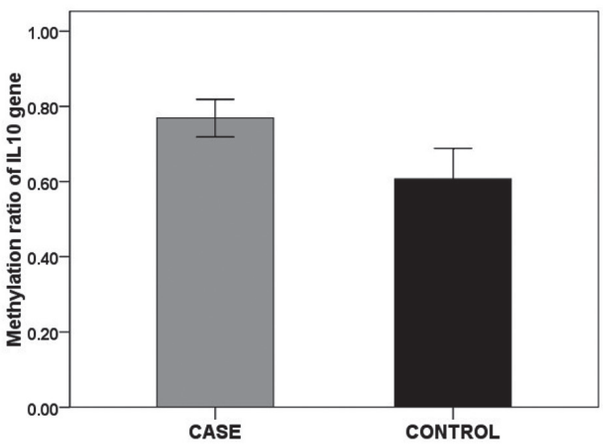

Fig. 1. Methylation ratio of IL-10 gene.

Conclusion. Our study showed that hypomethylation of IL-10 gene promoter is probably the main reason for low expression of IL-10 mRNA in patients with BD.

References

1. COMMINS S, STEINKE JW, BORISH L: The extended IL-10 superfamily: IL-10, IL-19, IL-20, IL-22, IL-24, IL-26, IL-28, and IL-29. *Journal of Allergy and Clinical Immunology* 2008; 121(5): 1108-11.
2. FU L-H, MA C-L, CONG B, LI S-J, CHEN H-Y, ZHANG J-G: Hypomethylation of proximal CpG motif of interleukin-10 promoter regulates its expression in human rheumatoid arthritis. *Acta Pharmacologica Sinica* 2011; 32(11): 1373-80.
3. HEDRICH CM, BREAM JH: Cell type-specific regulation of IL-10 expression in inflammation and disease. *Immunologic research* 2010; 47(1-3): 185-206.
4. L, CONG B, ZHEN Y, LI S, MA C, NI Z *et al*.: Methylation status of the IL-10 gene promoter in the peripheral blood mononuclear cells of rheumatoid arthritis patients. *Yi chuan= Hereditas/Zhongguo yi chuan xue hui bian ji* 2007; 29(11): 1357-61.
5. DONG J, IVASCU C, CHANG H-D, WU P, ANGELI R, MAGGI L *et al*.: IL-10 is excluded from the functional cytokine memory of human CD4+ memory T lymphocytes. *The Journal of Immunology* 2007; 179(4): 2389-96.

P023

Subgroup classification of Behçet's disease using clinical information: analysis of a clinical database of patients receiving financial aid for treatment

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Introduction. Behçet's disease is an inflammatory disease of unknown aetiology that is characterised by multisystem vasculitis, oral and genital ulcers, and ocular inflammation. Behçet's disease is diagnosed with a combination of symptoms. The Ministry of Health, Labour and Welfare (MHLW) of Japan initiated an online registration system to provide financial aid to treat intractable diseases in 2003, including Behçet's disease.
Aims. The purpose of this study was to explore subgroup classifications based on clinical symptoms, age of onset, gender, and laboratory information including HLA-B51, using data from a Japanese clinical database of patients receiving financial aid for treatment from the MHLW.
Methods. We obtained the new application data from the clinical database of patients with Behçet's disease between 2003 and 2014. We analysed 12 items (10 items of symptoms and 2 items of laboratory data): sex, age of onset, recurrent oral ulcers, skin lesions, ocular inflammation, genital ulcers, arthritis, intestinal ulcers, vascular lesions, neurologic involvement, and laboratory data (pathergy test, HLA-B51). We performed Hayashi's quantification third methods (mathematically equivalent method to correspondence analysis) using HALBAU version 7 to identify important characteristics to divide Behçet's disease into subgroups.
Results. The new application data from the clinical database of patients

with Behçet's disease between 2003 and 2014 included about 9000 cases. However, there were 2218 cases that fulfilled the 12 items of information. We found three distinct clusters in the data: group A (male, ocular inflammation, HLA-B51-positive, neurologic involvement), group B (female, genital ulcers, onset age: <30 years, ocular inflammation-negative, HLA-B51-negative, neurologic involvement-negative), and group C (onset age: 30–39 years, skin lesions, arthritis). In this database, it is possible to confirm the severity changes and the appearance of special types on a yearly basis. In the next stage, we will confirm the severity changes and appearance of special types using the same database after several years for each subgroup. Our future goal is to investigate whether prognosis can be predicted from symptoms, laboratory data, and genetic information in the early stage of onset.

Conclusion. Using data from a Japanese clinical database from the MHLW, we analysed 2218 Behçet's disease cases. We found three distinct clusters of Behçet's disease. In the next stage, we will confirm the severity changes and appearance of special types with the same database after several years for each subgroup.

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P024

Differential clinical presentation of Adamantiades-Behçet's disease in non-endemic and endemic areas: retrospective data from a Middle-European cohort study

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Introduction. Middle-Europe is a non-endemic region for Adamantiades-Behçet's disease (ABD). Therefore, the clinical presentation of ABD patients may differ from those of endemic regions - with research needed into a potentially less severe form of ABD (1). So far clinical data are available for Germany and Italy, but not for patients living in Austria.

Aims. To assess demographical and clinical data in a Middle-European cohort of ABD patients, and compare the clinicl findings with those of a German, a Turkish and the ICBD cohort.

Methods. In a retrospective cohort study, in- and outpatients of an Austrian secondary and tertiary university hospital center were analyzed independent from the medical discipline involved. After ethical approval screening for ABD patients in the clinical information system resulted in 1821 documents from 1997 to 2016. Patients fulfilling the ICBD criteria were included. ABD symptoms and signs were identified by individual chart reviews. Findings were detailed for female and male patients as well as patients from Austrian and Turkish origin. The latter details were compared to the ICBD dataset, a German and a Turkish ABD cohort. SPSS (IBM, Version 20.0) was used for statistical analyses. Descriptive analyses were performed using the mean percentage. The Fisher's exact test was used to test for significances between groups.

Results. A total of 76 ABD-patients were identified with 39.1% Austrian and 37.0% Turkish origin, each 6.5% with Italian and Balkanese and each 2.2% with German, Armenian, Portuguese, Thai and Tunesian origin. With 5.6 (0-18), 10.0 (0-26) and 6.9 (±6.2) years, the average disease durations were comparable between the Austrian and the Turkish subgroup of the Innsbruck cohort and the cohort living in Turkey.

Genital aphthae and skin manifestations were more frequent, neurological, gastrointestinal and vascular manifestations less frequent in ABD patients of Turkish origin living in Austria compared to those living in Turkey (each $p<0.05$). When comparing the total Innsbruck cohort with the ICBD dataset, the Innsbruck cohort had less oral/genital aphthae and skin manifestations, but more musculoskeletal, vascular manifestations, gastrointestinal and lung manifestations. Innsbruck patients' data also reported more often a positive family history than in the ICBD dataset.

53.9% of Austrian ABD patients were women with an average male-to-female ratio of 0.86. (0.39 in patients with Austrian and 1.43 with Turkish background), and was 3.3 in patients with venous manifestations. The average age was 38.1 (16-64) years.

Conclusion. In this Middle-European ABD-cohort clinical presentations between patients of Austrian and Turkish origin do not strongly vary, whereas Turkish patients from the non-endemic Middle-European cohort present differently compared to patients living in Turkey. The role of such cohort analyses will increase, from the epidemiological as well as the management perspective.

Reference

1. LECCESE P, YAZICI Y, OLIVIERI I: Behçet's syndrome in nonendemic regions. *Curr Opin Rheumatol* [Internet]. 2017; 29(1): 12-16.

P025

Associations between clinical manifestations of Behçet's syndrome and work outcomes: results from a UK cross-sectional analysis

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Introduction. Behçet's syndrome (BS) exhibits significant heterogeneity in clinical manifestations, including orogenital ulceration, skin rash, arthralgia and ocular, venous, gastro-intestinal and neurological involvement. BS affects adults of working age, usually presenting between 20-40 years (1), and can therefore have significant impact on work outcomes, although published evidence regarding this is limited. The associations between clinical manifestations of BS (individual and cumulative) with employment status have not previously been assessed.

Aims. To 1) describe demographics, clinical manifestations, work outcomes and claiming of employment benefits in a UK BS cohort and 2) to explore the relationship between individual and cumulative clinical manifestations of BS and work outcomes.

Methods. A cross sectional analysis was performed using the Liverpool Behçet's Centre of Excellence clinical database. Inclusion criteria were clinical characteristics meeting International Criteria for Behçet's Disease (ICBD) diagnostic criteria and recorded employment data. Patients meeting ICBD criteria but thought unlikely to have BS on clinical review by our multi-disciplinary team were excluded. Demographics, clinical manifestations, work outcomes and use of employment related benefits were described. A binomial variable 'Out of work' was generated and defined as unemployment, sickness absence, or patients marked as retired but of working age, a carer or a homemaker if the patient had to stop work due to BS. Associations between Out of work and: 1) individual clinical manifestations of BS, and 2) number of clinical BS manifestations, were explored using multivariate logistic regression adjusted for age, gender, mean EQ5D score and socio-economic status. Odds ratios (OR) and 95% confidence intervals were calculated.

Results. 120 patients met inclusion criteria. Mean age was 41.1 years (s.d. 12.0) and 33 patients (28%) were male. The minimum number of clinical manifestations were two in order to meet ICBD criteria; the frequency of clinical manifestations in this cohort were 100% oral ulceration, 94% genital ulceration, 71% arthralgia, 43% skin rash and 20% ocular, 7% neurological, 6% vascular and 5% gastro-intestinal involvement. 37 patients (31%) were out of work with 44 patients (37%) claiming employment related benefits. With regard to the effect of individual clinical manifestations on work outcomes, ocular disease had a statistically significant increased risk for being out of work when assessed alone with OR 2.84 (95% CI 1.13, 7.13) but lost statistical significance when analysed in the multivariate model: OR 2.45 (95% CI 0.70, 8.60). With regard to cumulative clinical manifestations, patients with four or more clinical manifestations of BS had a statistically significant increased risk of being out of work with OR 5.57 (95% CI 1.33, 23.27) in comparison to patients with two manifestations in the multivariate model.

Conclusion. This study highlighta the significant burden of BS on work outcomes in this UK cohort. In particular, four or more cumulative BS manifestations were independently associated with being out of work in this young cohort. Further work is required to identify whether education or intervention in the workplace can help prevent disease related job loss in BS.

References

1. AMBROSE NL, HASKARD DO: Differential diagnosis and management of Behçet syndrome. *Nat Rev Rheumatol* 2013; 9: 79–89.

P026

Functional interleukin-18 gene polymorphisms might encode a risk factor in the development of recurrent oral ulceration

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Introduction. Recurrent aphthous stomatitis (RAS) presents one of the principal causes of recurrent oral ulceration. Behçet's disease (BD) is a multi-systemic inflammatory in which the presence of ROU is one of the diagnostic signs of this disease. Genetic factors and abnormal cytokine cascade are thought to play an important role in the development of both conditions.
Aims. A clinical investigation of the potential associations of two single nucleotide polymorphisms (SNPs) at positions–137 (G/C) and –607 (C/A) in the promoter region of the IL-18 gene, with a susceptibility to RAS and BD.
Methods. This case-control study included 80 RAS patients assigned as Group1 (Gp1), and 80 BD patients (Gp2), who were diagnosed according to The International Study Group (ISG) criteria for the diagnosis of BD (1990). Eighty (age and sex-matched) healthy subjects (Gp3) were also included. IL-18 SNPs at – 607 and – 137 regions were analyzed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. Serum IL-18 levels were measured in all our participants.
Results. This study included 112 (47%) females and 128 males (53%). Their age ranged from 16-46 years with mean ± SD 33.23±16.11 years. The genotype and allele distributions of the two SNPs did not differ significantly between patients with RAS and controls. However, the genotype and allele distributions at -607 SNP was significantly different between BD patients [CC (p=0.044), C allele (p=0.043), A allele (p=0.043)] and controls. IL-18 -607CC genotype (OR= 2, CI= 1.01-3.9) and C allele (OR= 1.59, CI= 1.02-2.48) were significantly found more among BD patients. The frequency of the GG genotype at position –137 was higher in both RAS (OR= 1.2, CI= 0.65-2.3, p= 0.5) and BD patients (OR= 1.4, CI= 0.76-2.7, p=0.27), but with no significant difference.
Conclusion. Although there was no evidence for a genetic association conferred by the two SNPs at positions –137 and –607 in the promoter region of the IL-18 gene with respect to a susceptibility to RAS, a positive association was found in case of BD patients regarding -607 promoter region.

P027

Cardiovascular risk in patients with Behçet's disease: a nationwide population-based dynamic cohort study

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Introduction. There are few studies regarding the correlation between Behçet's disease (BD) and cardiovascular risk.
Aims. To determine the overall cardiovascular risk in patients with BD compared to non-BD patients
Methods. BD patients (n=5,576; mean age, 43.35±11.88 years; male, 32.53%) without previous cardiovascular diseases were selected from the Korean National Health Insurance Database from 2010 to 2014. An age- and sex-matched control population of individuals without BD (n=27,880) was randomly sampled at a ratio of 5:1. Both cohorts were followed up for incident cardiovascular disease or until 2015.
Results. Myocardial infarction (hazard ratio [HR]=1.717 [1.08-2.73]) and stroke (HR=1.653 [1.094-2.498]) were significantly higher in BD patients than in the controls, but congestive heart failure was not (HR=1.202 [0.737-1.958]). BD patients showed a significantly higher mortality rate due to cardiovascular diseases (HR=1.823 [1.4-2.373]) compared to the controls.
Conclusion. Korean BD patients had a higher overall risk of cardiovascular disease. Physicians should carefully monitor patients with BD for the potential development of cardiovascular disease.

P029

Gender influence in Behçet disease: a bicentric Tunisian study

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Introduction. Behçet disease (BD) have been viewed to have a male predominance with more severe involvement.
Aims. We aimed to study gender influence in BD to see if this could be confirmed in the Tunisian context
Methods. We retrospectively reviewed the medical records of BD patients followed up in the Internal Medicine and the Ophthalmology Departments of Fattouma Bourguiba University Hospital (Monastir, Tunisia) between January 1990 and December 2017. BD was diagnosed according to the International Study Group for Behçet Disease criteria. A comparative study of clinical characteristics between males (group 1) and females (group 2) was performed.
Results. A total of 281 BD patients were included: 86 females (30.6%) and 195 males (69.4%) (Sex ratio M/F was 2.26). Mean age at diagnosis was 31.35 years (range, 12- 77 years). Familial history of BD was recorded in 13.2% of patients. Oral aphthosis was detected in 98.9 % of patients at presentation, genital ulcers in 76.2%, pseudofolliculitis in 78.3% and erythema nodosum in 10.7%. Ocular inflammation was found in 38.4% of the cases, neurological and vascular involvements were found in 10.3% and 26% of patients, respectively. Comparative study between females and males revealed that the latters were more prone to develop pseudofolliculitis (81.5% vs 70.9%; p=0.047), ocular manifestations (46.7% vs 20.9%; p=10^{-3}) and vascular involvement (30.4% vs 16.3%; p=0.013). Conversely, females develop more frequently erythema nodosum and articular manifestations (16.3% vs 6.2%; p=0.007) and (53.5% vs 38.1%; p=0.017), respectively
Conclusion. In the Tunisian context it seems that males are more prone to develop severe manifestations especially ocular and vascular involvement while females tend to develop milder manifestations.

P030

Clinical manifestations of Behçet's syndrome in a large cohort of Italian patients: focus on gender differences

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Introduction. Behçet's syndrome (BS) is a chronic multisystemic inflammatory disorder classified among primary vasculitis. The clinical hallmarks of the disease are mucocutaneous manifestations which include oral aphtosis, genital ulcers and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Although BS etiology is still unclear, both genetics and environmental factors (*i.e.* dietary habits, hygienic practices, infections and pollution) may contribute to BS onset and development. BS shows a peculiar geographic distribution with a higher prevalence in certain geographic areas of the globe. In European countries BS is included in the list of "rare" disease due to its low frequency in general population. Some evidences suggest that in non endemic regions the disease tend to be less severe and women seem to be more commonly affected (1-3).
Aims. The aim of this study was to investigate the clinical phenotypes of Italian BS patients who visited the Rheumatology Institute of Lucania (IReL) with respect to gender, HLA-B51 status and onset features.
Methods. We retrospectively evaluated 324 Italian patients (185 males and 139 females), seen consecutively at IReL from 1st January 2000 to 31th December 2017. Demographics, clinical features at onset and during follow-up and HLA status were obtained from a review of medical records. The analysis was limited to BS-patients who fulfilled the ISG criteria.
Results. 324 BS patients were identified in our database. 39 (17 males and 22 females) were excluded because did not satisfied ISG criteria and 285 (168 males and 117 females) resulted eligible for the present study. Results are summarized in Table I. We found statistically significant differences in papulopustolar lesions, posterior uveitis and deep venous thrombosis, which occur more frequently in males compared with females (83.3% versus 46.2%, 37% versus 18.8% and 8.3% versus 0.9% respectively; p<0.01).

Erythema nodosum (59% versus 41,1%, $p<0,01$), arthralgia (52.1% versus 31.5%, $p<0.01$) and intestinal involvement (11.3% vs 21.4% $p<0.05$) resulted more frequent in females compared with males. No differences were found in HLA status (M 67.9% vs F 61.5%) and arthralgia resulted more common as clinical manifestation at the disease's onset in females.

Table I. Clinical manifestations of Italian BS patients: gender differences.

Clinical Manifestations	Overall (285) n (%)	Male (168) n (%)	Female (117) n (%)	OR (95% CI)	p-value
Oral Ulcers (OA)	285 (100.0)	168 (100.0)	117 (100.0)	1.44 (0.00-9231)	NS
Genital Ulcers (GU)	171 (60.0)	95 (56.5)	76 (65.0)	0.70 (0.43-1.14)	NS
Erythema Nodosum (EN)	138 (48.4)	69 (41.1)	69 (59.0)	0.48 (0.30-0.78)	0.0029**
Follicolitits	50 (17.5)	32 (19.0)	18 (15.3)	1.29 (0.69-2.44)	NS
Papulopustolar lesions	194 (68.1)	140 (83.3)	54 (46.2)	5.83 (3.38-10.06)	0.0000**
Pathergy test	20 (45.5)	12 (7.1)	8 (6.8)	1.05 (0.41-2.65)	NS
Posterior uveitis	84 (29.5)	62 (37.0)	22 (18.8)	2.53 (1.44-4.42)	0.0010**
Anterior uveitis	51 (17.9)	29 (17.3)	22 (18.8)	0.90 (0.49-1.66)	NS
Panuveitis	24 (8.4)	17 (10.1)	7 (6.0)	1.77 (0.71-4.41)	NS
Episcleritis	4 (1.4)	2 (1.2)	2 (1.7)	0.69 (0.10-4.49)	NS
Arthralgia	114 (40.0)	53 (31.5)	61 (52.1)	0.42 (0.26-0.69)	0.0005**
Arthritis	74 (26.0)	44 (26.2)	30 (25.6)	1.03 (0.60-1.76)	NS
Deep venous thrombosis (DVT)	15 (5.3)	14 (8.3)	1 (0.9)	10.55 (1.37-81.35)	0.0054**
Superficial venous thrombosis (SVT)	33 (11.6)	18 (10.7)	15 (12.8)	0.82 (0.39-1.69)	NS
Neurological involvement	70 (24.6)	36 (21.4)	34 (29.1)	0.67 (0.39-1.15)	NS
Fatigue	72 (25.3)	37 (22.0)	35 (29.9)	0.66 (0.39-1.13)	NS
Fever	119 (41.8)	76 (45.2)	43 (36.8)	1.42 (0.88-2.31)	NS
Intestinal involvement	44 (15.4)	19 (11.3)	25 (21.4)	0.47 (0.24-0.90)	0.0208*
HLA-B51 positivity	186 (65.3)	114 (67.9)	72 (61.5)	1.32 (0.81-2.16)	NS

Abbreviations: BS, Behçet syndrome; n, number of subjects; OR, odds ratio; CI, confidence interval
Notes: *statistically significant (p-value<0.05); ** statistically significant (p-value<0.01)

Conclusion. In our cohort of Italian BS patients the disease results slightly more prevalent in males. Gender-related differences were observed for posterior uveitis, DVP and papulopustolar lesions which are more frequent in males whereas EN-like lesions, arthralgia and intestinal involvement are more frequently observed in females. These data confirm that BS tend to be less aggressive in Italian female patients. No sex-differences are observed in modalities of onset and HLA-B51 status.

References

1. LECCESE P, YAZICI Y, OLIVIERI I: Behçet's syndrome in nonendemic regions. *Curr Opin Rheumatol* 2017; 29(1): 12-16.
2. HATEMI G, SEYAHI E, FRESKO I, TALARICO R, HAMURYUDAN V: One year in review 2016: Behçet's syndrome. *Clin Exp Rheumaology* 2016; 34 Suppl. 102: 10-22.
3. PIPITONE N, BOIARDI L, OLIVIERI I, CANTINI F, SALVI F, MALATESTA R *et al*.: Clinical manifestations of Behçet's disease in 137 Italian patients: results of a multicenter study. *Clin Exp Rheumatol* 2004; 22 (6 Suppl. 36): S46-51.

P031

Quantitative evaluation of vascular parameters with optical coherence tomography angiography (OCTA) in patients with Behçet disease

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Introduction. Optical coherence tomography angiography (OCTA) is a non-invasive high resolution technique for imaging the microvasculature of the retina.
Aims. To evaluate the OCTA features of patients with Behçet Disease.
Methods. A total of 23 patients with Behçet Disease without ocular involvement (mean age 45.7; 49.5% female) and 29 healthy age and sex matched control subjects (mean age 51.4; 46.7% female) were involved in the study. We measured foveal avascular zone area, vessel density in the parafoveal region and flow index in superficial and deep capillary plexuses evaluated by OCTA . The flow index was measured as detected flow signals within the fovea centered 3 mm diameter area manually.
Results. Foveal avascular zone area was significantly larger in eyes with Behçet Disease than in control group in both the superficial and deep capillary plexuses (0.331 mm^2 vs 0.240 mm^2, $p=0.004$ and 0.352 mm^2 vs 0.257 mm^2, $p=0.003$, respectively). The mean capillary vessel density in the parafoveal region was lower in eyes with Behçet Disease than in control group for both superficial and deep capillary plexuses (55.3% vs 55.4%, $p=0.966$ and 64.0% vs 63.8%, $p=0.740$, respectively). The mean flow index was lower in eyes with Behçet Disease than in control group in superficial and deep capillary plexuses (13.154 vs 13.504, $p=0.185$ and 14.089 vs 14.530, $p=0.189$, respectively).
Conclusion. These results show that macular vascular changes can be seen in Behçet patients.

P032

Possible association of 3p12.3 and 6q25.1 with Behçet's disease in a Japanese population

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Introduction. Behçet's disease (BD) is currently thought to be triggered by various genetic as well as environmental factors. It is well established that BD is strongly associated with the human leukocyte antigen (HLA) class I allele, *HLA-B*51*, in many different ethnic groups. We previously reported four candidate loci (3p12, 6q25.1, 12p12.1 and 22q11.22) for BD outside the HLA region in a genome-wide association study (GWAS) with a Japanese population (300 BD patients and 300 controls) using 23,465 microsatellite markers (1).
Aims. We investigated whether the four candidate loci are associated with BD in a larger cohort of Japanese patients and controls.
Methods. We used previous GWAS data with a Japanese population (612 BD patients and 740 controls) using 500,568 single nucleotide polymorphisms (SNPs) (2). After sample and SNP quality control, a total of 792 SNPs in the four loci from 611 patients and 737 controls were used for statistical analyses.
Results. Of the four loci, SNPs in 3p12 and 6q25.1 showed a marginal but significant association with BD (lead SNP: $p=0.000063$, $pc=0.0496$ in 3p12; $p=0.000040$, $pc=0.032$ in 6q25.1). On the other hand, SNPs in the other two loci, 12p12.1 and 22q11.22, were not significantly associated with BD ($pc>0.05$).
Conclusion. This study suggests that 3p12 and 6q25.1 may contribute to the risk of BD. To confirm the findings, future validation studies with other independent populations are needed.

References

1. MEGURO A, INOKO H, OTA M, KATSUYAMA Y, OKA A, OKADA E, YAMAKAWA R, YUASA T, FUJIOKA T, OHNO S, BAHRAM S, MIZUKI N: Genetics of Behçet disease inside and outside the MHC. *Ann Rheum Dis* 2010; 69(4): 747-754.
2. MIZUKI N, MEGURO A, OTA M, OHNO S, SHIOTA T, KAWAGOE T, ITO N, KERA J, OKADA E, YATSU K, SONG YW, LEE EB, KITAICHI N, NAMBA K, HORIE Y, TAKENO M, SUGITA S, MOCHIZUKI M, BAHRAM S, ISHIGATSUBO Y, INOKO H: Genome-wide association studies identify IL23R-IL12RB2 and IL10 as Behçet's disease susceptibility loci. *Nat Genet* 2010; 42(8): 703-706.

P033

Differences in clinical manifestations of Behçet's syndrome by gender: cross-sectional analysis in a UK cohort

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Introduction. Geographical variations in genotype and phenotype of Behçet's syndrome (BS) are reported (1, 2). Previous meta-analysis of international cohorts has highlighted differences in clinical manifestations of BS by gender (3). A comparison of BS clinical manifestations by gender has not been analysed previously in a large UK BS cohort.
Aims. 1) To compare the clinical manifestations of BS in a UK cohort by gender and 2) to compare this to published international data.
Methods. A retrospective cross sectional analysis was performed using clinical databases at the Liverpool and Birmingham BS Centres of Excellence. Patients with a multi-disciplinary diagnosis of BS or International Study Group (ISG) diagnostic criteria were included. Clinical manifestations and

HLA-B51 positivity were compared by gender. T-tests and chi-squared tests were used for continuous and categorical data respectively and a p value of 0.05 or less was considered statistically significant.
Results. 433 patients met inclusion criteria (140 males, 32.3%). As depicted in Table I, male patients were younger and had significantly higher rates of ocular and vascular involvement, papulopustular skin rash and HLA-B51 positivity. Female patients had significantly higher rates of genital aphthosis and arthralgia.

Table I. Demographics and clinical manifestations of BS compared by gender (*statistically significant).

	Male (n=140)	Female (n=293)	p value
Age (years), mean (s.d.)*	41.2 (12.5)	44.1 (11.9)	0.02
Recurrent oral aphthosis, n (%)	139 (99.3)	291 (99.3)	0.97
Genital aphthosis, n (%)*	111 (79.3)	278 (94.9)	<0.01
Papulopustular skin rash, n (%)*	69 (49.3)	107 (36.5)	0.01
Erythema nodosum, n (%)	29 (20.7)	56 (19.1)	0.70
Skin aphthosis (n, %)	7 (5.0)	8 (2.7)	0.23
Uveitis, n (%)*	81 (57.9)	99 (33.8)	<0.01
Retinal vasculitis, n (%)*	39 (27.9)	36 (12.3)	<0.01
Central nervous system involvement, n (%)	16 (11.4)	20 (6.8)	0.11
Large vein thrombosis, n (%)*	22 (15.7)	19 (6.5)	<0.01
Arterial thrombosis or aneurysm, n (%)	4 (2.9)	7 (2.4)	0.77
Thrombophlebitis, n (%)*	10 (7.1)	5 (1.7)	<0.01
Gastro-intestinal involvement, n (%)	8 (5.7)	25 (8.5)	0.30
Arthralgia, n (%)*	68 (48.6)	180 (61.4)	0.01
Ethnicity (British or White), n (%)*	90 (64.3) (n=126)	238 (85.9) (n=277)	<0.01
HLA-B51 positive, n (%)*	14 (58.3) (n=27)	9 (20.0) (n=45)	<0.01

Conclusion. Similar to published international cohorts, male patients with BS in the UK have higher rates of ocular and venous involvement, papulopustular skin rash and HLA-B51 positivity and lower rates of genital aphthosis and arthralgia in comparison to female patients. However, the extent to which these differences are attributable to ethnicity is unclear.
References:

1. LEONARDO NM, MCNEIL J: Behçet's Disease: Is There Geographical Variation? A Review Far from the Silk Road. *Int J Rheumatol Hindawi* 2015; 2015: 1-7.
2. SIBLEY C, YAZICI Y, TASCILAR K, KHAN N, BATA Y, YAZICI H *et al*.: Behçet syndrome manifestations and activity in the United States versus Turkey -- a cross-sectional cohort comparison. *J Rheumatol* 2014; 41: 1379-84.
3. BONITSIS NG, NGUYEN L, B L, LAVALLEY MP, PAPOUTSIS N, ALTENBURG A *et al*.: Gender-specific differences in Adamantiades-Behçet's disease manifestations: an analysis of the German registry and meta-analysis of data from the literature. *Rheumatology* (Oxford) 2015; 54: 121-33.

P035

How the genetic evolution happened in Behçet's disease along the Silk Route?

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Introduction. The multiple risk factors involved into the pathogenesis of Behçet's disease (BD) making this complex auto-immune disorder hardly have a clear explanation for its underlying mechanism. Although the essential role of genetic factors in BD has been confirmed by enormous amount of interesting studies, including nine genome-wide association studies (GWAS) in various ethnic populations across the world, there are many questions arise about the function of genetic still leaking of evidence.
Aims. In our previous studies, we observed that in the same disorder such as BD, the related genes, even the related individual single-nucleotide polymorphisms (SNPs) play quite different role in patients with different ethnic background. The aim for this study is to identify different genes involoved in BD patients with different ethnic background.
Methods. We selected fifteen SNPs from six genes (STAT3, UBAC2, TCFBR3, PTPN22, GIMAP4 and IL10) which have been identified as high risk factors in BD patients in previous studies in other population along the sik route. Then repeated the DNA genotyping in a case-control study in British cohort.
Results. Our current results showed two rs1310182 and rs2476601 polymorphism in PTPN22 was strongly associated with the susceptibility to BD in U.K cohort, but have less effect in Turkeys population as compare with health controls and even not existing in Han-Chinese BD patients. The rest thirteen SNPs(rs3825427, rs9517668, rs9517701 and rs7999348 in UBAC2 louis, rs1805110 in TGFBR3, rs1522596 in GIMAP4, rs6503695, rs2293152 in STAT3 and rs1518111, rs3024505 and rs3024490 in IL10) have no significate difference in British BD patients as compare with health controls, even they showed strongly associated with BD in other two cohort Han Chinese and Turkish studies. The haplotype analysis using a logistic regression model for haplotype-specific associations revealed more interesting findings, where even these SNPs did not showed direct relationship with BD in UK cohort, but their combination gave promising clues. The haplotype AAGG and CTAA in gene UBAC, haplotype CA in STAT3 and the haplotype GAC in IL10 showed significate different in BD patients as compared with health participates in UK cohort.
Conclusion. In conclusion, our finding independently confirm, extend and refine the association of BD with STAT3, UBAC2, TGBR3, GIMAP4, PTPN22 and IL10 in different BD patients' cohort. We further confirmed that SNPs are not only worked alone but also collaboration with others in the pathogenesis of the disease, which gave a clue that the epistasis (gene-gene interactin) definity have to be considered as an important component of heritability in complex disease such as BD. The function research of these epistasis is on going in our group but these different gene association of BD in various populations warrant further investigation.

P036

Male-to-female ratio in Behçet's syndrome: meta-analysis of population-based studies

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Introduction. There is uncertainty with regard to potential sex differences in the occurrence of Behçet's syndrome (BS), both in general and in terms of regional variations in male-to-female (M/F) ratios. Sex ratios reported from cohort studies are potentially skewed because of sex-specific variations in disease expression (1), which may result in preferentially recruiting males or females across medical specialties.
Aims. This study's aim was to investigate the M/F ratio in BS reported from population-based prevalence surveys, which minimize the effect of selection bias.
Methods. The study was based on a recently published comprehensive literature review for population-based prevalence surveys in BS (2); for the purpose of the present analysis, the literature search was updated to March 2018. For the present study, only surveys reporting on the sex distribution of identified BS cases were eligible. The M/F ratio in each individual study was calculated as the ratio of the M/F distribution in BS cases and in the background population; for studies not specifically mentioning the counts by sex for the background population, we considered a sex ratio of 1:1 with equal numbers by sex. Pooled estimates were generated by meta-analysis by using the standard inverse-variance method for random-effects models and maximum likelihood standard estimator for computing the amount of heterogeneity. Heterogeneity of effects among studies was quantified by the I^2 test. Subgroup analyses and meta-regression analyses were performed to explore potential between-study heterogeneity with the following moderator variables: geographic area (6 areas), study design (census vs sample surveys), classification criteria (International Study Group vs other criteria), year of publication (across 4 calendar periods), and reference type (peer-reviewed vs grey literature).
Results. The analysis was based on 31 studies from 19 countries, including 2 recent publications (3,4), and a total of 19,238 prevalent BS cases. The overall pooled M/F ratio was estimated at 1.23 (95% CI: 0.94–1.61) with high heterogeneity (I^2=83.6%). The overall results and results stratified by geographic regions are shown in the Figure. Univariate meta-regression

analysis revealed no effect modification on the M/F ratio for geographic areas (p=0.134), study design (p=0.548), classification criteria (p=0.559), year of publication (p=0.897), or reference type (p=0.077). The M/F ratio estimate for the Asian subcontinent was 1.29 (95% CI 0.76–2.17) after removing 1 large study (3).

Conclusion. Our findings do not support a significant sex predilection in BS occurrence, both in general and within geographic regions. Slightly increased M/F ratios in BS, more prominent in Middle Eastern countries, could also reflect the higher severity of male BS with less underrecognition of diagnoses. The two-fold female predominance in Asian countries is in line with cohort studies but needs to be viewed with caution because it relied on a single large study.

References

1. BONITSIS NG *et al*.: Gender-specific differences in Adamantiades-Behçet's disease manifestations: an analysis of the German registry and meta-analysis of data from the literature. *Rheumatol Oxf Engl* 2015; 54: 121-133.
2. MALDINI C *et al*.: Exploring the variability in Behçet's disease prevalence: a meta-analytical approach. *Rheumatol Oxf Engl* 2018; 57: 185-195.
3. KIM JN *et al*.: The prevalence of Behçet's disease in Korea: data from Health Insurance Review and Assessment Service from 2011 to 2015. *Clin Exp Rheumatol* 2017; 35 Suppl. 108: 38-42.
4. MADANAT WY *et al*.: The prevalence of Behçet's disease in the north of Jordan: a hospital-based epidemiological survey. *Clin Exp Rheumatol* 2017; 35 Suppl. 108: 51-54.

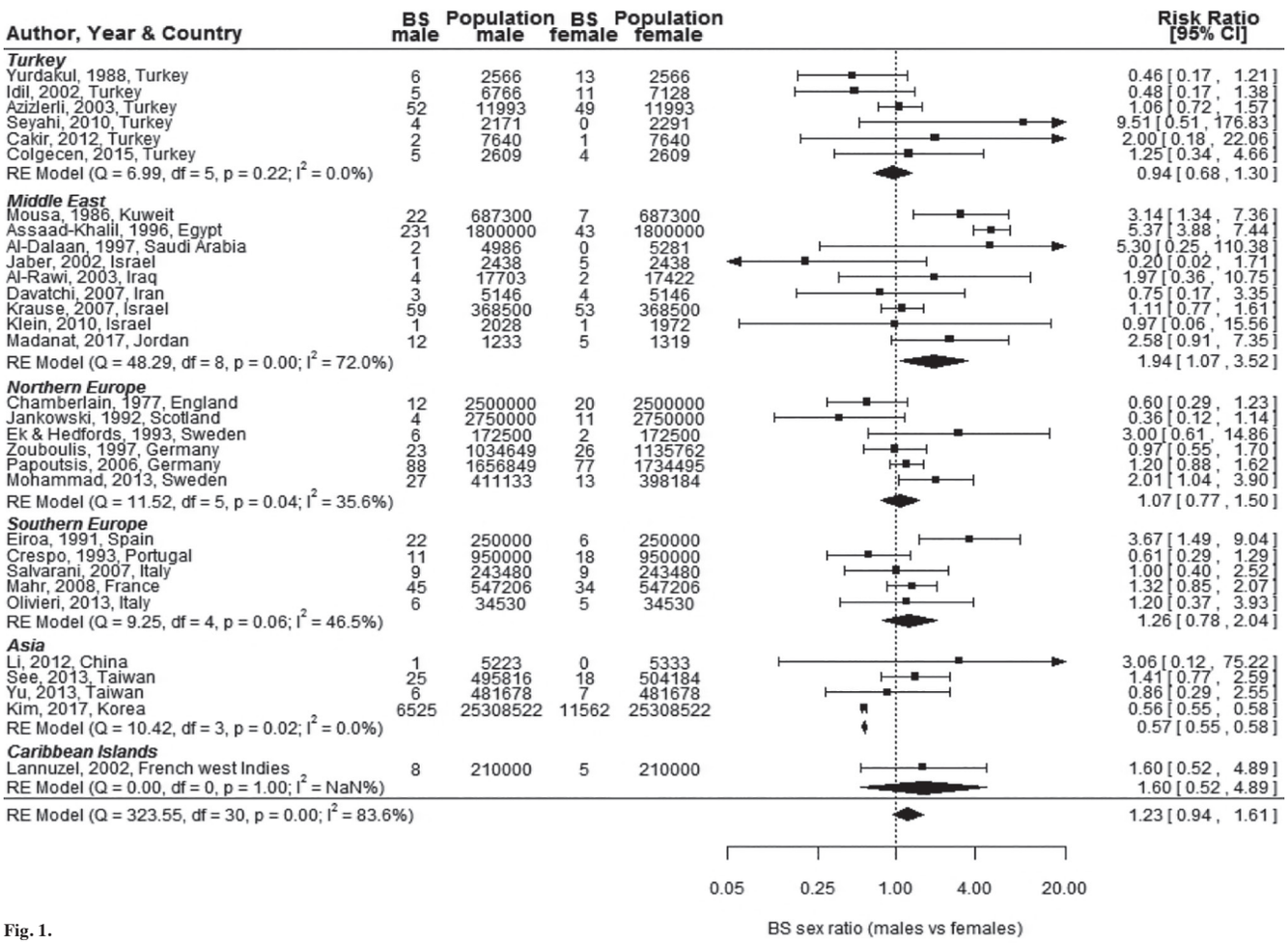

Fig. 1.

P037

More severe disease with multi organ affection in American versus Iranian Behçet's patients: a retrospective comparative cohort study

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Introduction. Behçet's disease (BD) is a rare vasculitis that affects vessels of variable size and results in multi-organ inflammatory disease. At-risk populations are most prevalent in the Middle East and East Asia, along the ancient Silk Road. Clinical data on BD in Western countries, especially in the United States of America (US), are scarce.

Aims. To compare the clinical features of BD patients from a tertiary referral center located at the West Coast of the US with a cohort of BD patients from a tertiary referral center in Iran.

Methods. Comparative analysis of a retrospective cohort of 56 BD patients evaluated at Stanford University Hospital (SUH) between 2000-2016, and a cohort of 163 patients from the BD Registry at Tehran University of Medical Sciences was done. Clinical, demographical, laboratory and treatment data were retrieved from medical records. Comparisons of cohorts were carried out using descriptive statistics along with parametric and non-parametric testing according to the type of data distribution.

Results. The SUH patients were younger (22.3 vs. 26.3 years p<0.05); were more often women (69.6% vs. 38.7 p<0.05) and had longer disease duration (16.8 vs. 12.0 years p<0.05). Genital ulcers, skin, joint, neurological, vascular, cardiac and pulmonary manifestations were all significantly more common in the Stanford cohort. Ocular lesions occurred more frequently in Iranian BD patients (53.4 % vs. 21.4% p<0.05), with the biggest difference seen for retinal vasculitis. 38 % of American patients had 4 or more organ systems involved, compared to only ~10% of Iranian BD patients.

We compared the SUH cohort with four other American BD cohorts from New York University Hospital, (NYU I n=634), Michigan (n=114), NIH (n=35) and NYU II (n=77). Consistently, all American cohorts had a predominance of female patients (64-80%). Ethnic and racial backgrounds differed between cohorts, with Stanford having the most diverse population and the lowest percentage of white patients. We found a lower age of onset in the Stanford cohort. The rates of superficial phlebitis, lower limb thrombosis/DVT and pulmonary aneurysms were comparable between Stanford, NYUI, and/or Michigan. CNS- and GI involvement were similar between Stanford , NYUI and NIH/NYUII (CNS 16-20%, GI 27-42%), with Michigan having lower rates for both GI and CNS (5.3% respectively). In general, the Stanford cohort was more similar to the NYUI cohort except for considerably higher rates of HLA-B51 and positive pathergy test in the SUH cohort.

Conclusion. BD patients from the West Coast of North America have a more severe disease course when compared to Iranian BD patients, as demonstrated by earlier onset and a higher rate of multi-organ involvement. The high risk of Iranian BD patients to develop vasculitis of ocular structures suggest that there may exist distinct pathomechanisms driving ocular versus non-ocular BD.

References

1. MAHR A *et al*.: *Arthritis Rheum* 2008; 58: 3951-3959.
2. DAVATCHI *et al*.: *Clin Rheumatol* 2010; 29: 823-33.
3. CALAMIA K *et al*.: *Arthritis Rheum* 2009; 61: 600-4.
4. SIBLEY C *et al*.: *J Rheumatol* 2014; 41: 1379-84.
5. KILIAN N, SAWALHA A: *Eur J Rheumatol* 2017; 4: 239-244.

P038

2018 update of the German Registry of Adamantiades-Behçet Disease

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Introduction. The registered charity German Registry of Adamantiades-Behçet Disease (ABD) provides data of 881 ABD-patients, which are permanent residents of Germany.

Aims. 31 clinics and practices transferred patients' data to the registry via standardized registration forms.

Methods. Demographic data, frequencies of manifestations, familial occurrence and potential prognostic signs have been evaluated.

Results. Of the 881 documented patients of the German Registry, 335 (39.2%) patients were of German and 345 (43.7%) of Turkish descent, along with 31 other countries of origin.

The prevalence in Germany can be estimated to be 1.1 per 100,000 (0.5 per 100.000 among people of German descent). First manifestation of the disease was predominantly in the third decade of life (median age: 26 years). The full disease developed in 2.9 years on average (median: 3 months). The median age of full clinical picture of ABD was 29 years.

Most frequent features included oral aphthae (98.1%), cutaneous lesions (63.9%), genital ulcers (64.2%), ocular manifestations (46.1%), arthritis (55.3%), vascular complications (21.1%), CNS-involvement (11.9%) as category of neurologic manifestation (20.4%), prostatitis-epididymitis (11.7%), gastrointestinal (10.0%), pulmonary (2.9%), cardiac (2.3%), kidney involvement (1.7%), and positive pathergy test (27.2%). Among skin manifestations, folliculitis (52.2%), erythema nodosum (38.6%), pyoderma (12.5%), skin ulcers (11.0%) and superficial thrombophlebitis (12.2%) were noted.

As the most severe complications blindness (5.9%), meningoencephalitis (3.8%), disabling arthritis (2.2%), fatal outcome (1.0%), hemoptysis (0.9%) and gastrointestinal perforation (0.6%) were registered. Most frequently reported onset symptoms included: oral apthae (83.4%), uveitis (4.7%), joint manifestation (3.1%), genital ulcers (2.9%) and erythema nodosum (1.1%). The following most common second symptoms in the course of the disease were reported: genital ulcers (41.8%), ocular manifestations (14.9%), erythema nodosum (14.4%), oral aphtae (11.6%), folliculitis (6.7%), joint manifestation (5.7%) and superficial thrombophlebitis (1.7%).

There was a positive family history in 11.9% among the entire collective of the German Registry. In case of German origin, family history was lower than in case of Turkish (3.7% versus 14.3%; $p<0.001$). Patients of Turkish descent showed androtopism in contrast to those of German descent (female:male 1.9:1, $p<0.001$). Androtopism was also documented in the whole collective (1.3:1).

Conclusion. The kind of first manifestation influenced the speed of diagnosis: In case of arthropathy, the average interval to diagnosis was significantly extended with 60 months compared to uveitis (15.5 months), superficial thrombophlebitis (13 months) or erythema nodosum (19 months) as onset signs. In Germany, the delay from the complete clinical syndrom to diagnosis took averagely more than 2.5 years.

Turkish patients suffered more often from uveitis compared to Germans (59.6 vs. 40.4%, $p=0.02$) as well as from folliculitis (56.6 vs. 43.4%, $p=0,05$). In German patients prostatitis/epididymitis (17.4 vs. 7.6%; $p=0.02$) was more frequent than in Turkish patients. The HLA-B5 antigen showed an association with uveitis ($p=0.001$) and gastrointestinal manifestations ($p=0.003$).

The registry gives a precise overview of the prevalence, ethnic, gender and age distribution, clinical as well as prognostic parameters. Late complications may be missing due to anonymisation. Supplementation by a follow-up-registry would give also an overview of the courses of the disease under therapy.

P040

Intestinal Behçet's disease associated with myelodysplastic syndrome with 8 trisomy: a case report and review of Japanese literature

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Introduction. A number of patients with Behçet's disease associated with myelodysplastic syndrome (MDS) with 8 trisomy has been reported. These patients frequently show with gastrointestinal involvement. Most of these cases are reported from east Asia, especially from Japan.

Aims. Here we report an intestinal Behçet's disease with 8 trisomy and review similar cases from previous reports.

Methods. A systematic literature review was performed in Japanese literature database (Ichu-shi) using the keywords (Behçet's disease) AND (myelodysplastic syndrome OR trisomy 8).

Results. A case was 55-year-old female. She was admitted to our hospital for several week history of fever, diarrhea, dyspnea, loss of appetite and loss of weight (4kg/3weeks). She has been diagnosed as having intestinal Behçet's disease over 11 years. She had presented with recurrent oral ulcers, arthritis, folliculitis and intestinal ulcers. She has been treated with methotrexate, but not with colchicine, salazosulfapyridine and 5-aminosalicylic acid which she was allergic to. On admission, laboratory data showed pancytopenia (hemoglobin of 6.4 g/dL, platelet of 57,000 /μL and WBC of 2,200 /μL) and inflammation (C reactive protein of 7.04 mg/dL). The colonoscopy revealed multiple ulcers throughout colon, which were worse than the previous examinations. Cytomegalovirus was not detected in the biopsied specimen. Bone marrow biopsy showed morphologic changes in erythroid without the increase of blast cells. Further chromosomal analysis detected chromosomal aberration including 8 trisomy: 48,XX,+8,+9,del (15) t(1;15) (q12; p11.2). The patient was diagnosed as the exacerbation of intestinal Behçet's disease probably caused by MDS-U (IPSS int-2, WPSS intermediate). Treatment with prednisolone 60mg daily gradually ameliorated the symptoms. The bone marrow transplantation for the treatment of MDS was not carried out because the patient had a past history of refractory cutaneous tuberculosis. After discharge from the hospital, the patient is followed up in an outpatient clinic without exacerbation of both Behçet's disease and MDS for two years.

In a systematic literature review, data from 28 manuscripts that met the inclusion criteria, reporting on 30 patients were analyzed. Several articles point out common clinical features in Behçet's disease comorbid with 8 trisomy MDS; the presence of intestinal lesion and the absence of uveitis. These patients were successfully treated with conventional glucocorticoid or TNF-alpha inhibitors.

Conclusion. Trisomy 8 may be involved in the concurrent manifestation of MDS and Behçet's disease with gastrointestinal involvement.

P042

Novel association of human leukocyte antigen class I allele with ocular Behçet's disease by imputation of dense genotype data

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Introduction. It is known that both genetic and environmental factors are important for pathogenesis of Behçet's disease. Human leukocyte antigen (HLA) class I have showed the strongest susceptibility as a genetic factor for Behçet's disease in genome-wide association studies for multiple populations. In addition, susceptibility of several HLA class I alleles have been reported[1)]. On the other hands, patients with Behçet's disease present various clinical manifestations, such as oral ulcer, eye involvement, skin lesions and genital ulcer. It is thought that there are associations between specific HLA class I alleles with each clinical manifestation.
Aims. To identify associations of HLA class I alleles for ocular Behçet's disease by imputation of genotyped data by the Immunochip (Illumina).
Methods. Genotypes of 8,147 SNPs located in the major histocompatibility complex (MHC) region (Chromosome 6; 28-34 Mb) were selected from genotype data including 1,900 cases and 1,779 controls. Genotyping data were imputed to type classical HLA alleles by SNP2HLA using the reference data collected by the Type1 Diabetes Genetic Consortium. Additional SNP genotypes from this region were also imputed IMPUTE2 after phasing by SHAPEIT. For quality control, markers with MAF<0.01 and Hardy-Weinberg equilibrium $p<1.0\times10^{-5}$ in controls were excluded. The concordance rate per allele in 2,186 samples for which *HLA-B*51* was directly typed. Numeric association tests in the additive model and regression conditional analysis were performed for statistical analysis. $p<0.0012$ was considered significant after correcting for the number of two-digit MHC class I alleles (n=42).
Results. In 1,900 cases, clinical information was available for 1,104 cases and 397 cases had ocular lesions. The concordance rate between imputed and genotyped *HLA-B*51* was 98.6%. After quality controls, imputation of the MHC region and classical HLAs showed the strongest association for *HLA-B*51* ($p=1.03\times10^{-55}$, OR 3.97, 95% CI: 3.29 - 4.80). The lead single nucleotide polymorphism is rs1050502, which is a synonymous variant of the HLA-B molecule and a tag SNP for *HLA-B*51*. Regression conditional analysis revealed independent associations of a disease risk allele, *HLA-B*27*, and protective risk alleles, *HLA-A*03* and *HLA-A*68*.
Conclusion. We conducted a large genetic study to reveal disease association of HLA class I for ocular Behçet's disease. We confirmed the strongest association of *HLA-B*51* and independent associations with *HLA-A*03* and *HLA-B*27* as reported in studies for Behçet's disease. In this study, susceptibility of *HLA-A*68* was newly identified by analysis in ocular Behçet's disease. These findings suggest that *HLA-A*68* is protectively involved in pathogenesis of uveitis.

References

1. OMBRELLO MJ, KIRINO Y, DE BAKKER PI, GUL A, KASTNER DL, REMMERS EF: Behçet disease-associated MHC class I residues implicate antigen binding and regulation of cell-mediated cytotoxicity. *Proc Natl Acad Sci USA* 2014; 111: 8867-72.

P043

Documentation and follow-up in a multicenter Registry of Adamantiades-Behçet's disease

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Introduction. In the German Registry of Adamantiades-Behçet's disease, 881 patients have been included from more than 30 institutions during the last 28 years. The registry has been the basis of several clinical studies. Patients enrollment is anonymous, thus no follow-up is possible within the framework of this registry.
Aims. Several aims motivate the installation of a multicenter follow-up registry: The follow-up of manifestations and course of the disease under therapy, the generation of epidemiological data referring to incidence and prevalence of the disease and the development of standards with respect to diagnostic evaluation and therapeutic management. Large sample sizes of patients will be necessary to obtain sufficient evidence. Direct comparisons between different therapies can be made under real conditions.
Methods. Clinically competent centers will be selected in order to transfer data and registration forms of Adamantiades-Behçet's disease (ABD) patients to the referral center. The database includes patient identification and the numbers of regular follow-up and additionally visits, including documentation of clinical symptoms, serology, medication and dosage. The clinical course is evaluated by documentation of the severity of each manifestation via scoring systems for clinical features such as oral ulceration, skin lesions, eye and gastrointestinal involvement, arthralgia, nervous system and major blood vessel involvement by activity forms. Every patient has to sign an informed consent to confirm knowledge about the rationale of the registry, the use of his or her data and experimental serum measurements for inflammatory cytokines.
Results. Overall function will be determined by new organ involvement, remission of old organ involvement, damage, quality of life, psychological well being, fatigue and acute phase response. The ophthalmology clinical examination schedule includes ophthalmologic scores for slit lamp biomicroscopy, gradings for vitreous haze, fundus, macular edema, visual acuity, and fluorescein angiography. The dermatology evaluation includes the number and overall pain score of oral ulcers, number and overall pain score of genital ulcers, number,localization and overall pain of erythema nodosum lesions, number and localization of papulopustular lesions. Documentation is on paper and a web-based system is being developed. Feasible case report forms have been designed and will be presented.
Conclusion. In contrast to the current German registry, anonymisation at the longitudinal registry will not be feasible as follow-up data have to be matched. To assess the long-term safety of therapies, the evaluation of the course of large patient cohorts in a long-term registry is of particular medical importance. In Germany, only azathioprine is explicitely approved for the treatment of ABD, cyclosporine A only for Behçet uveitis, and adalimumab for non-infectious intermediate/posterior uveitis. Due to the expansion of possible therapies, e.g. biologics, it is particularly important to acknowledge efficacy and safety of the compounds in long-term registry-based observational studies. The development of a follow-up registry for ABD patients may acknowledge comparative efficacy and safety of the compounds and will foster international cooperation.

P044

Influence of sex and age on clinical manifestations of Behçet's disease: data of 6627 patients from Japanese nationwide survey database

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Introduction. Both genetic and environmental factors are involved in the pathogenesis of Behçet's disease (BD). These factors are also implicated in development of various phenotypes in BD. While genetic factors are consistent throughout the lifespan, exposed environmental factors are accumulated in aging. Indeed, previous studies have shown that clinical presentations are partly dependent on onset age and sex in BD.
Aims. To investigate effects of onset age and sex on clinical features of BD symptoms using a Japanese nationwide survey database.
Methods. We analyzed clinical manifestations of BD in age- and sex- specific subgroups in the database of 7950 BD patients who were newly registered to the Japanese Ministry of Health, Labour and Welfare, from 2003 to 2014.
Results. A total of 6627 patients who met the revised International Criteria for BD were analyzed (male 2651, female 3976). The mean age was 39yo [IQR 31-50] with 1 year [0-4] of disease duration. Frequencies of ocular involvement and HLA-B51 were lower, and those of intestinal and neurological lesions were higher in this study compared with previous reports. In consistent with previous reports, ocular and vascular lesions were significantly more frequent in male than female, whereas skin lesions, genital ulcer, and arthritis were more in female. Age- and sex-specific subgroup analysis showed that individual manifestations were divided into three groups. The first was ocular involvement which was more frequent in male, but the male predominance disappeared in elderly. The similar pattern was found in

HLA-B51 and pathergy test. The second group consisting of skin manifestations, genital ulcer, and epididymitis had a peak of incidence from 20 to 50 years old. The last group including arthritis, vascular involvement, and neurological involvement showed gradually increasing incidence in aging. Intestinal involvement also showed age-dependent increase in addition to a small peak in young aged patients. Sensitivity analysis using International Study Group criteria replicated the results.
Conclusion. This study showed that clinical phenotype in early phase of BD was different depending on onset age and sex, suggesting involvement of environmental factors in clinical pictures of BD patients.

Reference

ISHIDO T *et al*.: Clinical manifestations of Behçet's disease depending on sex and age: results from Japanese nationwide registration. *Rheumatology* (Oxford) 2017; 56(11): 1918-1927.

P046

The important role of non-oral aphthous beginning and demographic factors on poor prognosis of Behçet disease

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Introduction. Although prognosis of Behçet disease(BD) is unpredictable, early evaluation of the demographic and clinical features are believed to help on this respect.
Aims. To analyze the correlation between demographic features and clinical manifestations particularly related to major (vital organ) involvement (VOI) at onset and during the course.
Methods. Our cohort is composed of 624 patients with BD (390 men, 234 women, M:F=1.67) diagnosed according to our dignostic criteria (Seoul 2000). Demographic features and clinical manifestations were carefully analyzed and possible correlations were investigated.These correlations were particularly looked for in non-aphthous (NAB) and aphthous beginning groups (AB). Major or vital organs included eye, heart, arteries and deep veins, lungs, GIS, CNS and amyloidosis. Results were statistically analyzed.
Results. Males were found to be more affected than women in many aspects except erythema nodosum. Males were significantly preponderated in most of the VOI.
Patients with early age of onset (<25yrs), present age less than 40, of male sex and with NAB had significantly more VOI. Some patients tend to develope multiple VOI together.
Conclusion. This study validated our previous findings that some demographic features and early clinical manifestations are helpful to predict the outlook of BD rather reliably.Therefore early evaluation of BD patients belonging to either AB or NAB group as to the demographics and clinical manifestations will be very helpful for the physicians to further follow-up, care and treatment.

P047

Epidemiological and clinical characteristics of Behçet's disease, descriptive study of 1646 cases

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Introduction. Behçet's disease is a systemic inflammatory vasculitis of unknown etiology**.**It's classically characterized by triple –symptom complex, oral and genital aphthous ulcers and uveitis. It can involve multiple organ system, joints, blood vessels, nervous system and digestive tracts. Peculiarly, the disease seems to show some clinical variability among different ethnic groups and geographical locations.
Aims. To analyze the demographics and the clinical aspects of Behçet's disease in Morocco in large cohort of patients (1646), and to compare them with other series in different ethnic populations.
Methods. Monocentric retrospective study on 1646 consecutive patients getting their healthcare at a tertiary internal medicine department over a period of 36 years. All the patients met de international criteria of the ISG for Behçet's disease.
Results. The cohort included 1646 patients, the male to female ratio was 2, 36. The mean age was 34, 3 (12-65). All our patients had oral aphthosis and 83.7% had genital aphthosis. Pathergy test was positive in 44.3%. Articular involvement was observed in 45.3%, the pattern was as follow, polyarthralgia in 63.3%, polyarthritis in 15%, oligoathritis in 14.2% and monoarthritis in 13,7% .it was deforming in 8 cases and destructive in 10 cases
Ocular involvement was noted in 59%, and consisted of uveitis in 86.2% and retinal vasculitis in 29.1%. Vascular disease was present in 19.13%, deep venous thrombosis in 90.8%. (74.4% Lower extremity deep venous thrombosis, 26.3% inferior and superior vena cava and 6 cases of Budd Chiari Syndrome). 38 patients had arterial disease, dominated by aneurysm lesions. 17 patients had cardiac involvement. 65 patients (35%) had neurological disease and was essentially parenchymatous. Digestive, pulmonary and renal disease were rather uncommon.
Conclusion. Behçet's disease is not infrequent in Morocco. We believe that its young population and geographic location plays an important role in its relatively high prevalence.

P048

Three cases of methotrexate-related lymphoproliferative disorder that developed during the treatment of chronic progressive neuro-Behçet's disease

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Introduction. Central nervous system involvement is one of the most serious complications in Behçet's disease (BD). This condition is referred to as neuro-Behçet's disease (NB) and can be classified into acute type (ANB) and chronic progressive type (CPNBD) based upon differences in the clinical course and responses to corticosteroid treatment. Recent studies have demonstrated the efficacy of methotrexate (MTX) and infliximab (IFX) for CPNBD. On the other hand, while MTX is considered to be an anchor drug for rheumatoid arthritis (RA), the development of MTX-related lymphoproliferative disorder (MTX-LPD) has been confirmed in some cases, which is considered a problem.
Aims. Recent studies have demonstrated the efficacy of methotrexate (MTX) and infliximab (IFX) for CPNBD. On the other hand, while MTX is considered to be an anchor drug for rheumatoid arthritis (RA), the development of MTX-related lymphoproliferative disorder (MTX-LPD) has been confirmed in some cases, which is considered a problem.
Methods. Herein, we report our experience with 3 patients who developed MTX-LPD during the treatment of CPNBD.
Results. *Case 1* (a 47-year-old male patient): This patient developed CPNBD when he was 28 years old. He began treatment with MTX at 32 years of age, and IFX was added at the 35 years of age. Since then, there has been no aggravation of his symptoms. At 45 years of age, he developed a refractory cutaneous ulcer in his right lower extremity that was diagnosed as MTX-LPD, based on skin biopsy results. After discontinuation of MTX and IFX administration, the ulcer was completely cured.
Case 2 (a 43-year-old male patient): This patient developed CPNBD when he was 28 years old. He began to receive MTX at 28 years of age. Since he developed fever and multiple cervical adenopathy at 42 years of age, he was diagnosed as having MTX-LPD, based on the results of lymph node biopsy. After discontinuation of MTX, and initiation of PSL administration (30 mg/day), the adenopathy improved immediately.
Case 3 (a 43-year-old male patient): The patient developed CPNBD when he was 31 years old. He began treatment with MTX at 31 years of age, and IFX was added in the same year. Since then, there has been no aggravation of his symptoms. At 43 years of age, MTX-LPD was suspected due to multiple cervical adenopathy and increase of soluble interleukin (IL)-2 receptor (sIL-2R) and thymidine kinase (TK), and thus MTX and IFX administration was discontinued. Immediately after discontinuation, the adenopathy and the levels of sIL-2R and TK were improved.
The MTX doses for Cases 1, 2, and 3 were 20, 15, and 17.5 mg/week, respectively, and the administration periods were 13, 15, and 12 years, respectively.
Conclusion. Although MTX is one of the effective drugs for CPNBD, careful attention should be paid to the development of MTX-LPD during its administration, as is done for RA.

P050

Tocilizumab in the treatment of severe and/or refractory vasculo-Behçet's disease: a single-centre experience in China

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Introduction. Vasculo-Behçet's disease(BD) is a life-threatening complication of BD. Biological therapy is always applied to patients who are refractory to steroid and immunosuppressant. TNF inhibitors have been proved to be effective in numerous studies. However, issues including poor response, loss of the initial efficacy over time, intolerance and relative contraindications limit the use of TNF-α inhibitors in BD patients. Thus, it is *necessary* to seek alternative *therapeutics* to treat the severe and/or refractory BD. Recently, some case reports have showed that tocilizumab(TCZ) was effective in severe and/or refractory BD, especially for neurologic and ocular manifestations (1, 2), but the efficacy of TCZ for vasculo-BD remains unknown.
Aims. To elucidate the efficacy and safety of TCZ for severe and/or refractory vasculo-BD.
Methods. We retrospectively analyzed seven vasculo-BD patients treated with TCZ in our center between 2014 and 2018.
Results. Seven patients (6 males and 1 female) were enrolled, with a mean age of 32.9±9.0 years old and median course of 91.3±37.5 months. Multiple arterial lesions were documented in all patients, including arterial aneurysm (n=5), stenosis (n=4), and occlusion (n=3), and multiple venous thrombosis were documented in two patients. Main locations for arterial lesions, with descending order of frequency, include subclavian artery (5/7), carotid artery (4/7), abdominal aorta (4/7), aortic arch (3/7), femoral artery (2/7), and coronary artery (2/7). Recurrent aneurysms together with graft occlusion or endoleak occurred in two patients who underwent endovascular stent placements. Concomitant medical conditions include hepatitis B infection in one patient, and latent tuberculosis infection in three patients who subsequently received anti-tuberculosis prophylaxis. Prior to TCZ therapy, all patients had failed to high-dose glucocorticoid in combination with multiple immunosuppressants. TCZ was administrated at 8mg/kg iv every 4 weeks for a median of 7 times, in combination with low-to-medium-dose corticosteroids and immunosuppressants. After a median follow-up of 19.4±9.0 months, all the patients achieved both clinical and serological improvements. One patient showed radiologic improvement of artery stenosis. The condition of the patient with endoleak after the stent placement remained stable without surgical intervention. No newly-onset arterial lesions or venous thrombosis were observed. The median ESR (18 vs 7 mm/h, $p<0.05$) and hsCRP level (30.6 vs 0.68 mg/L, $p<0.05$) were also significantly decreased. Furthermore, the dosage of corticosteroids was tapered from 27.1±16.5mg to 8.9±3.2mg ($p<0.05$), and immunosuppressants were tapered in number and dosage in three (42.9%) and three patients (42.9%), respectively. No serious adverse events or TB reactivation were observed.
Conclusion. TCZ, in combination with corticosteroids and immunosuppressants, was effective and well tolerated in severe and/or refractory vasculo-BD, with a favorable steroid- and immunosuppressant-sparing effect.

References

1. ADDIMANDA O, PIPITONE N, PAZZOLA G, SALVARANI C: Tocilizumab for severe refractory neuro-Behçet: three cases IL-6 blockade in neuro-Behçet. *Semin Arthritis Rheum* 2015; 44: 472-5.
2. MUSELIER A, BIELEFELD P, BIDOT S, VINIT J, BESANCENOT JF, BRON A: Efficacy of tocilizumab in two patients with anti-TNF-alpha refractory uveitis. *Ocul Immunol Inflamm* 2011; 19: 382-3.

P051

Trough levels of adalimumab and the appearances of anti-adalimumab antibody in non-infectious uveitis patients treated with Adalimumab

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Introduction. Adalimumab (ADA), a human anti-TNF-α monoclonal antibody has shown excellent clinical results in several immune-mediated diseases. However, it is also true that some patients show poor response to ADA in the course of treatment.
Aims. In this study, we investigated the correlation between the clinical response and the trough level of ADA or the appearance of anti-ADA antibody (AAA) in patients with refractory non-infectious uveitis including Behçet's disease who were undergoing ADA therapy.
Methods. Ten patients (5 males and 5 females) with refractory non-infectious uveitis were enrolled from January to September 2018. The etiology of uveitis was Vogt-Koyanagi-Harada disease in 5 cases, sarcoidosis in 2 cases, Behçet's disease, sympathetic ophthalmia and idiopathic non-infectious uveitis in one case each. They were treated with ADA in Hokkaido University Hospital for 6 months or longer and their clinical histories were obtained from medical records. The serum trough level of ADA and the level of AAA were measured with ELISA methods.
Results. The mean age was 52.1 years (range, 33-74 years) at the beginning of ADA treatment, and mean following-up period was 9.5 months (range, 7-11 months). The mean serum trough level of ADA was 49.8±33.2 ng/ml, and 4 of 10 patients (40%) were positive for AAA. The mean serum trough level of ADA was significantly lower in AAA-positive patients (24.1±22.9 ng/ml) than in AAA-negative patients (68.3±28.9 ng/ml), whereas there were no obvious differences in visual acuity, ocular findings or the prednisolone sparing effect between the two groups.
Conclusion. The serum trough levels of ADA were significantly lower in AAA-positive cases of non-infectious uveitis patients treated with ADA. The presence of AAA may weaken the therapeutic effects of ADA.

P052

Long-term efficacy and safety of adalimumab in Behçet's disease patients with non-infectious uveitis in the VISUAL III trial

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Introduction. Adalimumab has approved indications for the treatment of immune-mediated inflammatory diseases including non-infectious uveitis (1, 2) and intestinal Behçet's disease (BD; Japan only) (3).
Aims. To evaluate the long-term safety and efficacy of adalimumab in patients with non-infectious intermediate, posterior, or panuveitis associated with BD.
Methods. Adult patients who met treatment failure (TF) criteria, or who completed the VISUAL I/II trials without TF, were eligible to enter the open-label study VISUAL III (4). All patients received open-label adalimumab 40 mg every other week. Efficacy endpoints assessed through Week 78 of treatment in VISUAL III included proportion of patients with: no active inflammatory lesions in both eyes; anterior chamber (AC) cell grade ≤0.5+ in both eyes; vitreous haze (VH) grade ≤0.5+ in both eyes; and quiescence (defined as no active inflammatory lesions AND AC cell grade ≤0.5+ AND VH grade ≤0.5+). Mean best corrected visual acuity (BCVA) was also assessed. Missing data were reported using non-responder imputation (NRI) for binary endpoints and last observation carried forward (LOCF) for BCVA. Adverse events (AEs) were collected from first adalimumab dose in VISUAL III through the interim cut-off date of October 31, 2016.
Results. Of 371 patients (intent-to-treat population) analyzed in VISUAL III, 27 (7.3%) had a diagnosis of BD. The majority of patients with BD were male (22/27 [81.5%]) and predominantly of white race (18/27 [66.7%]),

with 3/27 (11.1%) of Asian race. At study entry, patients with BD had a mean (standard deviation) age of 33.9 (9.0) years and disease duration of 49.4 (39.6) months. A total of 17/27 (63.0%) patients were receiving immunosuppressants and 10/27 (37.0%) were receiving corticosteroids. The majority of patients overall had panuveitis (21/27 [77.8%]) and all patients with active uveitis at entry to VISUAL III (11/11) had panuveitis.
The percentage of patients with quiescence improved from 44.4% at Week 0 to 77.8% at Week 12 and remained stable through Week 78. Similar trends were observed for proportions of patients with no active inflammatory lesions and VH grade ≤0.5+ (Table). There was a decrease in the proportions of patients with AC cell grade ≤0.5+ (Weeks 0/78: 81.5%/77.8%), and mean logMAR BCVA of both eyes remained stable over time (Table).

Table I. Long-term efficacy of adalimumab in VISUAL III in patients with non-infectious uveitis associated with Behçet's disease.

	Week 0	Week 12	Week 30	Week 54	Week 78
Quiescence, % (95% CI)[a]	44.4 (25.5–64.7)	77.8 (57.7–91.4)	70.4 (49.8–86.2)	74.1 (53.7–88.9)	74.1 (53.7–88.9)
No active inflammatory lesions, % (95% CI)[a]	66.7 (46.0–83.5)	85.2 (66.3–95.8)	77.8 (57.7–91.4)	77.8 (57.7–91.4)	77.8 (57.7–91.4)
AC cell grade ≤0.5+, % (95% CI)[a]	81.5 (61.9–93.7)	88.9 (70.8–97.6)	85.2 (66.3–95.8)	85.2 (66.3–95.8)	77.8 (57.7–91.4)
VH grade ≤0.5+, % (95% CI)[a]	66.7 (46.0–83.5)	88.9 (70.8–97.6)	81.5 (61.9–93.7)	85.2 (66.3–95.8)	77.8 (57.7–91.4)
LogMAR BCVA, mean (95% CI)[b]	0.16 (0.03–0.28)	0.11 (0.01–0.21)	0.15 (0.03–0.28)	0.11 (0–0.21)	0.16 (0.02–0.31)

[a]NRI and [b]LOCF analysis; n=27 for all data.
CI, confidence interval.

Safety (events per 100 patient-years [E/100 PYs]) was comparable with previous VISUAL trials. Serious AEs and serious infections were observed at 8.8 and 5.8 E/100 PYs, respectively. Five events of vasculitis were reported in two patients with BD.
Conclusion. Increased quiescence and maintenance of visual acuity were achieved with long-term adalimumab treatment in patients with non-infectious uveitis associated with BD. No new safety signals were reported for this patient population in VISUAL III.
References

1. TAYLOR SR: *Eur Ophthalmic Rev* 2016;1 0: 17-18.
2. HUMIRA® (adalimumab): EU Summary of Product Characteristics 2018.
3. HISAMATSU T *et al*.: *J Gastroenterol* 2014; 49: 156-62.
4. SUHLER EB *et al*.: *Ophthalmology* 2018 Feb 8 [Epub ahead of print].

P053

Comparison of the treatment results of infliximab and interferon alpha in patients with Behçet uveitis

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Introduction. The visual prognosis and outcomes have been improved in Behçet uveitis with the use of interferon alpha and tumour necrosis factor alpha antagonists in the treatment (1-3). However, to the best of our knowledge, there are no data that compare the effectiveness of interferon alpha and tumour necrosis factor alpha antagonists in Behçet uveitis.
Aims. We aimed to compare the treatment results of infliximab and interferon alpha in patients with Behçet uveitis.
Methods. Medical records of 53 patients with Behçet's uveitis treated with infliximab or interferon alpha were retrospectively analysed. 20 patients were treated with intravenous infusions of infliximab at a dose of 5 mg/kg (Group 1) and 33 patients were treated with an initial dose of 4.5 million IU interferon alpha (Group 2). We compared the two groups by evaluating the mean number of uveitis attacks, visual acuity and intraocular inflammation at 6 and 12 months after the initiation of treatment.
Results. The mean duration of treatment was 20.8±18.1 months in Group 1 and 29.5±22.3 months in Group 2. Sixteen patients in Group 1 (80%) and 28 patients in Group 2 (85%) achieved remission. In both groups, the mean best-corrected visual acuity improved and frequency of relapses, aqueous flare levels, anterior chamber cells, vitreous haze score, macular edema and retinal vasculitis decreased significantly. In terms of these parameters, there were no significant difference between two groups. Three of the 20 patients in Group 1 (15%) and 6 of the 33 patients in Group 2 (18.1%) were switched to a different agent because of adverse effects.
Conclusion. Both infliximab and interferon were effective in controlling intraocular inflammation and decreasing relapse rate. Our results showed no significant difference between two agents in the control of intraocular inflammation.
References

1. AL RASHIDI S, AL FAWAZ A, KANGAVE D, ABU EL-ASRAR AM: Long-term Clinical Outcomes in Patients with Refractory Uveitis Associated with Behçet Disease Treated with Infliximab. *Ocul Immunol Inflamm* 2013; 21: 468-474.
2. MOLINS B, LLORENC V, HERNANDEZ MV, ESPINOSA G, DICK AD, ADAN A: Current and future treatments for Behçet's uveitis: road to remission. *Int Ophthalmol* 2014; 34: 365-381.
3. GUEUDRY J, SAADOUN D, WESCHLER B, LEHOAANG P, BODAGHI B: Long-term Efficacy of Interferon in Severe Uveitis Associated with Behçet Disease. *Ocul Immunol Inflamm* 2017; 25(1): 76-84.

P054

Effectiveness of benzathine penicillin in refractory ulcers of Behçet's disease

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Introduction. Prednisone therapy, thalidomide ,azathioprine, alpha interferon and recently anti–TNF-alpha inhibitors and interleukin 1 inhibitors are presently used in the resistant mucocutaneous lesions of Behçet's Disease (BD).We presented the Observation of patient with Behçet's Disease, despite treatment with azathioprine, then alpha interferon for his eye lesions, he developed resistant ulcers; the recovery from ulcers was obtained with Benzathine Penicillin (BP).
Aims. This observation illustrated the effictiveness of BP in refractory ulcers of BD and we recommend its use more frequently and to add BP in the EULAR recommendations for treatment of BD 2008, in resistant cases of mucocutaneous.
Methods. In 2013, BP at the dosage of 2.4 million units, every 2 weeks was used in this patient who had developed refractory ulcers, while he was treated with azathioprine, prednisone for his uveitis. Patient received 3 intramuscular injections. Colchicine at the dosage of 1mg /day was maintained. Serology of syphilis was negative. BP was reused in 2015 and 2017 at the same dosage: 2.4 millions units every 3 weeks, for resistant ulcers while the patient received alpha interferon, prednisone for his uveitis. He received 3 injections of BP in 2015 and also in 2017.
Results. OBSERVATION: Of 15 patients with BD treated successfully with BP, we presented this privileged case of one male who developed refractory ulcers, while he first received azathioprine, then alpha interferon for his eye lesions. The recovery from resistant ulcers was obtained with Benzathine Penicillin. A male 35 years old with family history of aphtosis. The onset of Behçet's Disease was 22 with oral ulceration in 2005. He developed in 2008 genital ulcer and uveitis in 2009 treated with pulse of cyclophosphamide combined with prednisone. In March 2013, while he was being treated for his uveitis with azathioprine, prednisone and colchicine 1 mg/day, he developed multiple oral ulcers that healed with BP. In October 2015, while treated with alpha interferon and Corticosteroids for his uveitis, he had developed 2 giants Genital Ulcers: diameter superior to 1.5 cm; the healing was obtained with BP. In 2017, He developed giant oral ulcer: diameter superior to 1cm, while he was treated with alpha interferon for his uveitis. The recovery was achieved with BP.
Conclusion. This observation illustrated that in some cases of refractory ulcers of BD, even azathioprine and alpha interferon are not efficient, and the recovery from refractory ulcers was obtained with Benzathine Penicillin. We confirm that the treatment with BP is rather easy in outpatients, it is efficient, it has a low cost and has'not a significant side effects. We recommend using more frequently BP in Behçet's Disease with refractory ulcers with this protocol: One injection of BP: 2.4 million every 3 weeks combinated to colchicine: 1mg/day; in total: 3 intramuscular injections. We support, infections hypothesis: Streptococcus, in the pathogenesis of BD.

P055

Anti-tumor necrosis alpha therapy in the management of refractory pediatric Behçets uveitis

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Introduction. Behçet's disease can cause sight threatening panuveitis. It is a realtively rare condition among pediatric uveitis patients, but can cause severe complications. There is limited data in the literature regarding the use of anti-tumor necrosis alpha therapy in refractory pediatric Behçet's uvetis cases.
Aims. The aim of this study was to evaluate the efficacy of anti-tumor necrosis alpha (Anti-TNF) treatment in the management of pediatric Behçet's uveitis, who failed conventional immunosuppressive therapies.
Methods. We reviewed the records of three pediatric Behçet's uveitis cases. Previous treatments, visual acuity and complications were specifically recorded.
Results. The first case was a 14 years old male patient. He was managed with azathiopurine + cyclosporine with systemic steroids for 4 months. Because of insufficient response, infliximab (IFX) 5mg/kg per 4 weeks was added to the treatment. He was stable under infliximab for 22 months and the infusion intervals were gradually increased to 8 weeks. His visual acuity was 0.7 OD and 0.8 OS at presentation, which improved to 1.0 bilaterally.
The second case was a 15 years old male patient. He was initially managed with azathiopurine + cyclosporine with systemic steroids for 5 months and IFX 5mg/kg per 4 weeks was added due to insufficient response. He had bilateral cataracts and was operated successfully without complications under IFX treatment. His visual acuity improved from 0.05 OD and 0.1 OS to 1.0 bilaterally.He was stable under infliximab for 22 months and the infusion intervals were gradually increased to 8 weeks. He needed INH treatment due to latent tuberculosis.
The third case was a 11 years old male patient. e was initially managed with azathiopurine + cyclosporine with systemic steroids for 5 months and IFX 5mg/kg per 4 weeks was added due to insufficient response. At the 18th infusion, he had anaphylaxis and IFX was switched to interferon-alpha. At the 6th month of interferon treatment, it was swithched to adalimumab 40mg/2wks because of insufficient response. He was stable for the last 6 moths under adalimumab. His initial visual acuity was 0.05 OD and 0.1 OS, and it improved to 1.0 in both eyes.
Conclusion. Anti-TNF treatments were successful in preventing visual loss in severe cases of refractory pediatric Behçet's uveitis.

P056

Vitamin D and Behçet's disease

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Introduction. Vitamin D deficiency is highly prevalent in patients with systemic inflammatory diseases as Rheumatoid Arthritis and Gougerot Sjögren's Syndrome. In our country, there is high prevalence of hypovitamin D. In our knowledge, there isn't study of Vitamin D and Behçet's Disease (BD).
Aims. To evaluate vitamin D deficiency in BD, its severity and its repercussions on patients with BD. To do prevention by dosing systematically Vitamin D in all patients with BD, even if they do not have symptoms related to vitamin deficiency .
Methods. Lab measurements included serum 25-OH vitamin D, calcium ,phosphorus and 24 hour calciuria were performed in these 17 patients with BD: 7 males and 10 females; 13 of them fulfilled all criteria of BD. Interrogation and Clinical examination of these patients discovered that, in addition to their symptomatology related to Behçet's Disease, some of them complained of asthenia, sleep disorders, paresthesia, myalgia and thoracic pain.
Results. Of these 17 patients with BD, 6 had very severe vitamin D deficiency: Inferior to 10 ng /ml: one male with osteoporosis related to high dosage of corticosteroids and 5 females: 4 of them had dress style covering. They complained of arthralgia, asthenia, paresthesia. Thoracic Pain is found in 3 females. 5 patients had important deficiency of vitamin D: 10 to 20 ng/ml: 4 females; one of them had thoracic pain: she was treated for a long times with corticosteroids. Vitamin D was performed systematically in 6 patients with BD. It was between 20 and 30 ng/ml. 5 males and one female. In these patients, the effect of vitamin D treatment improve considerably asthenia, paresthesia, myalgia and even thoracic pain and the quality of life.
Conclusion. In this preliminary study, vitamin D deficiency is frequent in BD. The very important deficiency is observed in females. The effect of vitamin D treatment improve considerably asthenia, paresthesia , myalgia and even thoracic pain. Serum 25-OH vitamin D should be performed systematically in Behçet's Disease, in order to correct a possible deficit on Vitamin D and improve quality of life of patients with BD.

P057

Long term follow-up of Behçet's syndrome patients treated with cyclophosphamide

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Introduction. Cyclophosphamide (CYC) remains an important treatment option for Behçet's syndrome (BS) patients with life-threatening conditions such as arterial aneurysms**.** However, several adverse events may occur with CYC and this has led to increased use of biologic agents such as rituximab in other vasculitides.
Aims. Our aim is to delineate the outcome and short and long-term adverse events with CYC use among BS patients.
Methods. We conducted a retrospective chart review of all BS patients treated with oral or intravenous CYC between 1976 and 2006. Patients were called and a standard form was used for collecting demographic characteristics, CYC indication, the reason for the cessation of therapy, cumulative dose of CYC and short-term serious adverse events necessitating the cessation of therapy and/or requiring hospitalization and long-term adverse events (malignancy and infertility).
Results. We identified 198 (M/W:184/14) patients who had received CYC. After a median follow up of 17 (IQR:9-26) years after the initiation of CYC therapy, 52 (26%) patients had died within a median duration of 4 (1-12) years, 33 (17%) were lost after a median follow-up of 9 (3.5-14) years, and 113 (57%) were contacted.
CYC was prescribed for vascular involvement in 132 (67%) patients, eye involvement in 52 (26%), central nervous system involvement in 5, both vascular and eye involvement in 7 and both vascular and central nervous system involvement in 2 patients. The median duration of CYC use was 12 (IQR:4-24) months and median cumulative dose was 13.5 (IQR:6-49) gr.
Among the 52 patients who died, reasons for death were vascular involvement in 26 (pulmonary artery aneurysm in 15, abdominal aorta aneurysm in 2, superior vena cava thrombosis in 2 and Budd-Chiari syndrome in 7), malignancies in 7, infections in 5, neurologic involvement in 2, ischemic stroke in 1, traffic accident in 1, and secondary amyloidosis in 1, esophageal varices bleeding in 1, and unknown in 5 patients.
Sixteen patients experienced serious adverse events associated with short term CYC use and 1 of them died due to infection. Among these adverse events, hemorrhagic cystitis occurred in 7 patients, infections in 4, leukopenia, acute myocardial infarction, anaphylactic reaction, azoospermia, liver toxicity, and severe nausea/vomiting in 1 patient each. Overall, 16 malignancies were observed in 14 (7%) patients after a median follow up of 25 (IQR:15-26) years. The malignancies were bladder carcinoma (n=4), lung adenocarcinoma (n=3), prostate adenocarcinoma (n=2), carcinoma of unknown primary origin, pancreas adenocarcinoma, t-MDS-AML, lymphoma, colon adenocarcinoma, squamous cell carcinoma and thyroid papillary carcinoma. Among the 113 patients we were able to question regarding infertility, 67 patients (59%) had children, 22 (19.5%) did not wish to have a child and 24 (21.5%) tried to have a child, but was not able to.
Conclusion. Short term serious adverse events occurred in 8% of the patients during CYC treatment. During long term follow-up malignancies occurred in 7% and infertility in 21.5% of the patients. These results underline the need for safer and effective alternatives to CYC for serious organ involvement in BS, similar to that in other vasculitides.

P058

Apremilast for the treatment of oral ulcers in Behçet's syndrome: a phase III randomized, double-blind, placebo-controlled study (RELIEF)

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Introduction. Oral ulcers (OU) are the most common sign of Behçet's syndrome and are observed in nearly every patient. Due to their severity and frequency of recurrence, OU can be disabling and have a substantial effect on quality of life. There is an unmet need for effective treatment for OU in Behçet's syndrome. Apremilast (APR), an oral phosphodiesterase 4 inhibitor that modulates inflammatory pathways, demonstrated efficacy in the treatment of OU of Behçet's syndrome in a phase II study.
Aims. To assess the efficacy and safety of APR for OU in patients with Behçet's syndrome who have active OU previously treated with ≥1 medication.
Methods. In this phase III, multicenter, randomized, double-blind, placebo-controlled study, 207 eligible patients were randomized (1:1) to APR 30 mg BID (n=104) or placebo (n=103) for 12 weeks, followed by a 52-week active-treatment extension. Patients had active Behçet's syndrome, with ≥3 OU at randomization or ≥2 OU at screening and at randomization, without active major organ involvement. The primary endpoint was area under the curve (AUC) for total number of OU over 12 weeks. AUC reflects the change in the number of OU over time, accounting for the recurring-remitting course of OU. Secondary endpoints included OU pain measured by the visual analog scale and the proportion of patients achieving resolution of OU (OU-free) at Week 12.
Results. AUC for total number of OU over 12 weeks was statistically significantly lower with APR 30 mg BID vs. placebo (129.54 vs. 222.14; $p<0.0001$), indicating a 42% reduction in AUC over 12 weeks. This treatment effect is supported by greater benefits with APR 30 mg BID vs. placebo as demonstrated by a reduction in the mean number of OU and OU pain (Figure), starting at Week 1 and continuing through Week 12, with a 48% reduction in number of OU and 61% reduction in OU pain at Week 12. The treatment effect was also supported by a significantly greater proportion of patients achieving OU resolution (52.9% vs. 22.3%; $p<0.0001$).
The proportion of patients with treatment-emergent adverse events (AEs) was comparable between APR and placebo during the placebo-controlled period (78.8% vs. 71.8%, respectively). Serious AEs were observed in 3 (2.9%) patients in the APR group (migraine, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, genital and fungal infections, OU flare, acne, acute febrile neutrophilic dermatosis, erythema multiforme).

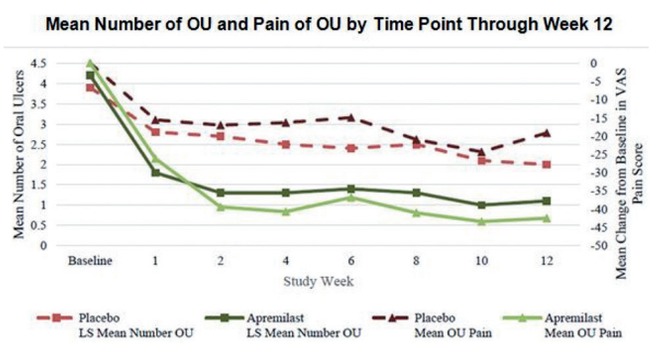

Fig. 1. Mean Number of OU and Pain of OU by Time Point Through Week 12.

Conclusion. In patients with Behçet's syndrome, APR effectively reduced the number of OU and resulted in a significantly greater proportion of patients who achieved OU resolution compared with placebo. The decrease in OU pain paralleled the decrease in number of OU over time. Safety findings were consistent with the known profile of APR.

P059

Efficacy and safety of interferon α2a as an add-on treatment for refractory Behçet's uveitis

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Introduction. Uveitis is one of the leading causes of morbidity in Behçet's patients which may result in irreversible vision loss (1). Evidence is accumulating that interferon (IFN) α2a might be a promising treatment for Behçet's Uveitis (BU) refractory to conventional immunosuppressive agents (2-4). The practical value of these studies, however, is limited by their heterogeneity in terms of ethnic and racial backgrounds of the patients, indication, dosage and duration of IFN treatment. In addition, while IFN was commonly given only with corticosteroids, whether and (if so) how it could be used as a combinatorial agent to conventional immunosuppressants remains to be further elucidated.
Aims. To investigate the efficacy and safety of IFNα2a as an add-on treatment for refractory BU.
Methods. Twenty-six refractory BU patients who received IFNα2a treatment in Peking Union Medical College Hospital between February 2015 and October 2017 were retrospectively reviewed. IFNα2a was used mainly as an add-on treatment for BU patients who underwent relapse under corticosteroids and conventional immunosuppressive agents. The primary outcomes were treatment success rate and changes in ocular relapse rates before and after initiation of IFNα2a. Disease activity, corticosteroid- and immunosuppressant-sparing effects, as well as side effects were secondary outcomes.
Results. A total of 26 patients (23 males and 3 females) with a mean age of 30.5±8.6 years were included. Eighteen patients (69.2%) were treated with at least 2 immunosuppressive agents before the initiation of IFNα2a. Treatment success was achieved in 24 patients (92.3%), and the median uveitis relapse rate decreased from 8 (range 2-12) to 0 (range 0-6) per patient-year ($p=0.000008$) during a mean follow-up of 13.6±6.0 months, corticosteroids were lowered in 20 cases (76.9%) and completely withdrawn in 2 (7.7%). In addition, immunosuppressive agents were reduced in number and dosage in 16 (61.5%) and 23 patients (88.5%), respectively, and were completely withdrawn in 5 cases (19.2%). No severe adverse events were observed and serum autoantibodies remained negative during the treatment of IFNα2a.
Conclusion. IFNα2a is effective and relatively safe in refractory BU, with significant steroid- and immunosuppressant-sparing effects.
References

1. TUGAL-TUTKUN I *et al*.: Uveitis in Behçet disease: an analysis of 880 patients. *Am J Ophthalmol* 2004; 138: 373-380.
2. ONAL S *et al*.: Long-term efficacy and safety of low-dose and dose-escalating interferon alfa-2a therapy in refractory Behçet uveitis. *Archives of Ophthalmology* 2011; 129: 288-294.
3. KOTTER I *et al*.: Treatment of ocular symptoms of Behçet's disease with interferon alpha 2a: a pilot study. *Br J Ophthalmol* 1998; 82: 488-494.
4. HASANREISOGLU M *et al*.: Interferon Alpha-2a Therapy in Patients with Refractory Behçet Uveitis. *Ocular Immunology and Inflammation* 2017; 25: 71-75.

P060

How long should we treat Neuro-Behçet's disease?

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Introduction. Neuro-Behçet's disease (NBD) is considered as one of the most serious organ involvement of Behçet's disease because of its long-term permanent disability. Immunosuppressives and immunomodulators are used in the treatment, but the duration of the prophylactic treatment is still not clear.
Aims. In this study, we tried to determine the optimum duration of the treatment by using the rate of relapsing patients over time.
Methods. We included all patients with NBD who were followed at our institution since 1973. The clinical course of patients with parenchymal involvement and cerebral venous sinus thrombosis were further analyzed using their data such as clinical and laboratory features, clinical course, re-

lapses, and the effect of treatment. The ratio of relapsing patients over time were estimated using Kaplan-Meier survival analysis.
Results. The clinical data of 430 patients (291 male, 139 female) were collected. Mean follow-up was 5.2±6.5 years. The patients were divided into three subcategories: parenchymal (p-NBD, 285 patients), cerebral sinus venous thrombosis (CSVT, 89 patients) and others (56 patients). Treatments included oral and parenteral steroids, oral and intravenous cyclophosphamide, azathioprine, mycophenolate mofetil and infliximab. Overall, 41.4% of the patients with parenchymal NBD (p-NBD) and 14.0% of patients with cerebral venous sinus thrombosis (CSVT) had at least one relapse. The mean time to the second relapse was 5.4±0.7 years in the p-NBD group and 13.7±1.3 years in the CSVT group (p<0.001). The annual risk of relapse decreases (ARR) to equal or less than 5% after five years in p-NBD, and two years in CSVT. The ARR continues to decrease to equal or less than 2% after seven years in p-NBD, and eight years in CSVT (Figure 1).

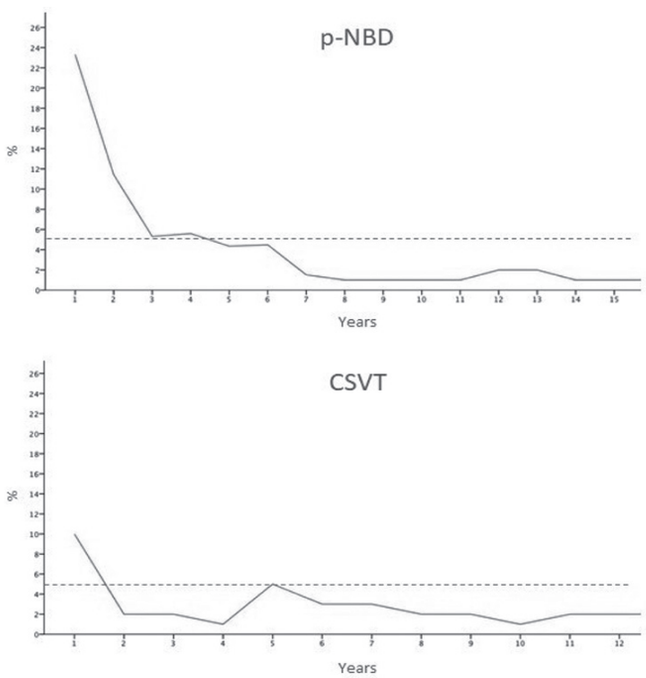

Fig. 1. Annualized risk of relapse of patients with parenchymal Neuro-Behçet's Disease (p-NBD) and cerebral sinus venous thrombosis (CSVT).

Conclusion. In this study, we present clinical features and treatment outcome of a large series of patients with NBD. Case-based decision approach is gold standard in the management of chronic diseases. However, our long-term follow-up data show that the risk of relapse is very low after seven years. Considering the cumulative increased risk of side effects and malignancy of immunosuppressive treatments, it is substantial to discontinue the prophylactic treatments after seven years in patients with NBD.

P061

Esophageal involvement of Behçet's disease responds to low dose of prednisolone: A single center experience

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Introduction. Gastrointestinal involvement of Behcet's disease (BD) increases mortality and morbidity, and moderate to high dose corticosteroid and/or immunosuppressant treatment is mandatory. Frequency of esophageal involvement in BD is very low compared to that of small bowel, and guildlines for the treatment of esophageal BD have not been established.
Aims. This study aimed to evaluate the optimal dosage of steroid for treatment of BD with esophageal involvement.
Methods. Retrospectively reviewed 755 consecutive patients with BD by International Study Group for BD in our institution from March 2014 to April 2018.
Results. Of the 755 BD patients, 118 underwent esophagogastroduodenoscopy (EGD) and/or colonoscopy due to gastrointestinal symptoms. Mean age was 41.2, female was 83 (70%). Forty-four out of 755 (5.8%) patients had gastrointestinal involvement: 39 terminal ileum, and 5 esophagus. None of them have both esophageal and ileal ulcers. In all patients with esophageal BD, immunohistochemical stains for HSV and CMV in biopsied tissue were performed. In all 5 patients with esophageal BD, prednisolone of 10 to 15 mg (median dosage: 0.28 mg/kg) per day was administered for one week, and tapered by 5 mg every week and stopped. All had complete clinical improvement and did not have recurrence during and after prednisolone tapering. Eight weeks off prednisolone, EGD was performed in 5 patients with esophageal BD and showed complete healing of esophageal ulcers. No adverse effects including peptic ulcer disease were found in 5 patients.

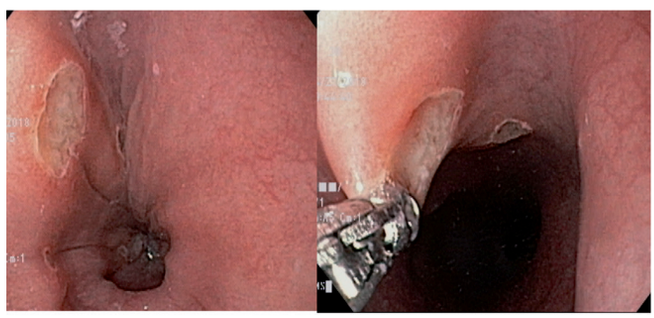

Fig. 1.

Conclusion. Esophageal BD without other gastrointestinal involvement responded to low dose prednisolone for a short period.

P062

Impact of thinning of retinal nerve fiber layer during Behçet's disease

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Introduction. Behçet's disease (BD) is a multisystemic vasculitis affecting all types of vessels. One of the most serious involvements during this disease is ocular involvement. Retinal injuries are very serious and can lead to blindness. Spectral domain-Optical Coherence Tomography (SD-OCT) is a tool which allows to study retina in detail. It is used in some ophtalmological diseases (e.g. glaucoma) and a few systemic diseases like multiple sclerosis in order to detect asymptomatic retinal complications. One of these complications is thinning of Retinal Nerve Fiber Layer (RNFL).
Aims. To study correlations between clinical presentation of BD and thinning of RNFL.
Methods. Twenty-five patients with BD (ICBD criteria) and seen in the department of Internal Medicine of our institution were included in the study. All of them had ophtalmological examination with SD-OCT. Patients were divided into 2 groups : group 1 with thinning of RNFL and group 2 without this abnormality.
Frequencies of ocular and systemic features were analyzed and compared in the two groups using the chi square test for qualitative variables and ANOVA test for quantitative variables.
Results. Twenty-five patients were enrolled. Their mean age at diagnosis was 40.16 years. The sex-ratio M/F was 1.08. Only 3 patients were in relapse in the moment of the SD-OCT (buccal aphtosis in all case and neurologic relapse in 1 case). Comparison of epidemiological and clinical characteristics between 2 groups is presented in Table I.
Table I. Comparison of frequencies of pevious and current features between 2 groups.
Conclusion. In our study, patients who had thinning RNFL presented significantly more frequently genital aphtosis. No other correlation was found in our study. We were limited by the small number of patients. A larger workforce seems necessary in order to better interpret the diagnostic and prognostic value of thinning of RNFL.

Table I.

Characteristics	Group 1 (n=13)	Group 2 (n=12)	P
Age at diagnosis (years)	41.23	39	0.6
Age at onset (years)	33.69	32.64	0.824
Sex-ratio M/F	1.16	1	0.582
Mean number of relapses	1.77	2.25	0.582
Previous features			
Buccal aphtosis	13	11	0.48
Genital aphtosis	**12**	**3**	**0.001**
Articular involvement	5	4	0.56
Pseudofillicullitis	8	6	0.43
Neurological involvement	1	4	0.136
Venous thrombosis	4	2	0.363
Arterial thrombosis	0	1	0.286
Aneuvrysm	0	0	-
Ocular involvement	4	3	0.55
Features in the moment of SD-OCT			
Buccal aphtosis	2	2	0.6
Genital aphtosis	0	0	-
Articular involvement			
Pseudofillicullitis	0	0	-
Neurological involvement	1	0	0.52
Venous thrombosis	0	0	-
Arterial thrombosis	0	0	-
Aneuvrysm	0	0	-
Ocular involvement	0	0	-

P063

Interferon-alpha for the management of lower extremity deep vein thrombosis in Behçet's syndrome: a case series

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Introduction. Lower extremity deep vein thrombosis (LEDVT) is a disabling complication of Behçet's syndrome (BS). Relapses are frequent and cause permanent disability due to post-thrombotic syndrome (1). The management of LEDVT in BS constitutes mainly of azathioprine (AZA) and corticosteroids (CS) as first-line agents (2). Interferon-α (IFN) has been used with good results in the management of eye involvement of BS. However, data regarding its efficacy for LEDVT has been scarce (3).
Aims. To evaluate the efficacy and safety of IFN for LEDVT in BS.
Methods. All BS pts who had a first episode of acute LEDVT since March 2010 are being prospectively followed with a standard protocol in our dedicated BS center. Acute LEDVT is confirmed by Doppler ultrasonography (DUS) at initial diagnosis and serial DUS assessment is performed. Our standard treatment strategy consists of AZA and CSs in pts with LEDVT. IFN has been used in pts who were refractory or intolerant to this regimen, or who had co-existing eye involvement. Our endpoints for assessing the efficacy of IFN have been recanalization of the index thrombus and prevention of relapses. Recanalization has been assessed in the transverse plane and defined as the ratio of the vein area at maximum compressibility to the non-compressed vein area. Good recanalization was defined as a ratio of at least 50%.
Results. 33 pts with LEDVT (26 M/7 F) were prospectively followed for a mean of 40.7±13.4 mo. IFN was started in 17/33 for mainly vascular involvement. In 2 pts IFN was started at the first episode of LEDVT due to co-existing uveitis. Seven pts were treated with IFN due to LEDVT relapses under AZA. In the remaining 9 pts, the reasons for switching from AZA to IFN were adverse events with AZA (n=2), relapse of superficial thrombophlebitis (n=4), leg ulcers due to severe post-thrombotic syndrome (n=2) and eye involvement (n=1). Among 17 pts treated with IFN (mean 29±20 mo), 3 pts already had good recanalization when starting IFN. In the remaining 14 pts, 13 (93%) had good recanalization under IFN. Two pts (11%) experienced relapses. One of the 2 pts who had a relapse had had poor recanalization despite IFN. In contrast, among the 29 pts treated with AZA with a mean follow-up of 20.2±15.8 mo, only 13 (45%) had good recanalization. 13 (45%) pts experienced relapses under AZA and 9 (69%) of those pts had poor recanalization. Overall we observed 23 LEDVT relapses in 15 pts. Relapse rates were 29%, 37% and 45% at 6, 12 and 24 mo respectively. The only adverse event with IFN causing drug withdrawal was thyroiditis in 1 patient.
Conclusion. Relapse rate for LEDVT in BS is high despite AZA treatment. IFN seems to be a promising agent for preventing LEDVT relapses and achieving good recanalization, an important predictor of relapse. The small number of pts and the lack of a parallel control group are the limitations of this prospective study

References

1. MELIKOGLU M: *Arthritis Rheumatol* 2014.
2. ALIBAZ-ONER F: *Medicine* (Baltimore) 2015.
3. CALGUNERI M: *Ann Rheum Dis* 2003.

P064

Frosted branch angiitis of Behçet's disease

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Introduction. Frosted branch angiitis (FBA) was caused lymphoma or leukemia, viral infections or auto-immune/inflammatory disease in which Behçet's disease (BD) accounted for half. Some mechanism of BD's pathogenesis may correlated pathology of FBA.
Aims. To present our FBA case and to analyses the correlation between BD and FBA with the review of the retreaters for FBA.
Methods. Presenting our FBA case, and comparing between our FBA case and the characteristics of other retreaters.
Results. [Case] A 29-year-old male with recurrent oral aphthous ulcers (OAU) and acneiform eruption (AE) was admitted to previous hospital complained with visual loss, high grade fever and poly-arthritis. Before the 5th days of the admission, diagnosing influenza B with headache and fever over 38 degrees Celsius he was taken laninamivir. After taking the agent, no small erythema punctatum, no drug rash, however, erythema nodosum (EN) on his arms and legs with edematous, bilateral ophthalmalgia were occurred with continuing his fever. Before the 3rd days, visual loss, uveitis and retinal bleeding were indicated by a ophthalmologist in the previous hospital. He was fulfilled Japanese BD criteria with uveitis, OAU, AE and EN, and arthritis. Thus, daily PSL 20 mg per os was started with Tenon capsule steroid injection, so his fever and EN, whose pathological findings was shown neutrophil involvements, were improved, but his iriitis and angiitis were not. On the 10th day, he was transferred our hospital, his laboratory data were shown positive inflammation: CRP 13.6 mg/dL, and frosted branch angiitis (FBA) was recognized. Infection and malignancy screening of serum and vitreous humor were negative, thus steroid pules therapy was performed, following PSL 0.5 mg/kg and cyclosporine were taking. Thereafter, his ocular vision improved as a below: right vision (RV), from finger movement to 20/70; left vision (LV), from finger counting to 20/20. After the three months was passed for his admission, he was discharged our hospital with tapering PSL. According to the ophthalmologist of our university, the FBA with BD like this case was different from the usual ocular angiitis of BD, fern-like fluorescence leakage from retinal capillary vessels. Thus, after a half year passed, macular grid laser photocoagulation and vitrectomy were performed against neovascularization, his ocular manifestations were finally composed: RV, 20/25; LV, 20/20. Around the 1.5-year was passed, he admitted our hospital with sudden onset of diarrhea and high grade fever. Colonoscopy was performed and deep ulcerations were found

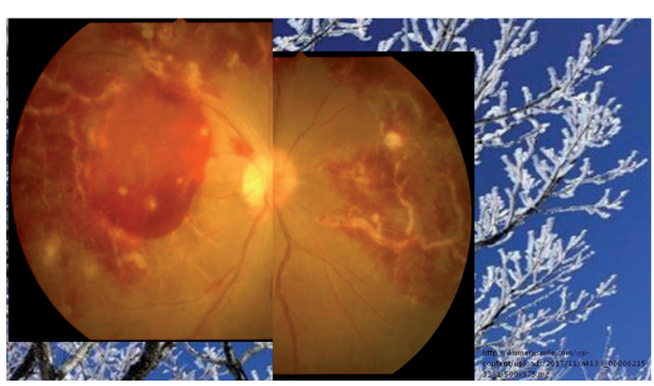

Fig. 1. The typical FBA's venous sheathing of the right eye fundus.

in ileocecum region. We diagnosed intestinal BD by Japanese BD diagnosing criteria with OAU, Skin lesions, arthritis, vascular lesions, and intestinal lesions. Injection of infliximab: anti-tumor necrosis factor alpha, and peros of mesalamine: 5-aminosalicylic acid (5-ASA) and prednisone were started. Now, the 3-year was passed, his symptoms were improved.
Conclusion. We believed that FBA was one of the ocular lesion of BD.
References

1. KWON SJ *et al*.: *Korean J Ophthalmol* 2013.
2. PORTERO A *et al*.: *Case Rep Ophthalmol* 2011.
3. AL-MUJIAINI A *et al*.: *Indian J Ophthalmol* 2011.
3. HANDRAN R *et al*.: *Pediatr* 2011.
3. JACKSON TE *et al*.: *Ocul Immunol Inflamm* 2011.

P065

Intra- and inter-observer reliability of a new uveitis damage score

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Introduction. Reliable assessment tools that would guide us to predict outcome and monitor medical treatment in ocular disease due to Behçet's syndrome (BS) are limited.
Aims. In this preliminary study, we describe a new uveitis damage score, test its intra and inter observer reliability and assess its association with visual acuity levels in a group of BS patients with eye disease.
Methods. Uveitis damage score was graded from 0 to 5 and described in Table. A total of 58 (46 M/12 F) patients with eye disease who were seen consecutively by the dedicated BS outpatient clinic were studied. Color fundus photographies were taken during the slit lamp examination, and the names of the patients' were masked. Visual acuity was measured at the same visit. Each fundus photograph was randomly numbered mixing the right and left eyes by an ophthalmologist (B.B.). Two other ophthalmologists (Y.O. and D. U) evaluated the photographs independently from each other. They repeated the same evaluation within 1 week. The level of agreement between and within observers was calculated using kappa (κ) statistics. The association between damage scores and the visual acuity was assessed with Spearman correlation test.
Results. The mean age of the patients 38.8±10.4 years and the mean disease duration for eye involvement was 13.7±7.9 years. There were 104 eyes (51 R/ 53 L) involved. The anatomical site of involvement was determined as posterior uveitis in 37 (16 R/ 21 L) (34%) and panuveitis in 67 (35 R/ 32 L) (64%). Kappa values calculated for intra-observer agreement were 0.72 and 0.84. Kappa value for inter-observer variability was calculated as 0.69. Additionally, damage scores and visual acuities correlated significantly well with each other for right (r=0.81, p<0.001) and left eyes (r=0.82, p<0.001).

Table. Uveitis damage score: definition of grades.

Grade 0	Vitreus opacity is present but there is no visible retinal structural change.
Grade 1	There is only vascular sheathing on the peripheral retina.
Grade 2	Peripheral vascular sheathing may progress centrally to the optic nerve, there may be pigment alterations in the macula and/or pallor of optic disc. The signs of structural damage are barely visible.
Grade 3	There are widespread perivascular sheathing, macular atrophic pigment alterations, moderate optic disc atrophy and visible choriocapillary changes.
Grade 4	There are total optic atrophy, extensive vaso-occlusive changes, diffuse pigment alterations along with atrophic changes in the choriocapillary level and in the ciliary body.
Grade 5	There is end stage structural damage in both anterior and posterior segments. Often, due to cataract and phytysis bulbi, fundus examination could not be done.

Conclusion. Intra and inter-observer agreement of this new uveitis damage grading was considerably good. Moreover, there was also good correlation between damage scores and the visual acuities.

P066

Outcome of invasive procedures done for venous thromboses due to Behçet's syndrome: A systematic literature review

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Introduction. Vascular involvement can be seen in up to 40% of the patients with Behçet's syndrome (BS) and lower extremity venous thrombosis (LEVT) is the most common manifestation. Immunosuppression (IS) is the mainstay treatment in BS. Its efficacy has been shown to reduce relapses and decrease mortality rate. Vascular interventions are not considered as an optimum management in BS because, they are either unsucesful or too risky because of the pathergy reaction. We have been aware of venous endovascular or surgical interventions in BS patients for some time. While the number of these patients grew, we observed that many had been occluded or complicated with infection.
Aims. In this study, we reviewed the literature specifically for these kind of invasive procedures performed for venous thrombosis in BS and analyzed their outcome.
Methods. Literature search for endovascular interventions in PubMed were performed. Systematic literature search in PubMed included the following keywords: Behcet OR Behcet* OR Adamantiades-Behçet* AND surgery OR surgical OR intervention OR stent OR bypass OR filter OR percutaneous OR angioplasty OR thrombectomy OR thrombolytic OR thrombolysis OR graft AND thrombosis OR thrombus from inception up to July, 2017.
Results. Of the 301 articles found, only 15 articles were suitable for review, consisting of 30 cases. The mean age of the patients was 35.2±10.7 years. Median follow-up period was 24 months (IQR 21). There were in total 13 cases with lower extremity venous intervention, of which 2 were initially unsuccessful. Six of the remaining 11 cases were re-occluded. Re-intervention to 5 of them could restore flow only in 2 cases. Invasive procedures of 8 Budd Chiari syndrome cases resulted with death in one patient and re-occlusion in another. Four of the 9 upper extremity/superior vena cava thrombosis cases resulted with re-occlusion. Anticoagulants were used in 27 (90%), IS were used in 13 (43%) patients. IS therapy was not initiated in 11/21 of patients with known diagnosis of BS.
Conclusion. In this review, initial endovascular or surgical interventions resulted in unfavorable results in 15 (50 %) of 30 BS patients with venous thrombosis. Follow up time was not available in 3 cases and was only one month in 1 case who were described as successful; thus their outcomes can be assumed as ill-defined. Unfavorable results after surgery or catheter puncture can be attributed to pathergy reaction or active vasculitis due to BS. Our study has limitations. This is rather a heterogeneous group of patients with mixed acute and chronic cases. The short follow up time in many of the case reports limit the validity of outcome assessment. Finally, we think that the indication of these vascular procedures is quite controversial. Moreover, these procedures requiring re-operations and re-hospitalizations cause great economic burden to healthcare system.

P067

Efficacy and tolerability of methotrexate therapy for refractory intestinal Behçet's disease: A single center experience

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Introduction. Intestinal Behçet's disease (BD) is often refractory to conventional therapies such as corticosteroids and thiopurines.
Aims. In this study, we assessed the efficacy and tolerability of methotrexate (MTX) in refractory intestinal BD.
Methods. We retrospectively reviewed 10 patients with refractory intestinal BD registered at the Inflammatory Bowel Disease Clinic of Severance Hospital, Seoul, Korea. We evaluated the efficacy and tolerability of MTX at 3 and 6 months.
Results. Of the 10 patients treated with MTX for refractory intestinal BD, four received MTX as a monotherapy and six received MTX with adalimumab. Of them, three patients (30%) at 3 months and four patients (50%) at 6 months responded to MTX, achieving steroid-free remission. Moreover, the serum C-reactive protein level was significantly decreased at 6 months compared with the baseline (p=0.039). The serum erythrocyte

Table. P066

Author, year	Gender, age	Involved veins	Invasive procedure	Followup (months)	Outcome
Thorell, 2015	F, 52	Subclavian, left brachiosephalic(SVCS), LEVT	SVC stent	12	Patent stent
Seinturier, 2014	F, 30	Right femoral, common iliac	Endovascular fibrinolysis, thrombectomy, thrombolysis failure. At 1 year baloon dilatation, stent	30	Asymptomatic
Li, 2014	2 patients* NA	LEVT*	IVC filter	24	Emboli resolution at 3 months, no relapse
Li, 2014	2 patients* NA	IVC hepatic (BCS)	IVC thrombectomy, HV balloon angioplasty	24	Recanalized
Celik,2013	F, 32	SVC, bilateral jugular, brachiocephalic, SVCS	Local thrombolysis	24	Asymptomatic
Geng, 2013	M, 40	Bilateral LEVT, IVC, PAA, left renal	IVC filter, PAA coil	9	No relapse
Jeong, 2013	F, 25	IVC, bilateral iliac	Thrombectomy, balloon angioplasty	1	No relapse
Yu, 2012	M, 36	SVC (No thrombosis), SVCS	SVC balloon angioplasty. At first week: SVC stent due to occlusion. 2 months later, excision and bypass due to stent thrombosis	12	No relapse
Tekbas, 2012	5 M patients* NA	Iliofemoral (also IVC in 2 patients)	PTA and stents in 3 patients, second intervention at first month due to reocclusion; unseccessful in other 2 patients	NA	Reocclusion
Tekbas, 2012	2 M patients* NA	Bilateral subclavian, brachiosephalic, internal jugular, SVC	PTA and stents; second interventions at first week and eight month due to reocclusion	48 and 36	Patent stents
Tekbas, 2012	E, NA	Subclavian	PTA	12	Patent vein
Tekbas, 2012	2 E patients* NA	Hepatic IVC stenosis (BCS), Iliofemoral	IVC stent, iliofemoral PTA	NA	Patent stents
Vandergheynst, 2008	M, 38	SVC (No thrombosis), SVCS	SVC angioplasty	36	Asymptomatic
Han, 2004	M, 45	Hepatic, IVC (BCS)	IVC baloon angioplasty, stent	NA	Patent stents
Kuniyoshi, 2002	M, 24	IVC (BCS)	PTA failure for 3 times, 11 months later: resection, thrombectomy, IVC graft	60	HV IVC reocclusion, resection, HV-right atrium bypass
Kuniyoshi, 2002	F, 58	HV, IVC (BCS)	At 6 months: resection, thrombectomy	5	Ileus, MOF, exitus
Uthman, 2001	M, 27	Right subclavian	Local thrombolysis, balloon angioplasty. At first month: balloon dilatation and stent due to reocclusion	6	No relapse
Radke, 2001	F, 29	Right iliofemoral, IVC, right renal	IVC filter,excised 8 days later due to occlusion	12	Asymptomatic
Sagdıc, 1996	2 patients* NA	İliofemoral	IVC filter in a patient; Palma op, Graft, AV fistula in other	28 and 31	No emboli in a patient; reocclusion at fifth month in other
Sagdıc, 1996	NA	SVC	Right innominate vein- right atrium bypass	24	Collaterals
Bismuth, 1990	M, 21	HV, IVC, BCS, intracardiac thrombus*	Mesoatrial shunt graft	4	Patent graft

sedimentation rate and disease activity index for intestinal BD score tended to decrease; however, there were no statistically significant differences. No severe adverse effects were observed during 6 months, and nausea was reported in two patients.

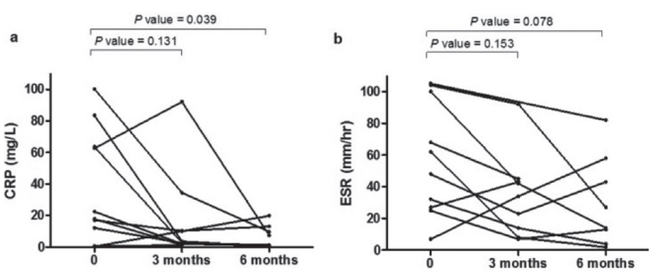

Fig. 1a. Serial changes in C-reactive protein (CRP) level and **b**. erythrocyte sedimentation rate (ESR) at 3 and 6 months.

Conclusion. MTX offers an effective treatment for patients with intestinal BD who are refractory to conventional therapies.

P068

Efficacy of the anti-IL17 Secukinumab in refractory Behçet syndrome: a retrospective chart review from the clinical practice

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Introduction. Behçet's syndrome (BS) is a systemic inflammatory condition characterised by a relapsing-remitting clinical course with different organ involvements (1). Current first-line pharmacological approach is based on corticosteroids and colchicine, with eventual use of Disease-Modifying Anti-Rheumatic Drugs (DMARDs) in refractory patients or as glucocorticoid-sparing agents (2). In case of severe and/or resistant manifestations, biologic agents may be required. To date, anti-tumor necrosis factor (TNF)-α, interferon (IFN)-α and anti-IL-1 drugs represent the mainstay of the biologic approach for BS (3). Although such biologics proved effective, occurrence of treatment failure or safety concerns may require therapeutic alternatives. Considering that inflammatory patterns sustaining BS mucocutaneous and articular manifestations are similar to those of other rheumatic disorders, such as psoriatic arthritis (PsA) and ankylosing spondylitis (AS), off-label use of biologics approved for the treatment of such disorders, such as the anti-IL17 Secukinumab, may represent a valid therapeutic strategy in refractory BS patients.

Aims. This study aimed to evaluate the efficacy of the anti-IL17 Secukinumab on active mucocutaneous and articular manifestations in refractory BS patients.
Methods. We retrospectively evaluated the medical charts of 5 female patients diagnosed with BS according to ISG/ICBD Criteria. All patients had active and disabling mucocutaneous and articular manifestations refractory to previous therapies with colchicine, conventional DMARDs and at least one anti-TNF-α. All patients received the IL17-inhibitor Secukinumab, at the initial regiment of 300 mg/monthly in the subject fulfilling the criteria for PsA, and at 150mg/monthly in the other four subjects with AS. Achievement of responses was assessed based on the number of oral aphthosis, as well as on the BDCAF score for BS activity, and BASDAI and ASDAS scores for the articular involvement. Complete response was defined as: i) decrease of 50% or more in the number of oral aphthosis; ii) BASDAI index <4; iii) ASDAS index <1.4; iv) decrease of 50% or more in the BDCAF index.
Results. The patient starting Secukinumab 300 mg/month successfully achieved complete response (CR) on both mucocutaneous and articular manifestations within 3 months from treatment beginning; specifically, the number of oral aphthosis decreased from 2 to 0/month, BASDAI from 4.55 to 3.05, BDCAF from 7 to 0, and ASDAS from 3.43 to 1.29. CR was stably maintained during all 9-month follow-up. Among the four subjects starting Secukinumab 150 mg/month, two achieved CR at month 6, but in one case relapse occurred in the following trimester. This patient and the other two that had not achieved CR at month 6 were switched to Secukinumab 300 mg/month. Within 3 months from the increase in dosage, all three subjects successfully (re)achieved CR.
Conclusion. To the best of our knowledge, this is the first study evaluating the efficacy of Secukinumab in the treatment of refractory BS. According to our findings, both 150mg and 300mg/month Secukinumab effectively improve BS manifestations in patients refractory to previous anti-TNF-α treatment, although Secukinumab 300 mg monthly resulted superior in inducing CR of both articular and mucocutaneous manifestations.

References

1. EMMI G1, SILVESTRI E, SQUATRITO D, D'ELIOS MM, CIUCCIARELLI L, PRISCO D, EMMI L: Behçet's syndrome pathophysiology and potential therapeutic targets. *Intern Emerg Med* 2014 Apr; 9(3): 257-65.
2. ALEXOUDI I, KAPSIMALI V, VAIOPOULOS A, KANAKIS M, VAIOPOULOS G: Evaluation of current therapeutic strategies in Behçet's disease. *Clin Rheumatol* 2011; 30: 157-163.
3. CASO F, COSTA L, RIGANTE D, LUCHERINI OM, CASO P, BASCHERINI V *et al*.: Biological treatments in Behçet's disease: beyond anti-TNF therapy. *Mediators Inflamm* 2014; 2014: 107421.

P069

Apremilast for Behçet's syndrome: results from a phase III, randomized, double-blind, placebo-controlled study in a Japanese subgroup

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Introduction. Apremilast, an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in a global, phase III, multicenter, randomized, double-blind, placebo-controlled study in patients with Behçet's syndrome and active oral ulcers previously treated with ≥1 medication. A subgroup analysis was performed for Japanese patients in this study.
Aims. To assess the efficacy and safety of apremilast compared with placebo over 12 weeks in the subgroup of Japanese patients with Behçet's syndrome in the study.
Methods. In the global study, 207 patients with Behçet's syndrome were randomized (1:1) to receive apremilast 30 mg twice daily (n=104) or placebo (n=103) for 12 weeks, followed by a 52-week active-treatment extension. Patients were stratified by region (Japan and Other). Patients had active Behçet's syndrome with ≥3 oral ulcers at randomization or ≥2 oral ulcers at screening and randomization without major organ involvement. The primary endpoint was the area under the curve (AUC) for the total number of oral ulcers over 12 weeks. Additional endpoints included the assessments of oral ulcers, including pain, overall disease activity (Behçet's Syndrome Activity Score [BSAS] and Behçet's Disease Current Activity Index [BDCAI]), and quality of life (QoL) at Week 12. The primary and secondary variables in the Japanese subset analysis were prespecified without adjustment for multiplicity. Nominal *P* values are presented.
Results. A total of 39 patients were included in the Japanese subgroup (placebo: n=20; apremilast: n=19). The subgroup analysis showed the AUC for oral ulcers was significantly lower in the apremilast group compared with placebo (115.9±40.4 vs. 253.3±38.5; p=0.0168), which is consistent with the findings of the overall study population (129.5±15.9 vs. 222.1±15.9; p<0.0001). Similarly, as observed in the overall population, significantly greater improvements were also shown in BSAS (p=0.0316), time to oral ulcer resolution (p=0.0081), complete response rate (p=0.0426), and maintenance of complete response of oral ulcers (p=0.0006) at Week 12 in the apremilast group. Numerical improvements were observed in oral ulcer pain, BDCAI, and QoL in the apremilast group; unlike the overall population, significance was not achieved, likely due to the limitation of the small sample size. Treatment-emergent adverse events (AEs) were comparable between the apremilast (73.7%) and placebo (75.0%) treatment groups. One serious AE (migraine) was reported with apremilast treatment. There were no AEs leading to discontinuation.
Conclusion. The Japanese subgroup analysis showed that apremilast reduced the number of oral ulcers and overall disease activity and had favorable effects on oral ulcer pain and QoL in patients with Behçet's syndrome and active oral ulcers over 12 weeks. The safety profile was consistent with the known safety profile of apremilast, and results were consistent with findings in the overall study population.

Poster Session 2

P070

Temporal trends in clinical manifestations of Behçet disease: comparative study between 1995 and 2017

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Introduction.
Behçet's Disease (BD) is a chronic systemic disease characterized by recurrent oral and genital ulcers and ocular inflammation. Recent evidence suggests that epidemiological and clinical expression of BD are changing over time
Aims. We aimed to study clinical manifestations of BD during the past 2 decades in the Tunisian context.
Methods. We retrospectively reviewed the medical records of BD patients diagnosed according to the International Study Group for Behçet Disease criteria admitted in the Internal Medicine or the Ophthalmology Department of Fattouma Bourguiba University Hospital (Monastir, Tunisia) between January 1995 and December 2017. A comparative study of clinical and epidemiological characteristics of the patients was performed between 1995-2005 (group 1) and 2006- 2017 (group 2).
Results. Of 225 patients with BD, 152 were male (67.6%) and 73 (32.4%) were female (sex ratio 2.08). The mean age at diagnosis was 32.6 years (range, 12-70 years). Familial history of BD was recorded in 12.9% of patients. Oral aphthosis was detected in 98.7% of patients at presentation, genital ulcers in 74.2%, pseudofolliculitis in 79.1% and erythema nodosum in 10.7%. Ocular involvement was found in 38.2% of the cases, articular manifestations in 43.1%, neurological and vascular involvement were found in 9.8% and 24.4% of patients, respectively.
Comparative study between group 1 (n=127) (56.4%) and group 2 (n=98) (43.6%) showed a significant increase of sex ratio (M/F) from 1.59 to 3 (p=0.025), a significant decrease in articular involvement (49.6% vs 35.1%, p=0.029) and a slight increase in ophthalmic involvement (33.1% vs 45.4%) without reaching significant difference (p=0.061).
Conclusion. According to our data, it seems that BD tends to affect less females with a decrease in the rate of articular involvement and a slight increase in ocular inflammation. Whether this reflects a real change in the epidemiology of BD or an awareness of the severity of ocular involvement leading to a best screening remains to be clarified by prospective studies.

P071

Sexual dysfunction in Behçet disease

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Introduction. Sexual dysfunction (SD) is common in chronic diseases, but little is known about the sexual dysfunction and mental health status in Behcet's disease (BD).
Aims. The aim of this study was to investigate the sexual dysfunction and mental health status in patients with BD.
Methods. A total of 51 BD patients and 50 healthy age and sex matched controls were included in this study. The sexual function and the mental health status of the patient and control groups were assessed using the Female Sexual Function Index (FSFI), international index of erectile function (IIEF) and SCL-90-R questionnaire. FSFI is used for evaluation of sexual function in women and has 6 domains: desire, arousal, lubrication, orgasm, satisfaction and pain. FSFI total SCL-90-R evaluate psychologic disorders and has 10 domains: somatic, obsessiveness, sensitivity in relationship, depression, anxiety, aggressiveness, phobia, paranoid, psychotic, additional questions.
Results. The mean total FSFI score for female patients and controls were 17.2±9.3 and 26.6±4.1, respectively (p=0.003). Dysfunction in all of the 6 domains of FSFI in the BD group was significantly more common than control groups. The mean total IIEF score for male patients and controls were 51.1±10.9 and 51.8±14.3, respectively (NS). There was no significant difference in the mean global intensity index (GSI) between the control and BD groups. Of the ten domains of SCL-90-R questionnaire only aggressiveness behavior in the BD group was significantly more common than control groups.
Conclusion. SD in males with BD is not more common than healthy controls. However, SD is more common in females with BD than in the controls.

P072

An unmet need for oral ulcer activity in patients with Behçet's disease: a multi-national study

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Introduction. Efficacy of current management approaches for oral ulcer treatment in routine clinical practice is insufficiently explored in Behçet's disease (BD) patients.
Aims. The aim of this multi-national study was to assess whether an unmet need for oral ulcer activity is present in patients with Behçet's disease.
Methods. Behçet's disease (n=197) patients from Jordan (n=50), Brazil (n=46), United Kingdom (n=41) and Turkey (60)(F/M: 100/97, mean age: 40,7±11,6 years) were included in this cross-sectional study. Data were collected by a questionnaire regarding oral ulcer activity during the previous month, treatment protocols and smoking patterns. Transformed BDCAF score was used to evaluate the general disease activity during the last month.
Results. In the whole BD group, 41,1% (n=81) of patients were treated with non-immunosuppresive medications (non-IS) and 53,3% (n=105) by ISs, irregular medication use/no medication was observed in 5,6% (n=11). The number and healing time of oral ulcers were 3,3±3,2 and 6,5±4,6 days, respectively in patients with active oral ulcers (n=114, 57,9%). The number of oral ulcers were significantly higher in patients treated with non-IS medications (4,04±3,9) and non-smoker patients (3,6±3,4) than those treated with ISs (2,5±2,1) and current smokers (2,3±2,1)(p<0.0001 and p=0.021, respectively). In binary logistic regression, non-IS medication use was found to be a predictive factor for oral ulcer activity (OR:2,3; p=0.011). Transformed BDCAF score was also lower in patients treated with ISs (4,02±3.5) than those using a non-IS treatment protocol (6,6±3,1)(p=0.009).
Conclusion. Since oral ulcer activity and global activity assessed by BDCAF were higher in patients treated with non-IS medications, an 'unmet need' was observed with milder, non-IS-based treatment protocols in a multi-national setting of clinical practice in BD patients.

P073

Assessment of severity and risk factors of post-thrombotic syndrome in vascular Behçet disease: muticentered retrospective study

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Introduction. Vascular involvement is seen in about one third of patients with Behçet Disease (BD). DVT (deep venous thrombosis) is the most common form of vascular Behçet Disease(VBD). Post-thrombotic syndrome (PTS) developing after a thrombotic event in lower extremity, is one of the major complications of DVT, and affects negatively patients' quality of life.
Aims. In this study, we aimed to assess the presence, severity and risk factors of PTS and venous disease spesific quality of life in VBD.
Methods. This study included 96 patients with BD (Female/Male:18/78, mean age: 38.8±8.74 years) having history of DVT from 3 tertiary Rheumatology centers in Turkey. Villalta scale was used to assess PTS. According to Villalta scale; PTS is present if score >4 and degree of PTS

mild, moderate and severe if score 5-9, 10-14, >14 respectively. The Venous Disability Score(VDS) and the Venous Clinical Severity Score(VCSS) were used for the assessment of venous disease. Venous disease-specific QoL was measured through Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom (VEINES-QoL/Sym) questionnaire. The Behçet Syndrome Activity Score (BSAS) questionnaire was used to assess disease activity. All patients were assessed with color Doppler ultrasonography(US) by experienced radiologists within 1 weeks following the clinical examination. In each patient, a total of 16 superficial and deep veins in both legs were assessed for the presence or absence of obstruction, recanalization, reflux, and collaterals.

Results. When vascular involvement developed, mean age was 32.7±8.65. Venous assessment was done after 6(0-26) years first vascular event. During venous assessment, median disease duration was 9 (0-34)years. Eighty (84.2%) patients were under ımmunsupressive (IS) treatment and 13 of these patients were under anticoagulation treatment in addition to ISs. Median IS time 37.5 (1-256); anticoagulation time 12(1-156) months. PTS was present in 57 (61.3%) out of 93 patients and severe PTS was present in 19 (19.8%) patients.There was no association between presence of PTS and sex, age during DVT and presence of relaps. There was no difference between patients with or without anticoagulant usage regarding PTS presence (p=0.817). Doppler US examination shows no abnormalities at 10 (10.6%) patients, 5 (50%) of these patients had PTS. Bilateral leg vessel involvement was present in 31(31.4%)patients. Fourty (47.6%) patients had both upper and lower leg vessel involvement. But we didn't find any associaton with PTS presence and doppler US findings such as bilateral involvement, upper and lower leg vessel involvement, reflux or trombosis at any vessel in the affected leg.When VBD patients with and without PTS were compared, VEINES-QoL/Sym, and VCSS were significantly worse. BSAS was also significantly higher in patients with PTS (Table I).

Table I. Clinical and venous assessment characteristics of patients with vascular Behçet disease.

		Post-thrombotic Syndrome		P Value
		No	Yes	
BSAS score (n:93)		10 (0-47)	20 (1-69)	.002
Standing time (hours)		8.09±3.9	8.24±3.97	.856
VCSS score (n:85)		2.27±1.64	6.54±4.09	.000
VDS	0	18 (50%)	11(19.3%)	.003
	1	15(41.7%)	34(59.6%)	
	2	3 (8.3%)	12(21.1%)	
Veines QoL total score (n:93)		97.19±17.8	77.75±17.3	.000
Veines symptom score		44.3±9.9	35.2±9.1	.000
CEAP		1.53±1.34	2.94±1.83	.000
DVT	1	24(40%)	36(60%)	.888
	2 and over	12 (36.7%)	21 (63.3%)	
Treatment	IS	13 (39.4%)	20 (60.6%)	.817
	IS+AC	17 (36.2%)	30 (63.8%)	
Treatment duration (months)	IS	39(1-200)	36 (3-256)	.600
	AK	12(1-60)	12 (1-156)	.772
Duration of trombosis (years)	<5	15 (40.5%)	22 (59.5%)	.872
	>5	20 (36.4%)	35 (63.6%)	
Compression stocking treatment	No	18 (42.5%)	24 (57.5)	.357
	Yes	12 (24.5%)	27(75.5)	

Conclusion. We found that PTS develops in more than half of the patients with VBD during follow-up. We didn't find any predictor factor for development of PTS. About one third of patient with PTS were severe PTS. Venous disease spesific quality of life is worse in VBD with PTS compared to patients without PTS. Our results confirm that PTS is very frequent clinical problem for physicians treating VBD in daily practice. During management of patients with VBD, PTS should be taken into account as much as preventing vascular relapses.

P074

Enhanced TLR-5 expression in pathergy-positive Behçet's disease patients indicates the importance of an innate-driven immune response

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Introduction. Behçet's disease (BD) is an auto-inflammatory vasculitis predominantly affecting the orogenital mucosa, skin and eyes.
It is characterized by a pathergic reaction, which is an excellent example of innate driven inflammatory reaction in BD. A skin prick test shows an exaggerated immune response to tissue damage, pointing towards a possible role for pathogen- or damage-associated molecular pattern recognition receptors, like toll like receptors (TLR).
Aims. Our aim of this study is to investigate TLR expression and function in Behçet's disease patients.
Methods. To investigate whether the auto-inflammatory nature and the pathergic reaction in BD are driven by a disturbed TLR-response we compared both TLR-expression by flow-cytometry and TLR-response by stimulation assay in 18 BD patients (both pathergy positive and negative) and 13 healthy controls.
Results. We show significant elevated expression of TLR 1, 2 in B-lymphocytes of patients compared to healthy controls. TLR 1, 2 and 4 are significantly higher expressed in both CD4 and CD8 positive T-lymphocytes of BD patients. Granulocytes of BD patients show significant higher expression of TLR 1, 2, 4 and 6. TLR 2 and 4 expression is significantly increased on monocytes of BD patients.
In pathergy positive patients, TLR 5 is significantly higher expressed compared to pathergy negative patients on B- and T-lymphocytes, granulocytes and monocytes.
Furthermore, TLR-2 and TLR-5 show an elevated response to stimulation with their cognate ligands.
Conclusion. Cells of patient with BD overexpress TLR-1, 2, 4, 5 and 6 in patients with BD, with an elevated TLR-response to stimulation of TLR-2 and TLR-5. Strikingly, in pathergy-positive patients, TLR-5 expression is even further augmented, possible pointing towards a microbial (flaggelin) driven pathogenesis of the pathergy phenomenon.
We believe our results indicate an exaggerated TLR-response drives the auto-inflammatory nature of BD.

P075

Influence of smoking on the manifestations at the onset and course of Behçet disease

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Introduction. Behçet disease (BD) is a multifactorial systemic inflammatory disorder. Recurrent oral aphthous ulcers (ROU) are the commonest manifestation of BD at the disease onset and course. However, 14-20% of the patients may not develop ROU at onset, and previous observations suggested that smoking may decrease the frequency of ROU in patients with BD.
Aims. This study aimed to investigate the role of smoking on ROU and other manifestations of BD at the onset and during the course of BD.
Methods. Study group consisted of 399 patients with follow-up records between 2010-2016 and who fulfilled the International Study Group (ISG) diagnostic criteria and provided reliable information about smoking. All patients were interviewed by MA about the smoking status and disease manifestations, and collected data were recorded using a standard form.
Results. Smokers were more frequent among males at the disease onset compared to females (52.5% vs 26.4%, p<0.001). Non-aphthous beginning (NAB) at the disease onset was more frequent among smokers compared to non-smokers (18.4% vs 6.8% in males, p=0.019; 22.9% vs 9.7% in females, p=0.038). Genital ulcer (GU) as initial finding was more frequent among smokers compared to non-smokers (32.5% vs 7.8% in males, p<0.001; 35.4% vs 17.9% in females, p=0.022). After the appearance of their first manifestation, both male and female smokers fulfilled the ISG criteria ear-

lier than non-smokers (median 36 vs 71 months in males, $p<0.001$; median 43 vs 74 months in females, $p=0.001$). Frequency of uveitis was higher in patients among smokers compared to non-smokers (47.4% vs 32% in males, $p=0.021$; 41.7% vs 22.4% in females, $p=0.017$). The first papulopustular lesion (PPL) developed earlier in smoker males than nonsmoker males (median 27 vs 53.5 months, $p=0.006$). Similarly, first PPL, erythema nodosum-like lesion, arthritis and deep-vein thrombosis develop earlier in smoker female patients compared to non-smoker females (median 36 vs 84 months, $p=0.025$; median 14.5 vs 60 months, $p=0.033$; median 41.5 vs 119 months, $p=0.018$; mean 31.7 vs 164.1 months, $p=0.042$, respectively). Smoking was identified as an independent risk factor for the development of GU (OR=1.7) and uveitis (OR=1.95) by logistic regression, but the overall risk of PPL was found to be decreased in smokers (OR=0.54).
Conclusion. This retrospective study revealed that smoking may contribute to the increased frequency of NAB in BD, and smoker patients may have differences in their disease course with a higher risk of GU and uveitis. These findings suggest that smoking may affect not only ROU but also other manifestations of BD with potentially higher impact on the disease morbidity.

P076

Clinical characteristics of neuro-Behçet's disease in South Korea

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Introduction. Neuro-Behçet's disease (NBD) is a serious form of Behçet's disease (BD) which is known to occur in 1.3–14.3% of the patients with BD (1). NBD can cause substantial disability and one third of the patients with NBD are known to fall into a progressive disease course (2, 3). Despite its clinical importance, it is difficult to comprehensively understand the clinical feature of NBD as the prevalence of NBD and its clinical manifestations show significant regional variations (4). In addition, until recently, there have been no well-established diagnostic criteria of NBD.
Aims. We intended to analyze the clinical and radiological characteristics of NBD patients in South Korea by utilizing recently suggested diagnostic criteria of NBD (5).
Methods. We retrospectively reviewed the medical records of patients between January 2000 and December 2017 at Severance Hospital, Seoul, South Korea. The patients who had the diagnosis code of BD were found by searching the electronic hospital database. Of these patients, we included the patients who were classified into definite or probable NBD based on the recently suggested international consensus recommendations (ICR) (5). The diagnosis of BD was based on the International Study Group criteria for the diagnosis of BD. We analyzed the clinical and radiological features of these patients.
Results. During the study period, 9817 patients who had at least one diagnosis code of BD were found. Of these patients, 1682 patients visited the neurology department. The frequent reason for visit to the neurology clinic included headache (45.4%), pain (12.5%), and dizziness (11.0%) or for the evaluation and management of cerebrovascular disease (9.9%) or peripheral neuropathy (8.7%). Among the patients who visited the neurology clinic, 93 patients met the ICR diagnostic criteria of NBD: 8 (8.6%) patients had non-parenchymal NBD (3 with cerebral venous thrombosis and 5 with acute meningeal syndrome) and 85 (91.4%) patients had parenchymal NBD. We further analyzed the clinical and radiological characteristics of 85 parenchymal NBD patients (Table). These patients consisted of 49 (57.6%) males and 36 (42.4%) females. Mean age at the onset of BD and NBD was 28.5±10.1 and 38.8±10.6 years, respectively. In terms of neurological syndrome, brainstem syndrome (43.5%) was most common, followed by multifocal (31.8%), spinal cord (11.8%), cerebral (9.4%), and optic neuropathy (3.5%). Thirty nine (45.9%) patients showed monophasic, 22 (25.9%) showed polyphasic, 13 (15.3%) showed primary progressive, and 11 (12.9%) showed secondary progressive course. Frequent symptoms of the patients included motor weakness (51.8%), dysarthria (44.7%), headache (44.7%), fever (30.6%) and sensory symptoms (27.1%). Frequent site of MRI lesions included brainstem (65.9%), white matter (44.7%) and basal ganglia (42.4%). In patients with spinal cord lesion, most of the lesions were located in cervical and/or thoracic cord. Contrast enhancement was observed in 50.6% and brainstem atrophy was observed in 32.9% of the patients.
Conclusion. The present study demonstrates the clinical and MRI characteristics of NBD patients in South Korea based on recently suggested diagnostic criteria. This study is based on the largest number of NBD patients in South Korea and the findings well correspond to the previous reports.

Table. Baseline characteristics of 85 NBD patients.

Characteristics	Clinical values
Age at onset of BD, years	28.5 ± 10.1
Age at onset of NBD, years	38.8 ± 10.6
Sex, male	49 (57.6)
Characteristics of BD	
Oral ulceration	82 (96.5)
Genital ulceration	56 (65.9)
Ocular manifestation	48 (56.5)
Skin lesions	65 (76.5)
Positive pathergy test*	4 (15.4)
HLA-B51 positive†	17 (73.9)
Neurological syndrome	
Multifocal/diffuse	27 (31.8)
Brainstem	37 (43.5)
Spinal cord	10 (11.8)
Cerebral	8 (9.4)
Optic neuropathy	3 (3.5)
Clinical course	
Monophasic	39 (45.9)
Polyphasic	22 (25.9)
Primary progressive	13 (15.3)
Secondary progressive	11 (12.9)

* Pathergy test was conducted in 26 patients.
† HLA-B51 test was conducted in 23 patients.
Values are expressed as number of subjects (%) or mean ± SD

P077

Can bosentan (Tracleer®) act as an immunomodulating agent in patients with Behçet's disease? A pilot study.

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Introduction. Behçet's disease (BD) is a vasculitis characterized by aphthous oro-genital ulcers, inflammatory skin changes and uveitis. Although treatment is mainly immunosuppressive, elevated endotheline-1 (ET-1) levels suggest a possible beneficial effect of treatment with an ET-1 receptor antagonist bosentan.
Aims. The aim of our study was to investigate the possible beneficial effects and safety of ET-1 inhibitor Bosentan in patients with Behcet's disease
Methods. To investigate the possible beneficial effect of the ET-1 inhibitor bosentan we performed a prospective double-blind placebo controlled pilot study into the effect and safety of bosentan on the disease activity in BD patients. Disease activity was measured using the Behçet Disease Current Activity Form. The primary objective of the study was to determine if bosentan is an effective treatment in patients with BD, secondary endpoints were safety, tapering of medication and the effect of bosentan on possible disease activity markers as ET-1, circulating endothelial cells (CEC), soluble interleukin-2 receptor (sIL2R) and cytokine levels.
Results. Ten patients were randomized to either bosentan or placebo. Overall no effect on disease activity was observed, although one patient responded clinically and continued treatment after study period. Except one SAE, bosentan seems safe to use. No effect on tapering of medication, CEC's, sIL2R and cytokine levels was found. In the bosentan group ET-1 levels were elevated during treatment period, without correlation with disease activity.
Conclusion. In conclusion, bosentan appears safe in BD patients, with possibly a positive effect on disease activity. We show one responding patient of five treated. Our observations should be confirmed and extended in a larger patient cohort to be of significant impact in the treatment options for BD.

P078

Assessing the sensitivity of ISG and PEDBD criteria in a UK cohort of children and young people with Behçet's disease

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Introduction. There are currently very little data on the incidence and prevalence of Behçet's disease (BD) amongst children and in particular within the UK and Republic of Ireland (ROI), or regarding the performance of the different disease classification/diagnostic criteria in paediatric cohorts.
Aims. This study was undertaken primarily to establish the UK and ROI incidence and prevalence of BD in children under 16 years of age (analysis in progress). Secondary aims were to define the clinical features and compare the different criteria used in the diagnosis of Behçet's: International Criteria for Behçet's Disease (ICBD), International Study Group (ISG) and Pediatric Criteria for Behçet's Disease (PEDBD) (1, 2, 3). These secondary aims are presented here.
Methods. A surveillance study of the UK and ROI was undertaken with the British Paediatric Surveillance Unit (BPSU) and the British Society of Paediatric Dermatologists (BSPD) between 2015-2017. The BPSU's system for the study of rare conditions is well established having been developed since 1986, to survey over 90 rare paediatric conditions. A monthly email was also sent to the BSPD, so that their members could notify any cases. All clinicians that notified a case were sent a questionnaire by the study team. Cases were defined as definite if they scored ≥4 on ICBD criteria. We calculated the sensitivity (with exact Clopper-Pearson confidence intervals) of ISG and PEDBD criteria compared to the ICBD (gold standard).
Results. Of 149 notifications received, following removal of errors, duplicates and cases which could not be followed up: 56/80 (70%) cases fulfilled the ICBD criteria. Of these 30/56 (54%) were prevalent, and 26/56 (46%) were incident cases. 32 (57%) were female and 24 (43%) male, with median age at onset 6 years (n=53), and median age at diagnosis 11 years (n=51). 48/53 (86%) of cases were White British and 8/53 (14%) non-White.

Table I. Showing comparison of clinical features in cases meeting ICBD, ISG or PEDB criteria.

	ICBD confirmed cases (N=56)		ISG confirmed cases (N=31)		PEDBD confirmed cases (N=29)	
Clinical features	**N**	**%**	**N**	**%**	**N**	**%**
Oral ulceration	56	100	31	100	29	100
Genital or perianal ulceration	52	93	27	87	26	90
Skin involvement:	28	50	24	77	23	79
Pseudofolliculitis	13	23	13	42	13	45
Erythema nodosum	10	18	10	32	10	34
Skin ulcers	6	11	6	19	5	17
Eye involvement:	14	25	12	39	12	41
Anterior Uveitis	8	14	8	26	8	28
Intermediate Uveitis	2	4	2	6	2	7
Panuveitis	1	2	1	3	1	3
Posterior Uveitis	0	0	0	0	0	0
Retinal Vasculitis	1	2	1	3	1	3
Visual loss	1	2	1	3	1	3
Neurological involvement:	7	13	5	16	6	21
Headaches	4	7	4	13	4	14
Central Venous Thrombosis	1	2	0	0	1	3
Sensorineural deafness	1	2	0	0	0	0
Aseptic Meningitis	0	0	0	0	0	0
Parenchymal Involvement	0	0	0	0	0	0
Other involvement:	22	39	11	35	9	31
Arthritis	8	14	6	19	6	21
Arthralgia	8	14	5	16	4	14
Abdominal Pain	7	13	4	13	3	10
Diarrhoea	2	4	1	3	1	3
Fatigue	2	4	2	6	2	7
Fevers	1	2	0	0	0	0

Table I shows clinical features in cases confirmed by each criteria. The sensitivity of ISG was 55.4% (95% confidence interval (CI) 41.5-68.7%) and 51.8% (95% CI 38.0-65.3%) for PEDBD.
All patients had oral ulceration, with genital ulceration being the next most common manifestation. Skin involvement occurred in 50-79% depending on criteria used. Eye involvement was seen in 25% of those confirmed using ICBD criteria with only one case of visual loss. Neurological/vascular involvement was only reported in one patient with central venous thrombosis.
Conclusion. BD in those under 16 years of age is extremely rare in the UK and ROI, and the majority are of White-British ethnicity. The commonest BD sub-type was the mucocutaneous variant with significant eye disease occurring less commonly than in other pediatric cohorts. In this cohort, ISG criteria appeared to have similar sensitivity to PEDBD criteria.

References

1. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. *J Eur Acad Derm Ven* 2014.
2. Criteria for diagnosis of Behçet's disease: International Study Group for Behçet's Disease. *Lancet* 1990.
3. Koné-Paut I, Shahram F *et al*.: Consensus classification criteria for paediatric Behçet's disease from a prospective observational cohort: PEDBD. *Ann Rheum Dis* 2015.

P079

Hypercoagulability as a cause of thrombosis in Behçet's syndrome: a systematic review and meta analysis

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Introduction. While thrombosis in Behçet's Syndrome (BS) is considered to be mainly caused by inflammation in the vessel wall, several prothrombotic factors have been studied with inconsistent results.
Aims. We aimed to perform a systematic review of clinical studies investigating the thrombophilic factors in BS.
Methods. The online database of PubMed was searched with the keyword "Behçet*" in four languages (English, German, French and Turkish) from inception up to May 2018. Titles and/or abstracts of all studies were screened independently by two reviewers (GG and BY) for studies reporting on thrombosis, fibrinolysis, endothelial factors and comparing BS patients with and without thrombosis. Conflicts were solved by a third reviewer (GH). The pooled odds ratios (0R) with 95% CI were calculated for binary outcomes and standardized mean differences (MD) were calculated for continuous outcomes by using RevMan 5.3.

Table I. Meta-analysis of studies with controversial results.

Prothrombotic Factor	Number of studies	Number of Behçet's patients		MD/OR (95% CI)
		With thrombosis	Without thrombosis	
Homocysteine	12	303	501	MD: 0.8 µmol/L (0.45-1.15)
Factor V Leiden mutation	7	185	361	OR: 2.33 (1.36-4.01)
von Willebrand factor level	3	54	148	MD: 0.44 IU/dL, (0.12-0.76)
tPA	4	90	174	MD: 0.06 ng/mL (-0.20-0.32)
Prothrombin gene mutation,	5	146	263	OR: 1.42 (0.47-4.26)
FVIII level	2	45	101	MD: -0.02 IU/dL (0.92-0.88)
Activated Protein C resistance	4	95	139	OR: 2.43 (0.91-6.50)

MD: mean difference, OR: odds ratio, tPA: tissue plasminogen activator

Results. Of 9664 articles, 9085 were excluded due to repetition and inappropriate study design after reviewing titles and abstracts. Full text review of the remaining 579 articles yielded 51 papers meeting our predetermined inclusion criteria.
A list of factors such as protein C, protein S, anti-thrombin III, plasminogen, plasminogen activator inhibitor, fibrinogen, thrombomodulin, factor 7, factor 12, thrombin activatable fibrinolysis inhibitor, lupus anticoagulants,

anticardiolipin antibodies, antiß2 Glycoprotein1 antibodies and methylenetetrahydrofolate reductase gene C677T mutation were not different in BS patients with thrombosis compared to those without thrombosis. On the other hand, angiopoietin-1 levels, P-selectin glycoprotein ligand-1, lipoprotein (a), platelet-activating factor seemed to be more frequent in BS patients with thrombosis in the few studies reporting on these, including a small number of patients.
Among the 7 parameters with controversial results across studies, meta-analysis showed significantly higher homocysteine levels, more Factor V Leiden mutation and higher von Willebrand factor levels in BS patients with thrombosis, whereas the pooled difference was not significant for tissue plasminogen factor, prothrombin gene mutations, factor VIII levels and activated protein C resistance (Table).
Conclusion. Among the several prothrombotic factors that were studied in BS patients, factor V Leiden mutations, high homocysteine levels and high von Willebrand factor levels may be associated with thrombosis in BS. Studies investigating all of these factors together in a large number of patients together with appropriate controls are needed to confirm these results.

P080

Canakinumab for Behçet's Disease Resistant to Standard Treatment (CanBeDisT) - an open-label single center pilot study

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Introduction. As Behçet's disease is suspected to be autoinflammatory rather than autoimmune, we initiated a pilot study with canakinumab, an IL-1 antibody which is approved for CAPS, JIA, AOSD and gout in Germany. The dosages were chosen according to those being effective in CAPS. Except interferon, TNF antagonists, other biologicals or cyclophosphamide all standard background treatments were permitted.
Aims. To evaluate the efficacy of canakinumab in treatment resistant BD.
Methods. Ten patients with treatment resistant BD, 6 males and 4 females, mean age 38 years, were included. Previous treatments before study entry were prednisolone and colchcine in all, azathioprine and methotrexate in 7, cyclosporine A in 4 and interferon alpha in 3.
Canakinumab dosage was 150 mg s.c. in case of remission at week 3, 150 mg were to be repeated after 8 weeks. In case of major response (improvement of the scores by 50% or more), the 150 mg s.c. injection was repeated at week 3 (visit 3) already.
In case of relapse after major response or remission later than week 3, a single additional injection of 300 mg canakinumab was applied. Trial duration was 24 weeks. Efficacy was measured by Behçet's current disease activity form BDCAF and BVAS.
Results. Study medication was combined with prednisolone below 10 mg/day in 8 (80%), colchicine in 3, azathioprine in 3, and cyclosporin A in 3, 1 patient had low dose steroids, colchicine and azathioprine on a stable dosage. 6 patients received a double dose of canakinumab due to relapse.
Mean BDCAF was 4.6 at screening, 4.1 at visit 2 baseline, 1.6 at visit 3, 2 at visit 4, 2.4 at visit 5 and 6, 1.33 at visit 7, 4,33 at visit 8 and 2 at visit 9.
Relapses occurred in 57.1% at visit 4, 40% at visit 5 and 6, 33.3% at visit 7 and 8, zero at visit 3 and 9.
BVAS at screening was at a median of 3, going down to 1.5 at visit 3, and to zero at visits 6 and 7 and 1 at visits 8 and 9.
8 (80%) patients did not reach the final visit due to relapses not responding to augmented canakinumab dosages or because of primary nonresponse (2 patients with ocular manifestations).
Conclusion. Canakinumab is effective for mucocutaneous manifestations or arthritis, but not for severe ocular manifestations. As there were many relapses (70%), with consecutive discontinuation of canakinumab in 80% before end of study the dosage of canakinumab at baseline may have been too low and should probably be augmented to 300 mg sc. as often necessary in autoinflammatory diseases (1). A prospective trial with higher dosages should be the next step.
References
1. KUEMMERLE-DESCHNER JB, HOFER F, ENDRES T, KORTUS-GOETZE B, BLANK N,WEISSBARTH-RIEDEL E, SCHUETZ C, KALLINICH T, KRAUSE K, RIETSCHEL C, HORNEFF G, BENSELER SM: Real-life effectiveness of canakinumab in cryopyrin-associated periodic syndrome. *Rheumatology* (Oxford) 2016 Apr; 55(4): 689-96.

P081

Another neuro-Behçet mimicking a spinal cord tumor case report

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Introduction. Neurological manifestations in Behçet's disease represent between 4 to 49% of systemic manifestations and remain, in the long term, the leading cause of morbidity and mortality.
Aims. We present a case of neuro Behçet with a rare neurological involvement.
Methods. Retrospective case repport
Results. It is the case of 24-year-old male patient admitted for gradual onset and progressive paraparesis, bladder and bowel incontinency. There was no history of trauma or headache.
On physical exam the patient was alert and oriented, cranial–nerve examinations were normal. Strength was 4/5 in the lower limbs bilaterally, sensation to pinprick was reduced on the trunk below T4, more pronounced on the left, hyperreflexia and positive Babinski sign. A picture consistent with a myelopathy.
Angio-MRI revealed a hyperintense gadolinium enhanced T2-weighted images and a discrete hypo intense enhanced T1-weighted lesion extending from C2 to C7, an aspect consisting of longitudinal extensive transverse myelitis, although neoplastic process was evoqued considering the pseudotumoraspect.
On the medical history, there was a clear story of recurrent oral and genital ulcers since the age of 25. Eye exam showed retinal vasculitis withintraretinal hemorrhage.
Bacterial and viral serology, autoimmune testing and CSF analysis were all normal. We retained the diagnosis of Behçet's disease with ocular and longitudinal extensive myelitis according to the 2014 International Criteria for Behçet Disease.
The patient received IVPulse steroid 1 gr/day for 3 days and IVcyclophosphamide along with physical therapy with good clinical response. A repeat MRI done one month later showed virtually complete resolution of the hyper signallesion confirming the diagnosis.
Conclusion. In Behçet's disease, a cerebral space-occupying lesion should lead to a diagnosis of pseudotumor cerebri. The correct diagnosis will determine an appropriate therapy and may prevent an inappropriate neurosurgical approach. The cortico and immunotherapy allowed a substantial regression of the lesion.
References
1. Benamour S1, Naji T, Alaoui FZ, El-Kabli H, El-Aidouni S: Neurological involvement in Behçet's disease. 154 cases from a cohort of 925 patients and review of the literature. Rev Neurol (Paris). 2006 Nov;162(11):1084-90.
2. Rodrigues MI, Loureiro C, Geraldo Couceiro A, Reis Ferreira C, Monteiro-Grillo M: Neuro-Behçet, pseudotumor cerebri and ocular signs: a rare association. GMS Ophthalmol Cases. 2013 Mar 25;3:Doc02. doi: 10.3205/oc000012.
3. Martínez-Estupiñán L, López-Longo FJ, Monteagudo I, Carreño Pérez L Pseudotumoral neurobehçet in a patient treated with anti-tumor necrosis factor alpha. Med Clin (Barc). 2015 Mar 9;144(5):235-6.

P082

Ocular involvement in Behçet Disease: clinical spectrum and predictive factors

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Introduction. Ocular involvement can affect 30% to 60% of patients with Behçet disease (BD), revealing the disease in up to 20%.
Aims. Our aim is to study predictive factors of ocular involvement in BD.
Methods. We retrospectively reviewed the medical records of BD patients followed up in the Internal Medicine and the Ophthalmology Departments of Fattouma Bourguiba University Hospital (Monastir, Tunisia) between January 1990 and December 2017. BD was diagnosed according to the International Study Group for Behçet Disease criteria. Ocular manifestations were first described than predictive factors were studied in univariate than multivariate analysis.
Results. Among 281 patients, 108 (38.4%) had ocular manifestations. Anterior uveitis was diagnosed in 17 patients (15.9%), panuveitis in 47 patients (43.9%), posterior uveitis in 23 patients (21.5%), intermediate uveitis in 13 patients (12.2%), optic neuritis in 4 patients (3.7%), central retinal

vein occlusion in 2 cases (1.9%) and orbital inflammatory pseudotumor in 1 case (0.9%). Ocular inflammation revealed the disease in 33 cases (11.7%). Uveitis was found to be unilateral in 20 cases (18.7%). Patients with ocular involvement were significantly less likely to have family history of BD (8% vs 17.9%; p=0.025), less likely to have oral and genital ulcers (97.2% vs 100%; p=0.028 and 63% vs 84.3%; p=10^{-3}, respectively). They were also less likely to have deep venous thrombosis (10.2% vs 20.3%; p=0.025) and mucocutaneous onset (61.3% vs 94.8%; p=10^{-3}). In multivariate analysis, we found that genital ulcers, deep venous thrombosis and mucocutaneous onset are protective factors for ocular involvement (OR=0.44, 95% CI= 0.23-0.84, p=0.013), (OR=0.34, 95% CI= 0.14-0.81, p=0.016), (OR=0.085, 95% CI= 0.03-0.16, p=10^{-3})

Conclusion. Prevalence of ophthalmic involvement in our cohort seems to be in agreement with previous published data. Patients with mucocutaneous onset, genital ulcers and deep venous thrombosis seem to be less prone to develop ocular manifestations.

P083

Allergic reaction to self-saliva in patients with Behçet's disease and related diseases

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Introduction. Behçet's disease (BD) is a systemic disorder characterized by commencing with recurrent aphthous stomatitis (RAS). Some of them are associated with HLA-B51. "Pathergy test" has been reported to be highly positive in BD patients, but recently the rate of reactivity is lower and its reactivity has been reported as a variant between the countries (1, 2). As we have indicated before, both BD and non-BD RAS patients who do not develop BD symptoms, tend to have hypersensitivity to oral *streptococci* (3, 4). Then, instead of "Pathergy test" we would like to propose the pricking with self-saliva as a new diagnostic method for BD (5).

Aims. To differentiate BD from the related diseases, we tied to prick with self-saliva instead of Pathergy test.

Methods. Twenty-five BD and 7 non-BD RAS patients and 12 disease controls including patients with herpes simplex virus infection, Lipschutz genital ulceration (GU) and erythema nodosum (EN) were tested by pricking with self-saliva of pure and sterilized self-saliva and saline control using a tiny stick.

Results. Almost 100% of BD patients classified with Japanese classification showed more than 5mm diameter-erythematous skin reaction 48 hours after pricking and non-BD RAS patients were found to show relatively weaker responses than those of BD patients. The responses to self-saliva seemed to be relatively stronger in BD patients with HLA-B51 gene than without the gene (average 13.5mm to 11.7mm), although the possessors of HLA-B51 were 33.3% among 15 BD patients including incomplete, complete and intestinal types of Japanese Classification. The responses were considered to be due to oral bacteria including streptococci, because almost no reactions by sterilized self-saliva were observed. The positive by old Pathergy test showed only one among BD patients (4%).

Conclusion. The self-salivary pricking is considered to be a significant way for BD diagnosis and might be differentiated from non-BD RAS showing weaker skin reactions. The cutaneous reactions were considered to be allergic reaction to oral bacteria including *streptococci* (3, 4). The results suggest that BD symptoms are caused by the vascular responses due to circulating monocytes fully immunized by oral *streptococci* in connection with the gene. It might be considered that non-BD RAS is locally immunized by oral organisms (5). Finally, we would like to propose the cutaneous reaction with self-saliva to make a diagnosis for BD patients and to suggest for a pathogenesis of BD and RAS.

References

1. SAKANE T, *et al*.: Current concepts: Behçet's disease. *N Eng J Med* 1999; 341: 1284.
2. DAVATCHI F *et al*.: Pathergy test in Behçet's disease: change in incidence over the time. *APLAR J Rheumatol* 2007; 10: 333.
3. KANEKO F *et al*.: A. Streptococcal infection in the pathogenesis of Behçet's disese and clinical effects of minocycline on the disease symptoms. *Yonsei Med J* 1997; 38: 444.
4. ISOGAI E *et al*.: Close association of Streptococcus sanguis uncommon serotypes with Behçet's disease" *Bifidobacterium Microflora* 1990; 9: 27.
5. KANEKO F *et al*.: Behçet's disease and related diseases-immune reactions to oral streptococci in their pathogenesis. *J Dermatol Res* 2016; 1: 1.

P085

An update on pulmonary artery involvement in Behçet's syndrome: more pulmonary artery thrombotic disease and a better outcome

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Introduction. Pulmonary artery involvement (PAI) is the most common form of arterial involvement in Behçet's syndrome (BS) and is a well-known cause of mortality and morbidity. A previous survey (1) by our group had analyzed the clinical characteristics and outcome in 47 pts with PAI registered between 2000-2007 and, as compared to our previous experience showed that: 1. the overwhelming male predominance was decreasing; 2. 1/4th of the pts had isolated pulmonary artery thrombosis (IPAT); and 3. the mortality rate was 26% after a mean follow-up of 7 yrs. Recently we had the impression the percentage of female patients was perhaps further increasing; the number of pts with IPAT were increasing and we started to use more biologics.

Aims. We aim to look at these assumptions formally in a recent group of BS pts with PAI.

Methods. We reviewed the records of 3390 pts with BS who were registered at our multidisciplinary clinic between Jan 2008 and Jan 2018. We identified 47 (42M/5F) pts with PAI and recorded all information regarding clinical characteristics, outcome, radiological studies and treatment.

Results. The prevalence of pts with PAI decreased from 1.9% to 1.4% in the recent cohort. The M/F ratio, the mean age at the onset of PAI and the frequencies of other vascular involvement were similar across the 2 cohorts. However, there were more pts with neurological disease (parenchymal) in the recent cohort. As usual, PAT or PAA were mostly bilateral and involved descending lobar arteries. On the other hand, types of PAI involvement at presentation had changed substantially: those with IPAT reached a share of 45%. Forty-five (96%) pts received cyclophosphamide pulses for a mean of 6±4 courses, which was significantly shorter compared to the previous cohort. Twenty-three (49%) pts received infliximab because of relapsing course, side effects or unresponsiveness for a mean follow-up of 8±4 mo while only 2 pts received anti-TNF's in the older cohort. 4 pts had lung surgery, lobectomies in 3 due to giant rapidly progressing aneurysms and a cavitectomy in 1. Bronchial artery embolization was done in 3 pts because of refractory hemoptysis. By Jan 2018, the outcome of information was available on 45/47 pts: 4 pts (8%) had died, 2 were lost to follow-up after 12 and 16 mo of follow-up and the remaining were alive after a median follow-up of 5 [IQR:3-9] yrs. The causes of deaths were massive hemoptysis in 3, severe pulmonary hypertension in 1. The survival has improved significantly in the recent yrs (Figure).

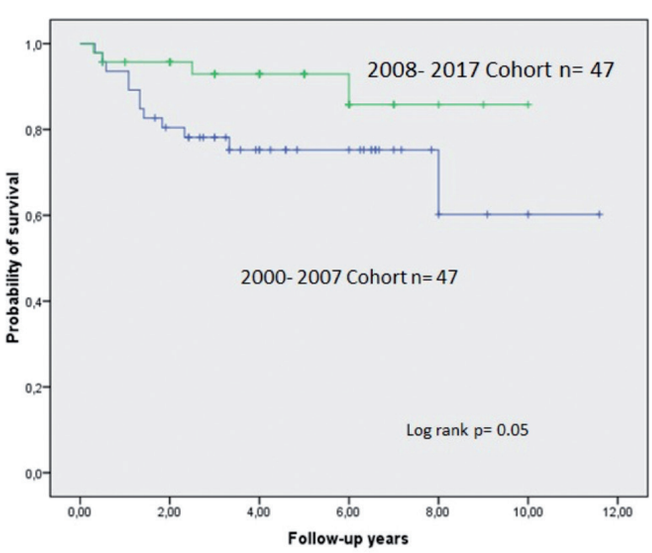

Fig. 1. Kaplan-Meier survival curve comparing two cohorts.

Conclusion. The surveys of 2 consecutive cohorts showed that the prevalence of PAI perhaps mildly decreased, IPAT type of involvement was

with considerably higher frequency and the outcome was getting better. Cyclophosphamide was still the first agent however its duration of use became much shorter and anti-TNF's were used in about half of the cohort. The survival seems to have improved significantly. This could have been due to a decreased severity of the type of PAI, with IPAT becoming the most frequent type and or a better management.

References

1. SEYAHI E: *Medicine* (Baltimore) 2012.

P086

New major organ involvement is lower in young male Behçets' compared to retrospective series: five-year results of a prospective cohort

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Introduction. Major organ involvement such as vascular or ocular disease, especially in young males, is one of the main causes of mortality and morbidity in Behçet's Disease (BD). However, the prognosis and predictors of major organ involvement is unsufficiently studied.
Aims. We aimed to follow young, male BD patients with only mucocutaneous symptoms which have the highest risk for new major organ involvement prospectively.
Methods. Thirty-six male patients with BD consecutively consulted in the outpatient clinics of Marmara University, Istanbul, 35 males with ankylosing spondylitis and 36 healthy males were included in the study. Bilateral upper and lower extremity venous doppler ultrasonography (US) and brachial and carotid arterial US (for assessing endothelial dysfunction) were performed in baseline visit for all study groups and in the first year follow-up visit for BD patients. Patients with BD were assessed prospectively with 3-6 months intervals and in any urgent visits.
Results. At baseline, the mean disease duration was 3.3 years. Venous insufficiency rate was higher in male BD patients without vascular events compared to healthy controls (BD vs HC: 30.5% vs 0%) and similar to patients with AS (BD vs AS. 30.5% vs 32%). Markers of endothelial dysfunction (FMD and NID) were similar between BD patients and healthy controls, however CIMT (Carotid intima media thickness) was significantly higher in BD (0.54 mm vs 0.47 mm, p=0.033). The mean follow-up duration was 56.6 months. Major organ involvement developed in 5 (13.8%, 3 vascular and 2 ocular involvement) patients during follow-up. Immunsuppresive (IS) therapy was required in 27% (n=10) of patients, due to major organ involvement in 5 (13.8%), refractory mucocutaneous symptoms in four (11%) and chronic arthritis in one (2.7%) patient. In the first year follow-up visit, endothelial functions and CIMT were observed to be significantly improved compared to baseline (Baseline vs Follow-up: 6.8±4 vs 10.9±4.5, p=0.003 for FMD**,** 0.55±0.13 vs 0.47±0.1 for CIMT, p=0.004). Patients requiring IS treatment in the follow-up had significantly lower FMD at baseline compared to the rest of the group (4.4 vs 8.5, p=0.005).

Table I. Venous wall measurements of lower extremity in study groups.

	Behçet's Disease (n=59)	Ankylosing Spondylitis (n=27)	Healthy Controls (n=28)	P Value
Age, years	32.5 (23-42)	32 (20-37)	31.5 (25-42)	0.23
Body Mass Index (kg/m2)	25.1 (18-33)	25 (18-32)	23.8 (20-29)	0.213
Right Common femoral VWT (mm)	0.8 (0.04-1.8)	0.3 (0.1-0.6)	0.25 (0.06-0.4)	**<0.001**
Left Common femoral VWT (mm)	0.8 (0.3-1.6)	0.3 (0.1-0.5)	0.2 (0.04-0.6)	**<0.001**
Right Great saphenous width (mm)	3.1 (0-6.4)	2.5 (1.1-3.5)	2.1 (1.3-3.5)	**<0.001**
Left Great saphenous width (mm)	3.1 (0-7.4)	2.6 (0.3-4.8)	2.4 (1.6-3.6)	**<0.001**
Right Small saphenous width (mm)	2.8 (0-5.3)	1.7 (1-3.1)	1.4 (0.9-3.7)	**<0.001**
Left Small saphenous width (mm)	2.7 (0-5.2)	1.8 (1.1-3.4)	1.6 (0.8-3.6)	**<0.001**
Left Great saphenous width (mm)	3.1 (0-7.4)	2.6 (0.3-4.8)	2.4 (1.6-3.6)	**<0.001**

VWT: Venous wall thickness

Conclusion. Our study demonstrated a lower incidence of major vascular events in male BD patients during prospective follow-up compared to historic controls in the literature. The decreased rate of baseline FMD in patients with later IS requirement suggest that FMD might be a predictor for major organ involvement in BD.

P088

Venous involvement in Behçet disease: clinical spectrum and predictive factors

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Introduction. Vascular involvement is frequent in Behçet disease (BD). Vascular manifestations are more frequently venous than arterial.
Aims. We aimed in this work to describe clinical characteristics, predictive factors and management of venous involvement during BD in the Tunisian context.
Methods. We retrospectively studied 281 records of BD patients followed between January 2004 and December 2017 in the Internal Medicine Department and who fulfilled the International Study Group for BD (ISGBD) criteria. We described first clinical features of BD with venous involvement then predictive factors were studied in univariate then multivariate analysis.
Results. Among 281 patients, 61 have had venous involvement. They were 82% males and 18% females with a mean age of 32 years (12 to 55 years). Superficial venous thrombosis were diagnosed in 18 patients (29.5%) associated or not to deep venous thrombosis in 46 cases (75.4%) as follow: upper arm (16.4%), inferior limb (37.7%), inferior vena cava (13.1%), superior vena cava (1.6%) and mesenteric vein (1.6%). Venous involvement was associated to arterial manifestations in 9 patients (14.8%). Treatment consisted in high doses of steroids in 42.6%, cyclophosphamide in 21.3% and anticoagulation in 79.3%. Predictive factors independently associated with venous involvement in BD are male gender (OR=0.3, 95% CI= 0.14-0.67, p=0.004), erythema nodosum (OR=4.2, 95% CI=1.7- 10.6, p=0.002), ophthalmic involvement (OR=0.46, 95% CI=0.24- 0.9, p=0.024) and orchi epididymitis (OR=4.8, 95% CI=1.42-16.38, p=0.012).
Conclusion. Venous involvement in BD is frequent in the Tunisian context consisting in deep and superficial veins. Male gender, patients with erythema nodosum, ophthalmic manifestations or orchi epididymitis are more prone to develop venous complications needing therefore a close monitoring. In addition to anticoagulant, treatment should associate steroids and immunosuppressors.

P089

Oral health is a mediator for disease severity in patients with Behçet's disease: a Multiple mediation analysis study

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Introduction. Oral ulcers with periods of remission and exacerbation can lead to poor oral health since they limit oral hygiene practices.
Aims. The aim of this study is to examine whether oral health as an infectious focus mediates disease course in patients with Behçet's disease (BD).
Methods. In this retrospective study, oral health of 194 BD patients was examined at baseline and follow-up periods by using dental and periodontal indices. The mean follow-up period was 4.5±2.8 years. The Behçet's disease severity score was calculated with higher scores indicating a more severe course. The reason for last dental visits was recorded as tooth extraction or regular control visits/planned treatments at the end of follow-up period. Mediation analysis evaluating direct and indirect causal effects was carried out to assess the effects of oral health on disease severity score during follow-up period in the study. Gender as one of the determinants of severe disease course is thought to be an independent variable in BD, whereas disease severity as an outcome measure is accepted to be a dependent variable. Possible mediators considered in the proposed model were: (i)

presence of dental caries (M_1) and (ii) tooth extraction (M_2) in the last dental visit. After mediation analysis, a bootstrap analysis with 1000 replications was applied to estimate mediation effects to generate 95% CI.
Results. Dental and periodontal indices were found to be higher at follow-up visit compared to those of baseline (p<0.05). Disease severity score was found to be higher in males (5.3±2.4) compared to females (4.4±2.5) during follow-up visit (p=0.005). Patients having tooth extraction at their last dental visit and patients with dental caries also had a more severe disease course (5.4±2.4 and 5.5±2.5, respectively) compared to the rest (4.2±2.3 and 4.4±2.4, respectively), (both p<0.0001). In multiple mediation analysis, disease severity score as a dependent variable was directly mediated by male gender (B=-0.8822, p=0.0145) and indirectly mediated through the presence of dental caries (B=0.9509 p=0.0110) and need of tooth extraction (B=0.8758 p=0.0128). Then, we also performed analysis with percentile bootstrap of two mediators and a need for tooth extraction was shown to be an effective mediator for severe disease course based on 1000 bootstrap sample.
Conclusion. Severe disease course in BD was directly mediated by male and indirectly mediated through the presence of dental caries and tooth extraction according to the mediation analysis. Therefore, better oral health should be aimed to eliminate microbial factors, which are a part of pathogenic processes, in the disease management.

P090

1 + 1 ≠ 3: Clinical challenges with a case of suspected neuro-Behçet's disease complicated with neurogenic pulmonary edema

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Introduction. Many diagnostic criteria for Behçet's disease (BD) exist. The current International Criteria for Behçet's Disease (ICBD) have higher sensitivity and accuracy while maintaining specificity when compared to criteria from the International Study Group for BD. A score ≥4 points indicates BD. Although incomplete BD and suspected BD are appointed in clinical studies, they are not endorsed. Incomplete and suspected BD are *e.g.* only acknowledged in Japanese criteria. As BD is diagnosed solely on clinical criteria, exclusion of other diseases regularly dictates ancillary procedures. This is not always optimal in limited resource settings.
Aims. To assess the clinical management of suspected BD patients with incomplete criteria.
Methods. To present a case of suspected BD with neurologic manifestations where immunosuppressive therapy is considered in a limited resource setting.
Results. We present a 42 year old male patient of East-Indian descent with hypertension and epilepsy since 2016 who visited the ER of the Academic Hospital Paramaribo in Suriname, South-America, five times in the past 1.5 years due to status epilepticus despite anti-epileptics. The last four times the patient also had dyspnea and bilateral pulmonary consolidations for which ICU admittance was mandatory. These consolidations subsided within 1 day and were due to neurogenic pulmonary edema (see Figure 1). MRI-brain showed mildly enlarged ventricles. Cerebral spinal fluid opening pressure and protein were 30 cmH2O and 0.47 g/L respectively, thus both elevated. Cell-count and inflammation markers were normal. Infections were not suspected and were excluded when possible in this limited setting (HIV, HSV, Syphilis; all negative). Basal available auto-immune serology (ANA, ANCA, ENA-6) was negative. No other features for auto-immune / -inflammatory disorders (including auto-immune encephalitis) were present except for oral ulcers >3 times a year. Seizures and raised intracranial pressure are recognized symptoms for neuro-BD. There were no other BD signs or symptoms. The patient scored 3 points on the ICBD. BD was suspected. Due to the refractory and fulminant course of the seizures treatment with corticosteroids were considered. This raises an issue as BD is not confirmed.

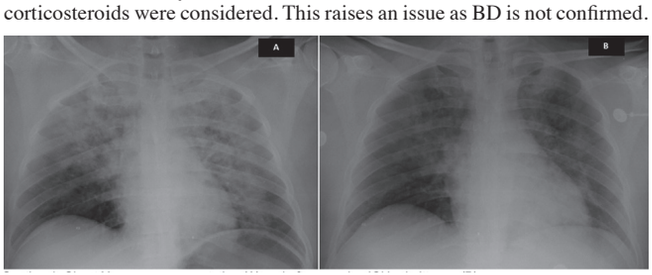

Fig. 1. Chest X-ray upon presentation (**A**) and after one day ICU admittance (**B**).

Conclusion. BD is a protean disease and disease manifestations vary per patient population. Neuro-BD on itself is diverse. In this case neuro-BD with neurogenic pulmonary edema is suspected. Although clinical reasoning may overrule clinical criteria and protocol this is not always desirable, especially when treating with potentially harmful medication. Caution should thus be exerted when assessing suspected BD with incomplete criteria, especially when options for ancillary tests are limited. Expert opinion can be of important value in this situation. Suspected BD with incomplete BD could be assessed for treatment outcome in further studies as this might aid in clinical decision making especially in limited resource setting.

P091

Mucocutaneous activity index as a patient-reported outcome measure in Behçet's disease: a multi-center study from Turkey

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Introduction. Organ-specific patient-reported outcome (PRO) measures may help management decisions of Behçet's disease (BD).
Aims. The aim of this prospective study was to evaluate the factors associated with the score of mucocutaneous activity index (MI), a validated patient-reported outcome tool, for Behçet's Disease (BD).
Methods. In this study, 834 BD patients (F/M: 441/393, age mean: 38.4±10.9 years) followed in twelve tertiary centres from Turkey were included. Validated mucocutaneous activity index (MI) and its subgroup activity indices regarding oral ulcer (CI), genital ulcer (GI) and erythema nodosum (EI) were assessed. Scores of each subgroup were between 0=inactive and 10=very active. Total MI score composed of these subgroups (0-30 points). Transformed Behçet's disease current activity form (BDCAF) was used to evaluate global activity.
Results. Active BD patients (n=567, 67,9%) were mainly in the mild group with mucocutaneous involvement (n=420). Disease duration was lower (9,7±6,9 vs 11,1±8,1 years, p=0.001) and patients were younger (36,4±10,2 vs 41,9±11,2 years, p=0.001) in the active group. The ratio of non-smokers was also higher in active patients (76,1% vs 67,6%, p=0.011). A higher MI score was observed in females (8,2±4,6) compared to males (7,3±3,9) among active patients (p=0.023). It was higher in females (8,1±4,3) than males (6,7±3,.6) in non-smokers (n=419) (p=0.002), whereas a significant relationship was not present in current smokers (n=132, p=0.85) with gender. MI score was also higher in patients whose disease durations were less than 5 years (6,5±2,6) than the others (4,7±4,7) (p=0.001).
Being a non-smoker (OR:1,7), disease duration less than 5 years (OR:2,4) and female sex (OR:1,5) were found as predictive factors for mucocutaneous activity according to binary logistic regression analysis (p<0.05). Increases in both MI score and BDCAF score were observed in immunosuppressive (IS) medication group (n=86; 9,6±5,3; 6,6±2,9) compared to non-IS group (n=316; 7,7±4,1; 5,5±2,5) in active patients with mucocutaneous involvement (p=0.001 and p=0.008).
Conclusion. Female gender, smoking and disease duration were associated with higher MI scores in our study. An organ-specific and reliable PRO measure such as mucocutaneous index might be a candidate scale for future clinical studies and clinical follow-up of mucocutaneous manifestations in BD patients.

P092

A case of retrosternal pain and high levels of d-dimers diagnosed as Behçet's syndrome

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Introduction. A 29-year-old man presented to the ER complaining of abrupt onset of retrosternal pain radiating to the back. The pain was continuous and aggravated by body movement and breathing. The patient had no significant past medical history and no risk factors for coronary disease, however, he reported two more similar episodes the last two months without any medical assessment.
The ECG recorded sinus bradycardia at a rate of 47 bpm with no evidence of ischemia. Vital signs were normal (T: 35,4°C, BP:120/70 mmHg, RR:14/

min). Cardiac troponin concentrations were 2.30 pg/ml (ref. 0-34.2) on arrival and 2.60 pg/ml 3 hours later. The patient was admitted for monitoring and further investigation in the Internal Medicine Department of our tertiary Institution.

Aims. Our goal is to provide information and support and to promote clinical research with the hopes of finding new treatments and a possible cure for Behçet's Disease.

Methods. Clinical findings on admission comprised tenderness on palpation of the sternum and right costochondral junction, normal cardiac sounds, also no evidence from chest auscultation was detected. Aphthous ulcerations of the mouth were present. The patient reported a 3-year history of recurrent aphthous ulcerations of the mouth, ameliorated once with corticosteroids and an episode of orcheoepididymitis but without genital lesions on the past. He also complained of low back pain with inflammatory pattern and morning stiffness.

Owing to the high d-dimers levels a CTPA was performed, revealed no evidence of pulmonary embolism. Echocardiogram showed normal ejection fraction and normal left ventricle contractility, without pericardial effusion. Lower extremity venous ultrasound was obtained demonstrating first degree venous reflux above the division of right saphenous, suggesting a small degree of venous valve failure of the right common femoral vein.

Results. Considering the past history of aphthous ulcerations, arthritis, orcheoepididymitis and the possibility of venous failure the diagnosis of Behçet syndrome was proposed.

Further investigation included ophthalmological evaluation with no significant findings, also assessment by the Reumatology and Dermatology team of our tertiary Institution. During hospitalization, the patient remained cardiovascular and respiratory stable, but with persisting episodes of chest pain. A complete ophthalmic examination was done without revealing any abnormalities. Additionally, laboratory work up revealed a marginally positive rheumatoid factor (24 IU/ml with reference values of >20 as positive test), collagen tests negative, ESR: 5, and normal acute phase reactants.

Conclusion. We report an unusual presentation of Behçet disease in a young adult who had several episodes of acute chest pain combined to increased levels of d-dimers before the final diagnosis of BD was established. The diagnosis was made based on clinical evaluation of aphthous ulcerations and venous failure as well as the past history of arthritis and orcheoepididymitis. Patient recovered after treatment with colchicine. Regular follow up assessment of the patient for a year period in the Outpatients Clinic confirmed clinical improvement and stability of laboratory findings.

References

1. D. VELISSARIS, S. KAROGIANNI, M. ANDREOU, A. FILIPPOPOULOU, S. N. LIOSSIS: Pathology Department of Patra's General University Hospital Rheumatology Department of Patra's General University Hospital.

P093

Predictive factors for work-day loss in a multi-center study in Behçet's disease: indirect costs for healthcare

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Introduction. In chronic diseases, work-day loss due to health problems is associated with indirect costs for healthcare management.

Aims. The aim of this multi-center study is to assess predictive factors for work-day loss as a productivity measure in Behçet's disease (BD).

Methods. In this cross-sectional, multi-center study, 834 BD patients (F/M: 441/393, age mean: 38.4±10.9 years) were included. Data were collected by a questionnaire regarding organ involvement, treatment protocols, disease duration (less than 5 years vs ≥5 years), smoking pattern, frequency of medical visits/ during the previous year (>4 visits vs ≤4 visits) and self-reported work-day loss during the previous year. Cut-off points of these variables were calculated according to median levels for the binary logistic regression analysis.

Results. Work-day loss was observed in 16,2% of the group (n=135). The majority of these patients were males (n=103, 76,3%). The mean work-day loss was 30,8±57,7 days (1-365 days) and was higher in males (31,7±54,2 vs 27,9±68,8 days, p=0.007). The mean age and disease duration were lower (34,3±8,4 and 7,04±6,04 years, respectively) in patients with work-day loss compared to others during the previous year (39,2±11,2 and 9,4±7,8 years, respectively, p=0.000). Increase in the work-day loss was prominent in patients with vascular involvement (19M/1F, 56,1±85,9 vs 26,4±50,6 days) (p=0.046), whereas no similar relationship was observed with any other organ involvement. Being a smoker (OR:1,7), disease duration less than 5 years (OR:2,05), male gender (OR:3,9) and more than 4 visits/previous year (OR:2,5) were found to be predictive factors for work-day loss according to binary logistic regression analysis (p<0.05).

Conclusion. Work-day loss was associated with vascular involvement in our study. Male gender, increase in the frequency of visits, being a current smoker and early period of the disease were predictive factors for work-day loss in patients with BD.

P094

Pulmonary Hypertension in Behçet's Disease

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Introduction. Behçet's disease (BD) is a systemic vasculitis that involvement of pulmonary arteries can be seen.

Aims. The aim of this study is to determine the prevalence and causes of pulmonary hypertension (PH) in BD.

Methods. We studied consecutively 154 BD patients who were fulfilled the International Study Group criteria for diagnosis of BD. All patients were evaluated with transthoracic echocardiography (TTE) for the presence of PH. BD patients were categorized according to the involved organs in 5 groups: group 1 mucocutaneus and articular, group 2 ocular, group 3 vascular, group 4 gastrointestinal and group 5 neurologic involvements. The presence of PH was defined as estimated sPAB ≥40 mmHg, by TTE. Every subject evaluated by a detailed medical history and physical examination was performed. Additional laboratory results were obtained from hospital file records.

Table I. Demographic and clinical features of Behçet's disease patients.

	All patients (n=154)	sPAP≥40 mm Hg (n=17)	sPAP<40 mm Hg (n=137)
Female, n (%)	62 (40.3)	6 (35.3)	56 (40.9)
Age, median (min-max)	41 (18-73)	46 (24-72)	40 (18-73)
Disease duration (months), median (min-max)	126 (6-540)	168 (12-540)	120 (6-480)
Diabetes Mellitus, n (%)	9 (5.8)	1 (5.9)	8 (5.8)
Hypertension, n (%)	26 (16.9)	5 (29.4)	21 (15.3)
Smoking, n (%)			
Never smoker	76 (49.4)	7 (41.2)	69 (50.4)
Current smoker	47 (30.5)	5 (29.4)	42 (30.7)
Ex-smoker	31 (20.1)	5 (29.4)	26 (19.0)
Oral ulcer, n (%)	154 (100)	17 (100)	137 (100)
Genital ulcer, n (%)	104 (67.5)	11 (64.7)	93 (67.9)
Erythema nodosum, n (%)	64 (41.6)	7 (41.2)	57 (41.6)
Papulo-pustular lesion, n (%)	35 (22.7)	3 (17.6)	32 (23.4)
Acneiform lesions, n (%)	105 (68.2)	8 (47.1)*	97 (70.8)*
Articular involvement, n (%)	35 (22.7)	4 (23.5)	31 (22.6)
Uveitis, n (%)	75 (48.7)	9 (52.9)	66 (48.2)
Pathergy, n (%)	40 (26)	6 (35.3)	34 (24.8)
Vascular involvement, n (%)	48 (31.2)	9 (52.9)**	39 (28.5)**
Pulmonary arterial involvement, n (%)	10 (6.5)	4 (23.5)***	6 (4.4)***
Neurologic involvement, n (%)	18 (11.7)	2 (11.8)	16 (11.7)
Gastrointestinal involvement, n (%)	12 (7.8)	1 (5.9)	11 (8.0)

sPAP: Systolic pulmonary artery pressure, min: minimum, max: maximum

* p = 0.04, ** p=0.04, *** p=0.003

Results. Demographic and clinical features of patients with and without PH was shown in table. PH was detected in 17 (11%) BD patients. PH frequency was higher in BD patients with vascular involvement than without vascular involvement (52.9% vs 28.5%; p=0.04). Ten (6.5%) patients had

pulmonary arterial involvement (PAI) which was more frequent in patients with PH than in those without (23.5% vs 4.4%; *p*=0.003). However, there was no significant difference between the predefined BD groups regarding the percentage of PH. Only 9 (52.9%) patients were symptomatic (NYHA FC >1). Left sided heart disease (Group II: 9 (52.9%) patients) was the leading cause of PH. Four (23.5%) patients had group IV PH and 75% (3/4) were symptomatic. Diastolic dysfunction was found in 32 (20.8%) patients and only 1 patient had systolic dysfunction. The number of patients with diastolic dysfunction was significantly higher in patients with PH patients as compare to patients without PH (8 (47.1%) vs 24 (17.6%), *p*=0.005).
Conclusion. PH is not infrequent in patients with BD. The most frequent cause of PH in BD patients was group II PH. There were also significant number of patients with group IV PH. Our data implicates that all BD patients with suspected PH should be carefully investigated for the presence of group II and IV PH. Pulmonary endarterectomy may be an option of treatment in inactive patients with group IV PH.

P095

A declining trend in frequency of secondary amyloidosis in Behçet's syndrome

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Introduction. A decline in the frequency of AA amyloidosis secondary to RA and infectious diseases has been reported.This is probably due to more effective treatment strategies. We had previously reported that although amyloidosis occurs in less than 0.5% of BS pts, it is one of the leading causes of death (1-3). We had an impression that the frequency of amyloidosis is decreasing among our pts with BS.
Aims. We aimed to determine the change in the frequency of AA amyloidosis over years in BS pts in addition to elaborating on clinical characteristics and outcomes.
Methods. We performed a chart review to identify all patients with amyloidosis in our BS center since 1976. We noted demographic characteristics, BS manifestations,age at BS and AA amyloidosis diagnosis, treatment modalities of these patients. Our endpoints were death and end stage renal disease(ESRD) requiring renal replacement therapy. The prevalence of AA amyloidosis was calculated separately for two periods (patients registered between1976-2000 and 2000-2017)
Results. Among our 9410 BS pts,27 (0.29%) had secondary amyloidosis. We identified 24 pts with amyloidosis among the 3820 pts in the earlier cohort and 3 additional amyloidosis among the 5590 pts in the recent cohort. The frequency of AA amyloidosis had declined from 0.62% to 0.054% in the recent cohort.M/F ratio was 22/5 and mean age at BS diagnosis was 29.5±7.4 years.Twenty-two (82%) of the pts with AA amyloidosis had major organ involvement (vascular inv. in 15, eye inv. in 13 and neurologic inv.in 2). Five (18%) of 27 pts had only mucocutaneous inv. AA amyloidosis was diagnosed after a mean duration of 9.8±6.7 years (mean age at AA amyloidosis: 39.3±9.3 years) and was confirmed with renal biopsy in 14 pts and rectal biopsy in 13. Eight pts had non-nephrotic range proteinuria at AA amyloidosis diagnosis. After amyloidosis diagnosis, 24 pts continued their previous immunosuppressives and colchicine. Two of these 24 were on anti-TNFs at the diagnosis of AA. Biologics were initiated in 3 pts who were most recently diagnosed to have amyloidosis, anti-TNFs in 2 and tocilizumab in 1. Fourteen (52%) pts had died after a median follow-up of 3 (IQR: 1-8.75) years, 3 were lost to follow-up just after AA amyloidosis diagnosis and 10 (37%) are still alive after a median follow up of 16 (IQR: 10-23) years.The reasons for death were infections in 5, related to ESRD in 5, subarachnoid hemorrhage, gastric adenocarcinoma, liver cirrhosis probably associated with amyloidosis and iatrogenic bowel perforation in 1 pts each. 10 (71%) of these 14 pts had developed ESRD before their deaths. Overall,15/27 pts developed ESRD after a median follow-up of 3.5 (IQR: 1.25-6.5) years after AA amyloidosis diagnosis. 5 of them had renal transplantation, all but 1 are still alive after 3, 4, 6, and 12 years. The last one died 11 years after transplantation due to subarachnoid hemorrhage as explained above.
Conclusion. AA amyloidosis appears to be a rare, but fatal complication of BS.Around 50% of pts died after a median follow-up of 3 years after AA amyloidosis.This study showed a decreasing trend of AA amyloidosis due to BS similar to that observed in other inflammatory and infectious causes.The shorter follow-up duration may be contributing for the lower prevalence of AA amyloidosis in the recent cohort.

References

1. YURDAKUL S: *Arthritis Rheum* 1990.
2. MELIKOĞLU M: *Rheumatology* (Oxford) 2001.
3. KURAL-SEYAHI E: *Medicine* (Baltimore) 2003.

P096

Management of refractory vascular Behçet's disease with TNF-α inhibitors: a retrospective multi-center case series

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Introduction. Vascular Behçet Disease (VBD) is observed in up to 40% of patients with BD and is one of the major causes of morbidity and mortality. Immunosuppressive (IS) treatments are the mainstay for VBD, however there are no randomized, controlled studies for its management.
Aims. We aimed to present the results of tumor necrosis factor-alpha (TNF-α) inhibitor use for refractory VBD.
Methods. We retrospectively collected data of 23 patients with VBD from three tertiary rheumatology centers in Turkey. All patients were refractory to corticosteroids (CS) and conventional immunsuppressives and were treated with TNF-α inhibitors. Clinical, demographic data and treatment outcomes were acquired from the clinical charts. Activity was assessed by the treating clinician according to clinical and laboratory signs of disease.
Results. The study included 23 patients (Male/Female:21/2) and median age was 35 (31-55) years. Median disease duration was 8 (1-24) years. In 6 patients, vascular involvement was the presenting symptom of BD. Median vascular event number was 2 (1-6). All patients were previously treated with conventional IS treatments (17 cyclophosphamide, 20 azathiopirine and 4 interferon-alpha) together with high dose corticosteroids. Infliximab (INF) in 21 patients and adalimumab (ADA) in 2 patients were chosen as first-line TNF-α inhibitors. All patients achieved remission within 3 months after the start of TNF-α inhibitors. Median metilprednisolone dose was decreased significantly after TNF-α inhibitor initiation (Table I) and stopped in 7 patients during follow-up without a relapse. In 4 patients, INF was switched to ADA (for secondary failure in 3 patients, allergic reaction in 1 patient). During follow-up, other reasons for discontinuation of TNF-α inhibitors was sustained remission in 2 patients, tuberculosis in 1 patient and new vascular event in 1 patient. One of the patients achieving sustained remission, relapsed after 6 months of drug-free period. At the last visit, 20 (2 ADA, 18 INF) patients were still under TNF-α inhibitor treatment with a median follow up of 14 (3-67) months and all were in remission. Seventeen patients had taken anticoagulant treatments in addition to ISs with median duration of 18 months (3-71). There was no difference in vascular events according to anticoagulant use (*p*=0.83). In 19 patients, thrombophilic risk factors were investigated and detected in six patients.

Table I. Clinical and laboratory characteristics of patients with vascular Behçet disease.

	Number of Patients, %		
Vascular Involvement Type			
Pulmonary aneurysm	7 (30.4%)		
Pulmonary aneurysm+Cardiac Involvement	4 (17.4%)		
Venous Involvement	12 (52.1%)		
Clinical Manifestations			
Mucocutaneous Involvement	23 (100%)		
Arthritis/Artralgia	4 (17.4%)		
Neurologic Involvemnet	2 (%8.7)		
Ocular Involvement	12 (%52.1)		
GIS	3/23 (%13)		
Patergy positivity	14/22 (63.6%)		
HLA-B51 positivity	2/7 (28.5%)		
Family history for Behçet Disease	6/23 (26.1%)		
	Before TNF inhibitors	**3.months after TNF inhibitors**	**P value**
Acute phase reactants			
Sedimentation, mm/hour	35.5(2-86)	12.5(0-31)	**<0.001**
C Reactive protein, mg/L	23.3(1-86)	7.3(2-54)	**0.007**
Metilprednisolone dose, mg/day	19.9(4-64)	5.7(0-20)	**0.001**

Conclusion. In our series, TNF-α inhibitors achieved clinical remission within 3 months in all patients and sustained remission was present in most of them after 14 months. TNF-α inhibitors seem effective and safe agents for the treatment of VBD patients refractory to conventional ISs.

P097

The influence of Behçet's disease flare-up on mood

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Introduction. Behçet's disease can be a very chronic debilitating disease especially during episodes of exacerbations. Besides its often severe physical effects, it also impose a significant psychological toll to those affected.
Aims. This study was aimed to describe the relationship between exacerbations of BD and mood among a BD cohort in the Midwest region of Ireland.
Methods. 28 patients who fulfilled the International Study Group for Behçet's Disease (ISGBD) diagnostic criteria and actively attending our rheumatology department were recruited. Patients were all interviewed through telephone calls. They were asked to provide a score between 0-10 (0-1=very poor, 2-3=bad, 4-6=fair, 7-8=good, 9-10=excellent) to reflect their mood over the past week. Patients who scored their mood below 7 were requested to list the underlying contributing factors leading to the low mood score.
Results. All 24 patients responded to the phone interview; 18 (64.3%) were females and 10 (35.7%) were males with mean age of 43.5 years. 14 (50%) patients rated a mood score of less than 7 with many listed more than one reason for their low mood. Majority of patients (71.4%) listed exacerbations of BD as the most common reason to worsen their mood, and this was followed by other health reasons (50%), family issues (35.7%) and problems related to work (21.4%). Within the past six months, 17 patients (60.7%) had exacerbations of BD. The symptoms of these exacerbations include oral aphthosis (76.5%), arthralgia (58.8%), genital ulcers (29.4%), fatigue (29.4%), intestinal involvement (11.8%) and skin involvement (5.9%). Interestingly, 4 (14.3%) patients were on antidepressant medication.
Conclusion. In addition to the detrimental effects on physical wellbeing, BD flare up has been shown in this study to have a significant impact on mood. Therefore, taking cognizance of the psychological aspect is crucial in the management of BD patients.

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Behçet's disease: outcome of pregnancy

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Introduction. Behçet's disease (BD) is the systemic vasculitis of unknown etiology with poliorganic pathology. Data on the outcome of pregnancy are discrepant.
Aims. To study the outcomes of pregnancies in BD patients.
Methods. The study included 12 patients with BD (according to ISBI criteria, 2014). (1). Average age of patients was 29.5 (25;35),and disease duration 7.4 (2;10.5). 100% of patients had relapsing aphthous stomatitis, other criteria: ulcers of genitals – in 41%, uveitis – in 41%, dermal lesion – 75%, erythema nodosum – 38%, articular syndrome – 41%, CNS lesion – 2 patients. 50% of patients had severe BD form according to Ch. Zouboulis classification (2) (due to generalized uveitis ,retina vasculitis and parenchymatous CNS lesion), the second half of patients had mainly dermal-mucous manifestations of the disease. Retrospective analysis of data concerning relationship between BD and pregnancy was performed.
Results. 34 full-term pregnancies in 12 patients resulted in 20 births of children (with cesarean section), 4 patients had 9 unfinished pregnancies: 1 due to medical reasons (rubella on the 7th week of gestation), the second was diagnosed "Neurobehcet", 5 cases of abortion before 12 weeks and two pregnancies resulted in the birth of healthy children. Two patients had abortion, one of them two times before 12 weeks. Two patients with BD had "standstill" pregnancies in history at 10 and 12 weeks, and two had miscarriage: one after 5 and 6 week and the other – 10 weeks.
BD debut with erythema nodosum and stomatitis during first full-term pregnancy born sound child.
Out of 20 children born from patients with BD only two had relapsing aphthous stomatitis and one – congenital glaucoma (from mother diagnosed "Neurobehcet").
Variants of BD severity and pathology of pregnancy (Table).

Table I. Variants of BD severity and pathology of pregnancy.

Severity and form of the disease	N=12(%)	Miscarriage, undeveloped pregnancy
Light	5(41.7)	3
Medium	1(8.3)	-
Severe	6(50)	2

Conclusion. Unfavorable outcomes of pregnancy were observed during different form of severity of BD. The above results were collected from all patients before proposed therapy, and it allows us to exclude the relation of the outcome of pregnancy with BD therapy.
References
1. International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD): The International Criteria for Behçet's Disease (ICBD).: a collaborative study of 27 countries on trhe sensitivity and specificity of the new criteria. *Journal of the European Academy of Dermatology and Venereology* 2014; vol.28, no. 3, 338-347.
2. Zouboulis C., Vaiopoulos G., Macromichelakis N *et al*.: Onset signs, clinical course, prognosis, treatment and outcome of adult patients with Adamantiades-Behçet's disease in Greece. *Clin Exp Rheum* 2003; 21 (Suppl. 30): S19-S26.

P099

Arterial involvement in Behçet's disease, a retrospective study of 38 cases

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Introduction. Behçet's disease (BD) is now recognized as a chronic multisystemic vasculitis classically characterized by a triad, oral and genital ulcers and uveitis. Vascular involvement is one of the major causes of mortality and morbidity.
Aims. To describe the demographic, clinical and prognosis aspect of vascular disease associated with in BD.
Methods. Retrospective study on 38 BD patients presenting arterial disease and treated at a tertiary internal medicine department over period of 36 years (1981-2017). All the patients met the international criteria of International Study Group. Arterial imaging consisted of Doppler ultrasound and CT-angiography.
Results. Out of a total of 1646 patients, 315 (19.13%) had vascular disease; 38 had arterial involvement (2.3%). 33 men and 5 female with a sex-ratio of 6.6. The mean age was 30 year-old (18-53), disease duration to diagnosis 6.1 years. Arterial aneurysm accounted for the majority of the cases, 33 patients (86.84%), 8 patients had occlusive disease and 8 patients had an arterial thrombosis.
Anatomical site distribution was as follow: 18 pulmonary, 6 abdominal aorta, 4 common femoral, 2 external iliac, 2 internal carotid and one right coronary artery lesion. 19 Patients had concomitant deep venous thrombosis. 4 patients presented a Hughes Stovin Syndrome.
We report an unusual case of coronary artery aneurysm associated with right ventricular thrombus presenting with an acute coronary syndrome.
All our patient received high dose corticosteroid and immunosuppressive therapy which consisted of IV cyclophosphamide and azathioprine. 10 patients underwent vascular surgery. 28 patients were treated medically. Eight patients treated medically had a positive outcome with complete regression of the aneurysms.5 cases of death were noted unfortunately.
Conclusion. Arterial damage during MB is rare, however it is life-threatening. It is necessary to think of it in the young person in an evocative context in order to be able to intervene before the stage of complications.

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Sweet syndrome lesions associated with Behçet disease: a true association?

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Introduction. Sweet syndrome (SS), or acute febrile neutrophilic dermatosis, is characterized by fever and erythematous papules, plaques, or nodules with a predominantly neutrophilic dermal infiltrate on histopathologic examination. It may be further categorized into classic, malignancy-associated, and drug-induced subtypes However, SS in association with Behçet's disease has been reported only in few patients.
Aims. We report tow patients who developed SS lesions during follow-up after the diagnosis of BD.
Methods. We studied the file whose developed SS lesions during follow-up after the diagnosis of BD.
Results. *Observation 1* A 46-year-old woman, who had been diagnosed with BD 17 years prior because of recurrent oral aphthae, arthritis and pathergy test positivity, was being treated by colchicine. She was admitted with arthritis of her wrists and ankles. Physical examination revealed 38.2° fever with cardiopulmonary auscultation without abnormalities, Dermatologic examination revealed painful, raised, erythematous papulesplaques, with variable dimensions , that were initially located on her arms, but then extended to her neck, trunk, forearms and wrists. Laboratory parameters were as follows: white blood cell count was 12 800/mm3 (neutrophils 9140/ mm3); CRP elevated to 124 mg / L, fibrinogen = 6.25g / L. ASO were all within normal limits. The pulmonary x-ray and abdominal ultrasonography results were unremarkable. Histopathologic examination of the skin biopsy taken from the erythematous plaque found on her right arm demonstrated a discrete spongiotic epidermis, abundant edema of the papillary dermis was observed, superficial and medium dermis were the site of a moderately abundant inflammatory infiltrate rich in neutrophils in leukocytoclasia, predominant around capillary vessels, without visible fibrinoid necrosis. The patient was diagnosed with SS associated with BD, and oral prednisolone 40 mg/day was initiated with colchicine. The pain and erythema decreased dramatically within 5 days.
Observation 2 A 55-year-old man, who had been diagnosed with BD 20 years prior because of recurrent oral and genital aphthae, arthritis and pathergy test positivity, was being treated by colchicine. He was admitted with fever. Physical examination revealed 38.2° fever with cardiopulmonary auscultation without abnormalities.Dermatologic examination revealed painful, raised, erythematous papules, and plaques located on his arms. Laboratory parameters were as follows: white blood cell count was 13 000/ mm3 (neutrophils 10140/ mm^3); CRP elevated to 70 mg / L. Histopathologic examination of the skin biopsy taken from the erythematous plaque found on his arm showed an abundant edema of the papillary dermis, superficial and medium dermis were the site of a moderately abundant inflammatory infiltrate rich in neutrophils, without visible fibrinoid necrosis. The patient was diagnosed with SS associated with BD, and oral prednisolone 50 mg/ day was initiated with colchicine.
Conclusion. Differentiation between Sweet syndrome associated with Behçet disease and Sweet syndrome lesions seen in Behçet disease is extremely difficult. One of the main distinguishing features is that HLA B51 is more common in BD, whereas HLA B54 is predominantly positive in SS. Another feature for differential diagnosis is the lack of fibrinoid necrosis on vessel walls in Sweet syndrome. In the histopathologic examination of our patients's biopsie, no fibrinoid necrosis was observed.

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Initial visit symptoms in probable Behçet's predictive of ISG criteria Behçet's: data from New York and Amsterdam cohorts

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Introduction. Behçet's syndrome (BS) is formally diagnosed using the International Study Group (ISG) criteria (1), where recurrent oral ulceration and any two other symptoms (recurrent genital ulceration, uveitis, skin lesions and pathergy positivity) are required. The allowance of various symptomology in the ISG criteria has led to the reporting of varied manifestations (1), and differences in clinical presentation can complicate BS diagnosis, especially in areas where the disease prevalence is low.
Aims. To explore clinical BS symptoms present at initial patient visit that are predictive of ISG criteria diagnosis at follow-up.
Methods. Data from consecutive patients monitored in outpatient clinics in New York and Amsterdam were abstracted. Patients were included if diagnosis at initial visit was "suspected" or "probable BS"; patients given a formal diagnosis by ISG criteria at initial visit or a non-BS diagnosis at initial visit were excluded. Demographic data, including ancestry/ethnicity, clinical symptoms, duration of symptoms and RAPID3 were abstracted from initial visit, with follow-up ISG status (defined as meeting criteria ISG+ vs not meeting criteria ISG-) abstracted from last visit. Ancestry/ethnicity were aggregated by endemic (Turkey, Asia, Middle and Far Eastern countries, Arabic countries and Northern Africa) versus non-endemic (Italy, Greece, Spain, Portugal as well as African-American and White NY).
Univariable logistic regression was used to screen initial visit clinical features and symptoms with follow-up ISG status. All variables that passed screening at $p \leq 0.10$ were included in the final multivariable model (2).
Results. 189 patients were included: 169 from NY and 20 from Amsterdam. 71 (37.6%) patients were classified as ISG+ with an average of 9.4 years (± 8.3 years) of symptoms. Age, gender, ethnicity, duration of symptoms at enrollment, duration of follow up as well as RAPID3 and almost all clinical manifestations at baseline were comparable between ISG+ And ISG- patients. Presence of morning stiffness, family history of BS, genital ulceration, labial ulceration, skin lesions, eye disease and retinitis were each identified in the univariable model as being possibly associated with prevalence of ISG+. The final multivariable model did not include correlated symptoms (*i.e.* genital and labial ulceration as well as eye disease and retinitis). In the final model, presence of morning stiffness, genital ulcers, skin lesions, and eye disease were associated with increased odds of ISG+, adjusting for age, symptom duration and family history (Figure). Area under the curve was 0.718, indicating acceptable predictive capability of the final model (2).
Conclusion. Based on our data, over a third of patients with suspected or probable Behçet's developed new manifestations over time that led to classification as ISG+ Behçet's. Despite development of these new manifestations, the presence of morning stiffness, genital ulcers, skin lesions, and eye disease at initial visit were independently associated with significantly higher odds in developing ISG+ Behçet's during follow up.
References

1. Criteria for diagnosis of Behçet's disease: International Study Group for Behçet's Disease. *Lancet* 1990; 335 (8697): 1078-1080.
2. Hosmer DW, Lemeshow S: *Applied Logistic Regression* (2nd ed), 2000. Wiley & Sons; New York.

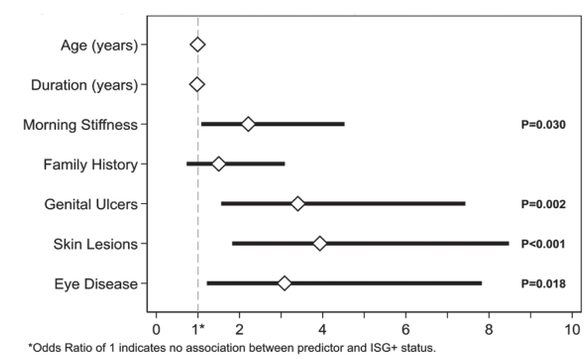

Fig. 1. Odds ratios and 95% confidence intervals from the logistic regression model prediciting ISG+ status.

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Clinical characteristics of parenchymal neuro-Behçet's disease: a single-center retrospective analysis

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Introduction. Neurological involvement is one of the most serious complications in Behçet's disease (BD). Parenchymal neuro-Behçet's Disease (p-NBD) accounts for the majority of NBD cases[1].
Aims. The aim of the study is to investigate the clinical characteristics of parenchymal neuro-Behçet's Disease.
Methods. We retrospectively reviewed all the medical records of BD patients admitted to Peking Union Medical College Hospitalfrom 2000 to 2016. The diagnosis of neurological involvement was based on the criteria of 2014 International Consensus on NBD[2]. Eighty-four BD patients without neurological involvement were randomly matched by sex and age as a control group. Clinical data including demographics, clinical features, laboratory and imaging studies, treatment and outcome, were extracted and analyzed.
Results. Of the 1009 BD patients hospitalized, NBD was documented in 62 patients (6.1%) and a total of 42 patients had parenchymal involvement (4.2%, male/female ratio 1.47:1). Their age at BD and the neurological onset was 30.0±11.1 and 35.3±12.1 years old, respectively. Neurological onset was concomitant with the onset of BD in 6 cases (14.3%). Pyramidal signs (21/42, 50.0%) and headaches (14/42, 33.3%) were the most common manifestations of p-NBD. On cranial MRI, the lesions were mainly in the midline structures and hyperintense in the T2-weighted image. The most common site of involvement was the brainstem (23/42, 54.8%) and the hemisphere (22/42, 52.4%). Spinal cord involvement was observed in 5 cases, 4 of which with cervical cord involvement. Thirteen cases had multifocal lesions. Compared with the controls, ocular involvement (uveitis, retinal vasculitis, scleritis) was more prevalent in p-NBD (35.7%) (p=0.041, OR=2.36,95% CI=1.03-5.44). Lumbar puncture revealed increased opening pressure in 8 cases (20%, 8/40) and mildly elevated CSF protein in 22 cases. Among the 20 patients with CSF cytological examination, 9 showed mixed pictures with lymphocyte predominance. All patients received corticosteroids and 23 (54.8%) received methylprednisolone pulse therapy(1g/d). Forty patients were treated with immunosuppressants, cyclophosphamide was the most commonly used immunosuppressant (39/42), and nine cases required multiple immunosuppressants combination. Biological agents (Infliximab, Tocilizumab, interferon-α2a) were administrated in six refractory p-NBD patients, all proved effective with significantly decreased Rankin score (p=0.002), as well as successful dosage tapering of corticosteroids and immunosuppressants. With a median follow-up of 28 months, 22 patients (61.1%) achieved clinical improvements, while 10 patients (27.8%) relapsed and 4 patients died (mortality rate 11.1%).
Conclusion. p-NBD is a disabling or life-threatening complication despite its rareness and occurs more often in male patients. Ocular involvement is a risk factor for p-NBD. Early identification and active treatment are essential for improving prognosis, glucocorticoids and immunosuppressants are the major therapies,and biological agents might be promising in treating refractory cases.

References

1. YOON D.-L *et al*.: Neuro-Behçet's disease in South Korea: clinical characteristics and treatment response. *Int J Rheum Dis* 2014; 17: 453-8.
2. KALRA S *et al*.: Diagnosis and management of Neuro-Behçet's disease: international consensus recommendations. *Journal of Neurology* 2014; 261: 1662-1676.

P103

Impaired oral ulcer suppression and composite index score in Behçet's disease: multinomial logistic regression analysis for oral ulcer activity

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Introduction. Factors associated with oral ulcer activity is unsufficiently explored with a patient-reported outcome (PRO) measure in Behçet's disease (BD).
Aims. The aim of this study was to assess factors associated with impaired oral ulcer suppression and Composite index score (CI), a validated patient-reported outcome measure for the assessment of oral ulcers, in BD.
Methods. In this cross-sectional study, 834 BD patients from 12 tertiary clinics in Turkey were analysed. Oral ulcer activity was assessed according to treatment protocols (immunosuppressive (IS) vs non-immunosuppresive (non-IS) treatments), gender, smoking pattern (non-smoker vs current smoker) and disease duration (less than 5 years vs ≥5 years). Disease severity was categorized as mild vs severe according to major organ involvement. Oral ulcer activity was evaluated by a "Composite index" score which include the presence of active oral ulcer (1 point), pain (5 points) and functional limitations (4 points) during the previous month (0-10 points). In active patients, the cut-off point of CI was selected as 6 points (the median value for low vs high oral ulcer activity (OUA)). The score was categorized as inactive (CI=0), CI<6 points for low OUA and CI≥6 points for high OUA groups. These categories were used as dependent variables in multinomial regression analysis according to inactivity vs low OUA and inactivity vs high OUA.
Results. The mean CI score, number and healing time of oral ulcers were 6.0±2.3, 2.9±2.7 and 7.1±4.1 days during the previous month in patients with active oral ulcers (n=543; 65,1%). The ratios of male gender (54,6%) and severe disease course with IS use (34,3%) were higher in inactive patients than low OUA (43,5% and 15,4%) and high OUA groups (42,8%; 16,8%) (p<0.05). Being a current smoker (32,6%) and disease duration more than 5 years (66,7%) were also associated with inactive oral ulcer pattern than low OUA (23,9% and 53,6%) and high OUA groups (22,9% and 56,5%) (p<0.05).
Decreases in the number (low OUA: 2,1±1,5 vs high OUA: 3,6±3,2) and healing time of oral ulcers (5,8±3,01 days vs 8,2±4,5 days) were seen in low OUA compared to those of high OUA (p=0.000 for both). Similarly, increases in scores of CI (high OUA: 7,8±1,3 vs low OUA: 3,9±1,3) and its subscales pain (4,1±0,9 vs 2,02±1,1) and functional limitation (2,7±0,8 vs 0,9±0,7) were seen in high OUA compared to those of low OUA (p=0.000 for all).
In multinomial regression analysis, mild disease course with non-IS use (odds ratio (OR): 3,04), mild disease course with IS use (OR:2,5), severe disease course with non-IS (OR:3,8) and disease duration less than 5 years (OR:1,8) were predictive factors for low OUA (p<0.05). In addition to all, being a current smoker (OR:1,5) was also associated with high OUA (p<0.05).
Conclusion. Composite index score as a PROM was associated with the disease course, treatment modalities and disease duration in BD. Being a non-smoker was also observed to be a critical factor for high oral ulcer activity. "Composite index" as an organ-specific activity index might be a candidate scale for the clinical follow-up and therapeutic studies in BD.

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Outcome of short-term Infliximab treatment for sight-threatening uveitis in Behçet's disease: a single center experience

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Introduction. Previous recommendations on the use of anti-TNF agents in BD included the administration of a single infusion of infliximab, 5 mg/kg for acute, unilateral, posterior uveitis with significant reduction of visual acuity (<0.2), whereas in cases of bilateral posterior eye segment inflammation a single infusion of infliximab could be used as a first-line agent to achieve a fast-onset response, along with the an appropriate immunosuppressive drug (Sfikakis PP *et al*., Rheumatology 2007). Moreover, our recent study suggested that long-term remission is feasible after discontinuation of successful continuous anti-TNF treatment given for severe BD, including ocular involvement (Sfikakis PP *et al*. Arthritis Rheumatol 2018).

Aims. We aimed to retrospectively examine whether long-term remission is also feasible for patients with ocular BD who received short-term infliximab.
Methods. We identified all patients with BD followed up in our center since 2001 at least once yearly, who received short-term biologic treatment for ocular disease, i.e. one to three IV infusions of Infliximab. Study's endpoint was the proportion of patients remaining in complete ocular remission for at least 3 years after cessation of Infliximab.
Results. We identified 13 patients who received one (n=2), two (n=1) or three (n=10) IV Infliximab infusions (5 mg/kg each) for sight-threatening posterior ocular inflammation, either at the first attack (n=6) or for relapsing uveitis (n=7). Infliximab was given as monotherapy (n=1), or as add-on to azathioprine (n=9) or to azathioprine in combination with cyclosporine (n=3). Twelve of thirteen (92%) patients had a complete initial response to Infliximab, whereas the remaining patient responded subsequently to Interferon. Of the 12 patients only one experienced a posterior uveitis relapse after 6 months. The remaining 11 patients (85%), aged 50±13.9 years, 64% male, disease duration 7.9±4 years, achieved sustained ocular remission for a mean of 7±3.8 years (range 4-14.3 years). Notably, 4/11 patients who achieved the study's endpoint were also able to discontinue azathioprine and are currently any drug free.
Conclusion. Sustained long-term remission is feasible in cases of BD uveitis receiving short-term IV anti-TNF treatment. Whether limited infliximab infusions should be administered promptly in all patients with posterior uveitis should be examined in additional studies.

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Oral ulceration in Behçet's disease: spot the difference!

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Introduction. Behçet's Disease (BD) is characterised by oral and genital aphthous ulceration and is complicated by multisystem involvement that includes eye, skin, joint and CNS lesions. As there is no diagnostic test for BD, diagnosis relies on clinical criteria. The International Study Group Criteria for BD requires the presence of minor, major or herpetiform aphthous ulcers at least 3 times in one 12 month period. Oral ulcers are frequently the first sign and present in nearly all BD patients (1). However, oral ulceration may present in a variety of forms and is a significant manifestation of several diseases,including Mucous Membrane Pemphigoid (MMP) and Irritable Bowel Disease (IBD) among others, making early diagnosis for the clinician challenging.
Aims. The aim of this study is to define the clinical characteristics of Behçet's ulcer which should allow differentiation from other causes of oral ulceration by an International Delphi consultation. By doing this, it will consequently feed into future clearer guidance for other non-oral medicine specialists of when the suspicion of BD in a patient with history of oral ulceration should be raised, and when to further investigate accordingly.
Methods. The Delphi method is a widely used and accepted method for seeking consensus among experts within a certain topic (2, 3). International BD experts will be invited to participate in this Delphi consultation and the following rounds will be conducted:
Round 1: The international panel of experts will be formed following invitation via email. The initial questionnaire will include forty clinical pictures which will be circulated to the expert panel to discuss variables and features for the inclusion in the aim to define the phenotype of the ulcers in patients with BD verses IBD, versus MMP and RAS.
Round 2: A questionnaire defining the clinical characteristics of these ulcers will be created. Participants will rank their agreement with each statement in the questionnaire The information will be summarised and included in a new version of the questionnaire for the participants to see.
Round 3: Participants will then re-rank their agreement with chance to change their score following disclosure of the results. A consensus should be reached
Results. Results of the Delphi consultation will be presented and further guidelines for the non-oral specialist will be formulated to enhance earlier and more accurate diagnosis of BD
Conclusion. This is the first time an attempt to define the specific clinical characteristics in oral BD through Delphi consultation has been conducted. We hope this international collaboration will allow increase awareness of BD as a possible differential diagnosis among other causes of oral ulceration within non oral medicine and non BD experts and reduce time from clinical onset to diagnosis in the hope of improving patient care and quality of life.
References
1. MAIN DM, CHAMBERLAIN MA: Clinical differentiation of oral ulcerationin Behçet's disease. *Br J Rheumatol* 1992; 31: 767-70.
2. THE DELPHI METHOD: An experimental study of group opinion. *Rand Corporation Dalkey* 1969.
3. ROWE AND WRIGHT: The Delphi technique as a forecasting tool: issues and analysis. *International Journal of Forecasting* 1999; 15: 353-375.

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Analysis of distribution pattern using lesion probability mapping in parenchymal neuro-Behçet's disease

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Introduction. One of the most disabling complications of Behçet's disease is neurological involvement. Neuro-Behçet's disease (NBD) is seen in 5-15% of the patients. NBD usually presents with parenchymal lesions or cerebral sinus venous thrombosis. Localization of the parenchymal lesions usually has a unique distribution pattern that involves the mesencephalo-diencephalic region and brainstem. However, there are inadequate studies that analyze the precise distribution pattern of the brain parenchymal lesions.
Aims. In this study, we aimed to define the distribution pattern of the parenchymal lesions in the brain using probability mapping.
Methods. We used non-standardized brain magnetic resonance images (MRI) of the patients with p-NBD. Boundaries of the lesions in the axial T2 weighted images were marked as polygons and converted into high definition raster datasets. Digitalized lesions are transferred onto a standardized brain template with 7 mm section thickness. Spatial analyses are performed to sum up intersected boundaries using GIS software.
Results. We included 52 brain MRI's of 50 patients with an acute lesion in our study. Based on the lesion topography, the most frequently affected regions were ponto-mesencephalic junction that is followed pons and thalamus. Interestingly, lesions tend to be localized in the central structures of the brainstem.
Conclusion. In this study, we employed a novel and simple technique to create lesion probability maps using non-standardized images. In the previous studies of p-NBD, brain lesions were localized using inexact anatomical regions. Our study provides visual probability maps with precise localizations. The reason why ponto-mesencephalic junction is more vulnerable in NBD may shed light on the pathophysiology of Behçet's disease.
References
1. AKMAN-DEMIR G, SERDAROGLU P, TASÇI B: Clinical patterns of neurological involvement in Behçet's disease: evaluation of 200 patients. The Neuro-Behçet Study Group. *Brain* 1999; 122(Pt 11): 2171-82.
2. KOÇER N, ISLAK C, SIVA A, SAIP S, AKMAN C, KANTARCI O, HAMURYUDAN V: CNS involvement in neuro-Behçet syndrome: an MR study. *AJNR Am J Neuroradiol* 1999; 20(6): 1015-24.

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Osteonecrosis in Behçet's disease: an iatrogenic secondary disorder or a downplayed comorbidity?

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Introduction. Behçet's disease (BD) is a multisystemic disease classified among the vasculitis. It's characterized by oral and genital aphthosis, cutaneous, ophthalmic, neurologic, or rheumatologic manifestations. BD patients with severe organ involvement such as ocular abnormalities require systemic corticosteroid in combination with other immunosuppressive agents. The prevalence, and often the severity of BD, is increased in the Middle East and the Mediterranean regions. Osteonecrosis (ON) is defined

as the death of bone marrow and trabecular elements due to interruptions of the blood supply to the bone.
Aims. The aim of this study is to present an unprecedented series of BD patients with concurrent osteonecrosis.
Methods. We used our database of BD population in our referral Behçet's clinic. In this case series, we aim to introduce a unique subgroup of 18 BD patients who developed ON throughout the course of disease.
Results. Total number of 18 BD patients were diagnosed with avascular necrosis. The development of avascular necrosis in one patient was distributed at different time points. In 15 patients, the elaborate chronology of clinical events were recorded. The mean time interval between arthralgia and diagnosis of avascular necrosis was 7.32 months. In the unique patient with four osteonecrotic joints, 5 months in hip joint and 18 months in shoulders. In AVN subgroup, oral aphthosis was the most common initial BD sign. Thirteen cases (72.2%) developed skin lesions in the course of disease. On the other hand, 14 cases (77.8%) ocular lesions developed. Among AVN patients, vascular lesions were comparatively more common (33.4%) than general BD population (6/18). These vascular lesions comprised of 4 deep vein thrombosis, 2 aneurism and 1 pulmonary vasculitis.
Conclusion. Joint pain without the evidence of arthritis must alert the clinician related with the risk of bone infarctions. In spite of rarely incidence, AVN is a costly complication of BD.

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Cardiac involvement in Behçet disease in a Tunisian cohort

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Introduction. Cardiac involvement in behcet disease (BD) is rare accounting for 1% to 6%.
Aims. We aimed in this work to describe clinical manifestations and therapeutic options of BD in a Tunisian context
Methods. We retrospectively studied 281 records of BD patients (mean age= 31 years, sex ratio M/F= 2.26) followed between January 2004 and December 2017 in the Internal Medicine Department and who fulfilled the ISGBD criteria. Only patients with cardiac manifestations were described.
Results. Cardiac involvement was seen in 6 patients (2.13%) with a mean age of 30 years (18 to 38 years). They were 5 males and 1 female. Cardiac manifestations were: pericarditis in one case (16.7%), myocarditis which was revealing the disease in 1 case (16.7%), intra cardiac thrombosis in 2 cases (33.3%) and myocardial infarction in 2 other cases (33.3%). Cardiac manifestations were associated to deep venous thrombosis, inferior vena cava thrombosis, pulmonaryembolism and arterial aneurysm in one case each. Extra cardiac manifestations were oral aphtosis (100%), genital aphtosis (83.3%), necrotic pseudofolliculitis (83.3%), erythema nodosum (16.7%) and ophtalmic manifestations (50%). Treatment consisted in high doses of steroids with 6 pulses of cyclophosphamide monthly relayed by azathioprine per os with a good outcome.
Conclusion. Even if cardiac involvement in BD is rare, it should be known by physicians especially cardiologists given that cardiac manifestations could be the revealing symptoms.

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The assessment of work productivity and activity impairment in patients with Behçet's disease: a multi-national study

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Introduction. Chronic diseases like Behçet's disease (BD) may affect work productivity and daily life activities.
Aims. The aim of the study was to evaluate work productivity and daily activity impairment in patients with Behçet's disease (BD) in a multi-national study.
Methods. Behçet's disease (n=197) patients from Jordan (n=50), Brazil (n=46), United Kingdom (n=41) and Turkey (60)(F/M: 100/97, mean age: 40.7±11.6 years) were included in this cross-sectional, multi-national study. Disease duration was 14.2±9.7 years. A questionnaire regarding the Work Productivity and Activity Impairment (WPAI) scale as a patient-reported outcome measure (PROM) and Behçet's disease Current Activity form (BDCAF) was used. Hours missed from work due to health problems and other reasons, hours actually worked and work productivity were evaluated by a 10-mm visual analogue scale (10-cm VAS, 0=no effect-10=severe effect) in currently employed patients (n=92). Daily activities (0=no effect-10=severe effect) for all patients (n=197) were evaluated by using WPAI during the last week. Absenteeism, presenteeism (reduced productivity at work), overall work impairment combining presenteeism and absenteeism in employed patients and daily activity impairment outside of the work were also calculated with WPAI. A transformed BDCAF score was used to evaluate the disease activity during the previous month.
Results. Employed patients (n=92, 46.7%) were younger (38,8±10,6 vs 42,4±12,3 years, p=0.045) and better-educated (12,1±3,7 vs 9,7±4,0 years, p<0.0001) compared to unemployed patients. Working hours were lower in females (32,4±17,7) than males (41,8±13,4) (p=0.01) in the employed group. In WPAI, scores of absenteeism (4,6±14,5), impaired productivity at work (35,8±30,7) and overall impairment (34,6±30,2) correlated with BDCAF score (5,1±3,3) in employed patients (r: 0,3 p=0.013; r: 0,3 p=0.005 and r:0,4 p=0.001). In addition, BDCAF score (5,3±3,4) also associated with impaired productivity at work (33,1±30,0) and overall impairment (31,6±28,8) in employed patients with major organ involvement (n=72, 36,5%) (r:0,4 p<0.0001 and r: 0,4 p=0.003).
Score of daily activity impairment (39,9±34,6) was lower in employed patients (33,7±31,5) than unemployed group (45,4±35,9 p=0.04). BDCAF score (3,9±3,4) correlated with daily activity impairment in the study group (r: 0,3 p=0.003). Moreover, daily activity impairment (39,7±35,5) also related with BDCAF score (4,6±3,6) in patients with major organ involvement (n=154, 78,2%).
Conclusion. Poor work productivity and impaired daily activity was observed in BD patients with major organ involvement, using WPAI as a patient-reported outcome measure. However, as two different time durations were evaluated (BDCAF for the last month and WPAI for the last week according to their scoring procedures), a weak correlation was observed among disease activity and work productivity/daily impairment.

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Juvenile onset Behçet's disease, a retrospective study of 60 patients

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Introduction. Behçet's disease (BD) is a multi-organ inflammatory disorder of unknown etiology affecting young adults .The usual onset of disease is between the second and the forth decade. It is rarely described in a children population, its prevalence is estimated at 0.9% - 7.6%.
Aims. To evaluate the clinical features of juvenile Behçet's disease and to compare them to the adult form.
Methods. We conducted a descriptive retrospective study of children with clinical diagnosis of BD presenting between 1981 and 2017. We collected 60 cases of juvenile Behçet's disease among a total of 1646 patients (3.64%) treated at a tertiary internal medicine department in Morocco. All patients met the classification criteria of the International study group. A juvenile BD was defined when the age of onset is less than 16 years old.
Results. There were 36 male and 24 female with a sex ratio of 1.5. The mean age of disease onset was 10.8 years (3-15). A family history of BD was found in 7 cases. Oral aphtosis was observed in 100%. Genital aphtosis was observed in 88.2%. Erythema nodosum was present in 26.7%, and cutaneous ulcers in 5%. Thirty seven patients (61.7%) had ocular involvement. Thirty three patients (55%) had arthritis, 6 patients (10%) had vascular disease, including 2 with superior vena cava thrombosis, 1 patient with internal jugular vein thrombosis and one patient had pulmonary artery aneurysm. 11 patients (17.7%) had neurological involvement, parenchymal disease in 7 patients, 3 patients had cranial nerve involvement and one patient had non parenchymal disease, and seven patients (11.7%) had gastrointestinal involvement.
Conclusion. Behçet's disease seems to have a different clinical phenotype in the children population. Familial form, neurological and digestive involvement are more frequent.

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A case of the Behçet's disease revealed by the panniculits

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Introduction. Panniculitis is an inflammation of the subcutaneous fat. Skin biopsy plays a critical role in the differential diagnosis of panniculitis. Many etiologies, including trauma, infectious disease and sometimes systemic diseases can be responsible for this disease. Its physiopathogy remains unclear. Few cases of Behçet's disease revealed by panniculitis were described in the litterature.
Aims. We report a case of panniculitis in Behçet's disease.
Methods. We studied the file of a patient with Behçet's disease revealed by panniculitis.
Results. 53-year-old patient with a history of central diabetes insipidus admitted for suspicion of panniculitis. He had a history of recurrent oral aphthous-like ulcers for 3 years. The physical examination revealed a genital and oral aphtosis and a positive pathergic test and dermohypodermal nodules sensitive, touching two legs and taking blue contusiform aspects. The neurological examination revealed a bilateralcerebellar syndrome and a pyramidal syndrome. In biology he had a biological inflammatory syndrome. Haemogram showed leukocytosis at 13400 / mm^3. Immunological assessment was normal. Brain imaging was normal. Infectious origin such as tuberculosis has been excluded. Histopathologic examination of the skin biopsy taken from the nodule showed the appearance of panniculitis. The diagnosis of Behçet's disease with neurological involvement associated with panniculitis was retained. The patient was treated with high dose corticosteroids and cyclophosphamide. Partial improvement in neurological involvement and panniculitis was noted. Four months later and during hospitalization for the 4th cyclophosphamide course, the patient experienced respiratory distress related to massive pulmonary embolism and died.
Conclusion. Panniculitis was rarely described during Behçet's disease. Deep biopsy is necessary to specify the type of involvement of the hypodermis and to propose a diagnostic hypothesis that will guide the management according to the etiology. As always, we must mention a pathology infectious reason for which to send part of the biopsy for bacteriological and mycobacteriological investigation. Our patient hadn't any infection and panniculitis lesions are related to Behçet's disease

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Leg ulcers in Behçet's syndrome: an observational survey in 24 patients

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Introduction. Formal experience with leg ulcers in Behçet's syndrome (BS) is limited. It is a relatively rare complication that can be seen during the course of mainly post-thrombotic syndrome. They can be difficult to manage and cause disability leading to unemployment and severe impairment in quality of life.
Aims. In this observational survey, we aimed to describe clinical characteristics of pts with leg ulcers.
Methods. A total of 24 pts (23 M/ 1F) that were seen in our out-patient BS clinic between May 2016 and January 2018 were evaluated with the help of a standardized questionnaire. Venous Doppler US and if necessary abdominal CT were used to evaluate localization of venous involvement. Biopsies were done if needed. Medical and other interventional treatments were recorded.
Results. The mean age at disease onset was 27.5±7.1 yrs (Table). The median time interval between the disease onset and ulcer development was 4.0 [2.5-11.5] yrs. The median follow-up was 7.8 [IQR: 2.9-14.2] yrs. Eleven (46%) were unemployed due to leg ulcers. Venous involvement was present in 20 pts (83%). Lower extremity vein thrombosis was present in all 20. It was mostly bilateral (15/20). The same 9/20 pts had other large vessel involvement. Four pts did not have any venous thrombosis or insufficiency. Histopathologic studies could be done in 3 and showed features of necrotizing vasculitis in 2 and venous stasis in the 3rd. A total of 12 pts (50%) had solitary ulcers while the remaining had 2 or more. We observed a total of 34 ulcers in 24 pts. They were mostly found around the medial malleolus (15/34) and the anterior surface of the tibia (14/34). Five pts had leg ulcers at unusual places such as lateral malleolus (n=2), popliteal fossa (n=1) and posterior surface of the tibia (n=2). Immunosuppressives including azathioprine, cyclophosphamide, interferon-alpha, infliximab and corticosteroids were used. Bed rest was advised to almost all. Iloprost infusions were given in 13 (54%) for a median duration of 6 mo. Additionally, larvae of Lucilia sericata were tried in 9 pts. Skin graft insertion was used in 2 pts, however, was successful only in 1. 17 ulcers in 11 (46%) pts healed in a median 24 mo [IQR: 9- 78]. In the remaining 13(54 %) pts 17 ulcers remained unhealed for a median 7 yrs [IQR: 5- 11], despite all treatment. The mean age at BS onset was significantly younger (24.4±5.4 vs 30.4±7.3 yrs; $p<0.05$) and the median time between disease onset and ulcer development was significantly shorter (3 [IQR: 1-4.5] vs 10 [IQR: 4-14 yrs, $p<0.05$] in pts with the healed ulcers. There were no apparent associations with the type of management and the severity of venous involvement.

Table. Demographic and clinical characteristics of the pts with leg ulcers in 24 pts with BS.

n (Male/ Female)	24 (23/1)
Mean age at disease onset	27.5 ± 7.1
Median time interval between disease onset and ulcer development,	4.0 [2.5-11.5]
Median follow-up duration	7.8 [2.9-14.2]
Unemployment due to the leg ulcers (%)	11 (46)
Eye disease, n (%)	7 (29)
Large vessel involvement (%)	9 (38)
Dural sinus thrombosis (%)	3 (12.5)
Vena cava sup.thr (%)	1 (4)
Pulmonary artery inv. (%)	5 (21)
Other arterial inv. (%)	1 (4)
Vena cava inferior-iliac vein thrombosis (%)	8 (33)
Lower extremity vein thrombosis (%)	20 (83)
Bilateral (%)	15 (62.5)
Femoral vein (%)	20 (83)
Popliteal vein (%)	14 (58)
Superficial vein (%)	7 (29)
No venous thrombosis or insufficiency (%)	4 (17)
Pts with a solitary ulcer (%)	12 (50)
Pts with more than 1 ulcer (>1) (%)	12 (50)
Pts with healed ulcers (%)	11 (46)
Pts with active ulcers (%)	13 (54)
Anatomical localization (total n =34)	
Medial malleolus (%)	15 (44 %)
Anterior surface of the tibia (%)	14 (41 %)
Other (%)	5 (5 %)

Conclusion. Leg ulcer develops mainly due to venous disease in the lower extremities. Peripheral arterial occlusive disease seems to be rarely associated. Leg ulcers may cause unemployment and be resistant to treatment. Ulcers that appear early during the disease course heal faster and are more responsive to treatment.

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Retrospective analysis of initial presentation findings of Behçet's syndrome throughout 4 decades

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Introduction.
There is some evidence that incident Behçet's syndrome (BS) might be becoming less severe (1, 2).
Aims. We compared clinical findings at presentation of BS patients registered in a large, long standing dedicated multidisciplinary outpatient clinic at 4 time points during a 40-year period.
Methods. There were 4 groups. Group 1 included patients registered in 1979- 1981, Group 2 those registered in 1990, Group 3 in 2000 and Group 4 in 2010. Only demographic and clinical findings at initial presentation were recorded on prepared forms.
Results. As shown in Table, over 4 decades, male/female ratio decreases gradually. While mean age at presentation does not change, the median disease duration got shorter. Almost all clinical manifestations except genital

ulcers and neurological involvement tended to decrease in frequency. This was also true when genders were separately analyzed. Importantly the severity of vascular and eye disease decreased. The slope of vascular disease was more obvious.

Table. Initial demographic and clinical characteristics of cohorts.

	Group 1 1979-81 cohort n=211	Group 2 1990 cohort n=170	Group 3 2000 cohort n=225	Group 4 2010 cohort n= 270	*P*
Male /Female	140/71	110/ 60	142/ 83	150/ 120	0.069
Male/Female ratio	1.97	1.83	1.71	1.25	
Mean age at disease onset	31.5 ± 8.3	30.9 ± 9.0	30.7± 9.3	32.3 ± 9.6	NS
Median disease duration	2.5 [1.0-6.0]	2.0 [1.0-5.0]	1 [0.5-3]	1 [0.6-4]	0.06
Mucocutaneous inv. , n (%)					
Genital ulceration	187 (88.6)	137 (80.6)	184 (81.7)	220 (81.4)	NS
Papulopustular lesion	174 (82.5)	130 (76.5)	187 (83)	185 (68.5)	<0.001
Erythema nodosum	132 (62.6)	88 (51.8)	101 (44.8)	112 (41.4)	<0.001
Ocular involvement, n (%)	107 (50.7)	107 (62.4)	97 (43.1)	129 (47.7)	0.001
Vascular involvement, n (%)	49 (23.2)	29 (17.0)	41 (18.2)	31 (11)	0.008
Large vessel involvement, n (%)	21 (42.9)	11 (38.0)	13 (31.7)	7 (22.5)	<0.001
Neurologic involvement, n (%)	7 (3.3)	6 (3.5)	5 (2.2)	10 (3.7)	NS
Arthritis, n (%)	79 (37.4)	37 (21.8)	53 (23.6)	56 (20.7)	<0.001

Conclusion. Our observations support the notion that incident BS might be getting milder. There might be a list of explanations for this observation. 1. It might be a true biological phenomenon due to changing environmental causes. In this line the significant decrease in papulopustular lesions could be due to a more sanitary environment while the rather unchanging frequency of neurologic involvement might be its possible independence from the environment. 2. It might be that the awareness of BS is increasing and we are recognizing less severe cases earlier. 3. Another explanation might be the more effective treatment these patients received before they were referred which was not specifically sought in this survey.

References

1. YOSHIDA A *et al*.: Comparison of patients with Behçet's disease in the 1980s and 1990s. *Ophthalmology* 2004.
2. CINGU AK *et al*.: Comparison of presenting features and three-year disease course in Turkish patients with Behçet uveitis who presented in the early 1990s and the early 2000s. *Ocul Immunol Inflamm* 2012.

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Renal involvement in Behçet's disease

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Introduction. Renal involvement is uncommon in Behçet's disease (BD).
Aims. The aim of this study was to investigate clinical and pathological characteristics of renal involvement in BD.
Methods. It is a retrospective analysis of 463 BD files in an internal medicine department over 18-year period. Patients who had renal involvement were included.
Results. Among BD patients, six men had renal involvement. Mean age at diagnosis of renal disorders was 30 year (extremes 23-53). Mean duration between BD diagnosis and renal disorders onset was 36.5 months (extremes 5-108). Five patients among six had vascular involvement (arterial aneurysm, deep venous thrombosis, vena cava thrombosis, Budd Chiari syndrome and intra-auricular thrombosis). Three patients had active disease at time of renal involvement onset; one patient had uveitis with retinal vasculitis, one had iliac artery aneurysm and the last had aortic aneurysm. Renal biopsy was performed in three cases; IgA nephropathy in one patient who presented with proteinuria at 4.35 g/24h and microscopic hematuria, mesangial proliferative glomerulonephritis in one patient (proteinuria was 1.3 g/24) and amylodisis in one patient. Amylodosis was diagnosed in two other patients who presented with intensive nephrotic syndrome, and was based on salivary gland biopsy and abdominal fat pad aspiration. Amylodosis was AA type in all cases. The sixth patient had isolated proteinuria at 0.5 g/24h. No patient had renal failure. Two patients with amylodosis were treated with prednisone 1mg/kg/day and the third one was given chlorambucil. Patients with active disease were already treated with immunosuppressive drugs and prednisone. Two patients died (heart failure and liver failure). Two patients were lost to follow up and three patients had good outcome with decreased proteinuria.
Conclusion. In different BD series like in our patients, amylodosis was the most frequent type of renal involvement. IgA nephropathy was also described in BD patients. Routine screening with urinalysis should be carried out for early detection of renal involvement.

References

1. ALTIPARMAK MR, TANVERDI M, PAMUK ON, TUNÇ R, HAMURYUDAN V: Glomerulonephritis in Behçet's disease: report of seven cases and review of the literature. *Clin Rheumatol* 2002; 21(1): 14-8.
2. KOSEMEHMETOGLU K, BAYDAR DE: Renal amyloidosis in Behçet's disease: clinicopathologic features of 8 cases. *Int Urol Nephrol* 2013; 45(3): 785-94.
3. ARDALAN MR, SADREDDINI S, NOSHAD H, EBRAHIMI A, MOLAEEFARD M, SOMI MH *et al*.: Renal involvement in Behçet's disease. *Saudi J Kidney Dis Transplant Off Publ Saudi Cent Organ Transplant Saudi Arab* 2009; 20(4): 618-22.
4. CHO SB, KIM J, KANG S-W, YOO T-H, ZHENG Z, CHO S *et al*.: Renal manifestations in 2007 Korean patients with Behçet's disease. *Yonsei Med J* 2013; 54(1): 189-96.

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Articular manifestations in Behçet's disease. A report of 121 cases

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Introduction. Articular manifestations in Behçet's disease (BD) is quite common and polymorph. Inflammatory arthralgia of the large joints is the most common manifestation.
Aims. The aim of this work is to estimate the prevalence and establish the epidemiological, clinical, therapeutic and evolutive profile of the articular manifestations.
Methods. We conduted a retrospective study of 296 patients who were followed for BD in our department, between Ocober 2005 and December 2017. All the patients fulfilled the international study group on Behçet's disease diagnostic criteria. Radiological assessment and antibody testing were obtained in all patients with arthritis.
Results. Articular manifestations were noticed in 121 out of 286 patients (40.8%), ranking third after cutaneo-mucosal and ocular manifestations of the disease. 65 male, 56 female (sex ratio=1.16), the mean age was 36.12 years at the time of diagnosis of BD. Joints involvement were the first disease manifestation in 19.8% (n=24). Inflammatory arthralgia was the most common manifestation and observed in 68.59%. Monoarthritis, polyarthritis, and oligoarthritis were observed in 7.4%, 10.7%, and 14.87%, respectively, most often occurring intermittently (70.24%). Knees (n=87) and ankles (n=65) were the most affected joints. A pelvi-axial involvement was noted in 5 patients, isolated lumbar pain in 6 patients. Unusual forms were observed: 1 case of pseudogout, 2 cases of destructive arthritis and 1 case associated with ankylosing spondylitis. The therapeutic options differ according to the clinical profile of the patients. 66 of the patients having concomitant visceral involvement requiring oral corticosteroids or/and immunosuppressants, had good clinical course. Among the 55 patients having mostly articular disease, 46 responded well to colchicine, non-steroid anti-inflammatory drugs or/and local corticosteroids. While 9 patients required low dose corticosteroids (n=4), methotrexate (n=2), hydroxychloroquine (n=2) and azathioprine (n=1).
Conclusion. Joint involvement in BD is generally benign, not engaging the functional prognosis. However, some cases can be particularly recurrent and destructive, for which new therapeutic alternatives can be proposed: azathioprine or even anti TNF. In our patients, the majority presented serious organ involvement and was treated aggressively making the articular disease paucisymptomatic.

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Recurrent venous thromboembolism disease during Behçet disease

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Introduction. One of the more frequent complication of venous thromboembolism disease (VTED) is recurrence that the occurrence have an etiological and therapeutic repercussions. the recurrent venous thromboembolism disease (RVTED) can occur during Behçet disease (BD).
Aims. To define the profile of RVTED during BD.

Methods. We compared 2 groups of patients admitted between January 2005 and December 2013. in our department for management of RVTED :
Group 1 (G1) : patients having BD as risk factor of VTED
Group 2 (G2): patients not having BD.
We excluded patients who were not admitted and those who had records with a lot of missing data.
Results. Between 1045 patients admitted for first venous thrombotic episode during the study period, 318 (11.2%) patients had RVTED. The mean age of these patients was 49.31 years. The sex-ratio was 1.87 (77 men and 41 women). Patients having RTVED relevant to BD (n=33; 28%) were significantly less frequent than those included in G2 (n=85; 72%). Numbers of recurrences were similar between 2 groups (1.34 in G1 and 1.13 in G2). The first episode of RVTED was revealing significantly (p=0.02) more frequently (p in G1 (57.5%) than in G2 (41.1%).
The mean age in G1(34.48 years) was significantly lower (p<0.05) than in G2 (55.07 years). The sex-ratio in G1 was 10, significantly higher than (p<0.05) in G2 (1.23). the average delay of risk factor diagnosis was similar between 2 groups (8.86 months in G1 and 9.65 months in G2. Frequencies of old patients and bedrest were significantly lower in G1 (p<0.05 and p=0.014 respectively) (6% and 3% in G1 respectively ; 20% and 36.4% in G2 respectively). The first episode of RVTED interested significantly more frequently (p=0.004) lower extremiities in patients without BD (95.2%) than in patients with BD (75.7%), but without significant differences concerning venous network and extent of these thrombosis. Frequencies of pulmonary embolism and others thrombotic localizations were similar between 2 groups. Comparaison of frequencies of the use of different therapeutic means and frequencies of different complications are presented in Table I.
Conclusion. The fact that endotheliopathy is the main pathophysiological basis of thrombosis during BD explain that RVTED were less recurrent in patients with BD than in those without BD.

Reference

1. NETZER NC, STOOHS RA, NETZER CM, CLARK K, STROHL KP: Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999; Oct 5; 131(7): 485-91.

Table I.

	Group 1 (BS patients with SVCS) (n=28)	Group 2 (BS patients with vascular involvement without SVCS) (n=80)	Group 3 (BS patients with no vascular involvement) (n=59)	Group 4 (Healthy controls) (n=80)	*p* value
Age, mean ± SD, years	44.3 ± 9.7	42. 1 ± 7.8	41.9 ± 5.9	42.7 ± 9.7	0.051
Disease duration, mean ± SD, years	18.7 ± 9.4	14.6 ± 7.7	12.5 ± 6.5		***0.001***
Hypertension, n (%)	4 (14.3)	6 (7.5)	2 (3.4)	4(5)	NS
BMI, mean ± SD	26.8 ± 4.7	26.4 ± 3.9	26.2 ± 3.3	27.0 ± 3.5	NS
High risk for OSA, n (%)	16 (57.1)	12 (15)	5 (8.5)	9 (11.3)	***< 0,001***

P117

Increased frequency of obstructive sleep apnea syndrome in Behçet's syndrome patients with vena cava superior thrombosis

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Introduction. Superior vena cava syndrome (SVCS), is a medical emergency and can also be seen in Behçet's syndrome (BS). Contrary to the severe outcome seen in malign conditions, SVCS in BS usually has a benign course, complicated rarely by hemoptysis, pleural effusion and a chylothorax. We had noted that BS patients with SVCS frequently complained of sleep disturbances, snoring and sleep apnea, suggesting an obstructive sleep apnea (OSA) disorder.
Aims. We aimed to determine the degree of risk for OSA among BS patients with SVCS and suitable controls using the Berlin questionnaire, a screening questionnaire for OSA with a high sensitivity and modest specificity (1).
Methods. Because of the lower frequency of female patients with VCSS (n= 2), only males were included. We studied 28 BS patients with SVCS (Group 1), 80 BS patients with vascular involvement without a SVCS (Group 2), and 59 BS patients with no vascular involvement (Group 3). Also 80 apparently healthy individuals (Group 4) of similar age and gender to BS patients were studied. The Berlin questionnaire was used to assess risk of OSA (1). Polysomnography was performed in patients at high risk for OSA according to the Berlin questionnaire.
Results. There were no differences regarding demographic characteristics, disease duration and variables associated with OSA among the groups (Table). The Berlin questionnaire categorized 57.1% (16/28) of the BS patients with SVCS (Group 1) as having a high risk for OSA and this was significantly higher compared to that found in the control groups. The frequency of those at high risk for OSA was 15%, 8.5%, 11.3% in Group 2, 3 and 4, respectively (p>0.05). Until now, polysomnography was performed in 12 subjects (5 patients with SVCS, 1 patient with vascular involvement without a SVCS and 6 healthy controls). OSA was detected in 3/5 patients with SVCS and 1/1 patient with vascular involvement without a SVCS and 4/6 healthy controls.
Conclusion. This study shows that BS patients with a history of VCSS are at high risk of OSA. This is probably due to the external pressure of the significant venous collaterals on the upper airways.

P118

Nodular regenerative hyperplasia in a patient with Behçet's disease and Budd-Chiari syndrome, receiving Azathioprine

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Introduction. Nodular regenerative hyperplasia (NRH) is rarely reported in patients with Behçet's disease (BD). Azathioprine (AZA) a drug frequently prescribed for the treatment of various BD manifestations, is considered to be one of the causes in the development of NRH.
Aims. We describe a 21 years old Arab male from Jordan, who presented with with recurrent abdominal pain, hepatosplenomegaly, and ascites, he had a 9 years history of recurrent oral ulcers, retinal vein thrombosis, IVC and left common iliac thrombosis and arthritis, 4 years ago developed Budd-Chiari syndrome (BCS), his grandfather had history of BD. He was given elsewhere methylprednisolone followed by oral prednisolone and Cyclophosphomide IV for 6 doses then maintained on AZA 100mg/day and colchicine 1mg/day. In addition he was on daily low molecular weight heparin.
Methods. On evaluation, the patient was alert. No jaundice or lymphadenopathy. An abdominal examination revealed hepatoslenomegaly, ascites and dilated collateral veins , pathergy test was positive. Hb 13.0 g/L, platelets 118 x 10^9/L, CRP 9.9mg/L (n <5.0), liver function tests revealed total protein 5.76 (n 6.4-8.3), albumin 3.8 g/dl, ALT 63.9 U/L, AST 51.5 U/L, GGT 285 U/L(n 12-64), alkaline phosphatase 146U/L(n 40-150), INR 1,18, renal function tests were normal, LDH, alpha –fetoprotein, CA 19.9 and CEA were normal. Screening for thrombophilia including anti cardiolipin antibodies, homocystine and Factor V Leiden were normal.
Abdominal ultrasound (US) showed enlarged liver with irregular contour and coarse heterogeneous nodular echo texture. There are multiple solid mass lesions noted in both lobes of the liver, the largest measuring about 4x3.5 cm. The portal vein and its branches appear dilated and patent with upper abdominal collaterals. The spleen enlarged
with about 7.3x6.7 cm solid mass lesion in the lower pole of the spleen. There is a gross ascites 2000 ml ascetic fluid aspirated which consisted of mesothelial cells and was negative for malignancy.

Liver biopsy showed Nodular areas devoid of fibrous tissue and portal tracts are seen in one core suggestive of NRH. Upper endoscopy is planned. Heparin and AZA was discontinued, dose of prednisolone was increased to 1mg/kg, plus diuretics. Mycophenalate mofetil 500mg x1 was started
Results. Our patient fulfilled ISG criteria for BD, he had BCS and developed NRH, The US report raised the possibility of malignancy, taking into consideration that some cases with BCS and IVC obstruction were reported to be complicated by the development of hepatocellular carcinoma. NRH is an uncommon liver condition as a result of obliterative vasculopathy and associated with chronic use of medications, namely AZA, which was reported to be one of the causes of NRH, especially in patients having TPMT mutations.
Conclusion. BD should be considered in the differential diagnosis of patients presenting with NRH and splenomegaly, in countries were the disease is prevalent. AZA should be used with extreme caution and close follow up in BD patients with BCS.

P119

Increased vein wall thickness in Behçet's syndrome

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Introduction. Lower extremity vein thrombosis (LEVT) is the key feature of vascular involvement in Behçet's syndrome (BS).Vein wall thickness (VWT) is proposed to be a surrogate marker of venous disease. A pilot MR study done in 7 BS patients and controls, had demonstrated increased VWT and signal enhancement in the lower extremity veins of BS patients without vascular disease (1). Another study, using USG, found that VWT was increased among BS patients without vascular disease compared to patients with ankylosing spondylitis and healthy controls (2).
Aims. We reassessed VWT in proximal lower extremity veins in BS patients with LEVT and suitable controls in a formal, masked protocol.
Methods. We studied 47 (40 M/ 7 F) BS patients with LEVT, 50 (43 M/ 7 F) BS patients without any vascular involvement and 38 (31 M/ 7 F) age and gender matched apparently healthy controls. Two independent radiologists, blinded to the diagnosis of BS, used USG to measure VWT of common femoral vein (CFV), superficial femoral vein (SFV) and vena saphena magna (VSM) in both legs.
Results. As shown in Table I, mean age at disease onset and the disease duration were similar between BS study groups. The mean age at thrombosis onset of the patients with LEVT was 26.4±5.8 years. There was good concordance between the 2 observers (kappa: 0.9) The mean VWT was significantly increased among both BS patients with LEVT and those without any vascular involvement when compared to the healthy controls while those with LEVT had the thickest veins.

Table I. Disease duration and VWT.

	BS with vascular involvement (n=47: 40 M/ 7 F)	BS without vascular involvement (n=50: 43 M/ 7 F)	Healthy controls (n=38: 31 M/ 7F)	P value
Age, years	37.06 ±5.26	36.98 ±4.47	34.87 ±7.22	0.296
Disease duration	10.96 ±6.45	9.68 ±5.89	-	0.310
Vein wall thickness, mean ± SD, mm				
Right CFV 1st observer	0.91± 0.67	0.69 ± 0.15	0.57 ± 0.11	0.001
Right CFV 2nd observer	0.93 ± 0.76	0.70 ± 0.18	0.58 ± 0.09	<0.001
Left CFV 1st observer	1.04 ± 0.85	0.66 ± 0.11	0.56 ± 0.07	<0.001
Left CFV 2nd observer	1.09 ± 0.83	0.69 ± 0.16	0.57 ± 0.07	<0.001
Right SFV 1st observer	0.79 ±0.38	0.60 ± 0.11	0.51 ± 0.9	<0.001
Right SFV 2nd observer	0.80 ± 0.42	0.62 ± 0.13	0.52 ± 0.07	<0.001
Left SFV 1st observer	0.88 ± 0.38	0.62 ± 0.12	0.49 ± 0.09	<0.001
Left SFV 2nd observer	0.90± 0.40	0.63 ± 0.13	0.51 ± 0.07	<0.001
Right VSM 1st observer	0.60 ± 0.22	0.52 ± 0.11	0.43 ± 0.07	<0.001
Right VSM 2nd observer	0.64 ± 0.25	0.53 ± 0.13	0.46 ± 0.08	<0.001
Left VSM 1st observer	0.67 ± 0.23	0.53 ± 0.11	0.42 ± 0.09	<0.001
Left VSM 2nd observer	0.65 ± 0.27	0.53 ± 0.11	0.43± 0.07	<0.001

Conclusion. VWT of proximal deep and superficial lower extremity veins was found to be increased among BS patients without any clinical and radiological vascular involvement.

References
1. AMBROSE N *et al*.: Magnetic resonance imaging of vein wall thickness in patients with Behçet's syndrome. *Clin Exp Rheumatol* 2014.
2. ALIBAZ-ONER F *et al*.: Venous vessel wall thickness in lower extremity is increased in male Behçet's disease patients without vascular involvement. *Ann Rheum Dis* 2017; 76 (Suppl. 2): 417.

P120

Patients with (suspected) Behçet syndrome: clinical presentation of 101 patients

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Introduction. Behçet's syndrome (BS) is a systemic vasculitis, which is most commonly seen along the Silk Road countries. In our center patients with (suspected) BS are seen and data on clinical presentation recorded. They are classified according to the International Study Group (ISG) criteria. Patients are considered ISG criteria positive when they have oral ulcers and 2 of the following genital ulcers, uveitis, skin laesions like e. nodosum and pathergy test positivity.
Aims. To analyse the first 101 patients of our cohort.
Methods. Cross-sectional cohort of patients with (suspected) BS in a non-endemic region.
Results. We included 101 patients, 73 of whom are female (72%), with a mean age of 39.9 years. Thirty-six of the patients came from Turkey, 22 from other Mediterranean/Arabic countries, 29 Whites / Caucasians, 10 from Asia and 4 patients were black.
ISG positive Behçet's syndrome was present in 37 patients (36.6%), in 45 the diagnosis was probable (44.6%) and in 19 patients (18.8%) it was concluded no BS was present.
The majority of ISG criteria positive patients were also female (76%, n=28). Clinical symptoms are described in Table I, for the entire population as well as ISG criteria positives only. The number of patients with loss of visual acuity in the patients with eye involvement is 5 of 27 in the entire cohort *i.e*.19% (95 confidence interval 8.2-36.7%), in the ISG positive Behçet patients there were 3 out of 16 (19%, 95% confidence interval 6.6-43.0%).
Colchicin, Prednisolone and Azathioprin were prescribed in 61 (60%), 47 (47%) and 25 (25%) patients respectively. TNF blockade was given, before entrance in the cohort, to 6 patients (3 of whom used more than 1 type). Furthermore, Methotrexate, Cyclosporin and Dapsone were prescribed in 10, 6 and 4 patients, respectively. Thalidomide was given to two (both developed neuropathy) and cyclophosphamide to 1 patient.
The mean RAPID3 score was 4.41, mean patient global was 5.75 and mean VAS Fatigue was 6.57 (all on a scale from 0 to 10).
The mean ESR was13.0 mm/hour (ranging from 1 to 51).

Table I. Clinical presentation of 101 patients with (suspected) Behçet Syndrome.

Manifestation	All, N=101 N, (%)	ISG positive, N=37 N, (%)
Oral aphthae	95 (94)	37 (100)
Genital aphthae	57 (56)	33 (89)
Skin involvement	37 (37)	27 (73)
Eye involvement	27 (27)	16 (43)
Loss of Visual Acuity	5 (19)#	3 (19)#
Venous thrombosis	5 (5)	2 (5)
Thrombophlebitis	11 (11)	7 (19)
Arterial involvement	2 (2)	1 (3)
CNS vasculitis	8 (8)	5 (14)
Gastro-intestinal involvement (diarrhea)	18 (18)	9 (24)
Arthritis	30 (30)	16 (43)
Epididymitis	2 (7)*	2 (22)*
Positive pathergy test	17 (17)	13 (35)

% of patients with eye involvement *% of male patients

Conclusion. In the first 101 patients of our cohort the disease was present in 37 patients, *i.e*. 37% (ISG criteria positive). Of them prevalence of disease manifestations are in agreement with other cohorts. The number of females is comparable to cohorts in other nonendemic regions (2). The percentage of patients with loss of visual acuity seems relatively high (2), when compared to other cohorts from nonendemic regions, it should be noted that the 95% confidence interval is wide

References
1. CRITERIA FOR DIAGNOSIS OF BEHÇET'S DISEASE: International Study Group for Behçet's Disease. *Lancet* 1990. 335(8697): 1078-80.
2. LECCESE P, YAZICI Y, OLIVIERI I: Behçet's syndrome in nonendemic regions. *Curr Opinion Rheumatol* 2017; 29: 12-6.

P121

Off-label use of biological agents in refractory Behçet's disease in Morocco

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Introduction. Behçet's disease is a chronic relapsing multisystem inflammatory disorder of unknown etiology, Ocular and neurological involvements are among the most serious and challenging manifestations of the disease.
Aims. To assess the efficacy of biological therapy in refractory ocular and neurological manifestations of Behçet's disease.
Methods. We report a retrospective study on 16 patients presenting ocular and/or neurological disease refractory to conventional immunosuppressive therapy, consisting of pulse cyclophosphamide and high dose corticosteroids, and requiring biologic therapy.
All the patients fulfilled the classification criteria of the International Criteria for Behçet's Disease (ICBD, 2014) and in Morocco treated at a tertiary internal medicine department over a 4 year period, 2014 to 2018.
Twelve patients had ocular disease, 8 received Infliximab, 5mg/kg IV infusion at week 0, 2, and 6 weeks then every 8 weeks, and 4 received Adalimumab, 40 mg every 2 weeks SQ.
Three patients had neurological disease and were treated with Tocilizumab, 8 mg/Kg IV infusion every 4 weeks.
The main outcome measures were the degree of anterior and posterior Inflammation and visual acuity improvement assessed on the Monoyer decimal scale. Patients with Neuro-Behçet were evaluated for symptom improvement and magnetic resonance imaging (MRI).
Results. Of the 16 patients included, 11 were male and 5 were female with sex-ratio of 2:1. The mean age was 30.6 years (18-44). The mean duration to diagnosis was 4.3 years (1-18).
12 patients had advanced bilateral ocular involvement, especially panuveitis, retinal vasculitis, serous retinal detachment and macular involvement. Vision acuity at diagnosis was estimated at counting fingers in 9 patients and 1/10 in 3 patients.
All Neuro-Behçet patients had parenchymal neurological disease, 4 brainstem, 2 hemispheric and 1 cerebellar involvement. 3 patients had concomitant ocular and neurological disease.
The overall response rate - complete and partial remission - was 83% and 80% for ocular and neurological disease respectively.
2 patients relapsed after going into remission, both of them were on Adalimumab.
Conclusion. Recent studies have shown biological agent to have remarkable efficacy in managing refractory Behçet's disease. Their use as first line therapy seems appropriate in critical presentations. Large clinical trials are needed to specify their use in the upcoming new guidelines.

P122

Work productivity is impaired in patients with Behçet's syndrome

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Introduction. Behçet's syndrome (BS) is most active during young adulthood and working years, thus affecting productivity. Work disability was previously reported especially among BS patients with eye, vascular and joint involvement.
Aims. In this study, we aimed to evaluate the work productivity and instability of patients with BS compared to ankylosing spondylitis (AS) patients and healthy controls (HC).
Methods. 125 (103 M/22 F) consecutive BS patients who were routinely followed in our dedicated BS center were studied. Patients with AS (30; 25 M/5 F) who were followed in the rheumatology outpatient clinic of our unit and HC (30; 18 M/12 F) were included as controls. Work Productivity and Activity Impairment Questionnaire (WPAI), Work Productivity Survey (WPS), Work Instability Scale (WIS) were used. Quality of life was assessed with the Behçet Disease Quality of Life (BDQoL) scale and disease activity with the Behçet's Disease Current Activity Index.

Table Characteristics of the included subjects.

	Behçet's syndrome (n=125)	Ankylosing spondylitis (n=30)	Healthy controls (n=30)
Male, n (%)	103 (82)	25 (83)	18 (60)
Mean (SD) current age,	36.1 ± 7.8	36.7 ± 6.9	31 ±8.1
Mean (SD) disease duration	8.1 ± 5.7	8.1 ± 5.7	N/A
WIS (mean±SD)	12.2 ± 9.8	11.4±5.6	6.1±4.3
WPAI-Absenteeism (mean±SD)	10.0±18.6	7.7±18.1	1.7±7.0
WPAI-Presenteeism (mean±SD)	37.0±29.5	32.1±24.6	9.3±21.0
WPS-Absenteeism (mean±SD)	1.8±4.2	1.3±3.4	0.1±0.3
WPS -Presenteeism (mean±SD)	4.2±7.0	4.1±6.2	1.2±3.3
BDCAF (mean±SD)	4.1 ± 2.7	N/A	N/A
BSAS (mean±SD)	22.5 ± 17.9	N/A	N/A
BDQoL (mean±SD)	19.7 ± 8.2	N/A	N/A
BASDAI (mean±SD)	N/A	3.4 ± 1.7	N/A
BASFI (mean±SD)	N/A	3.0 ± 2.8	N/A

N/A: Not applicable; Behçet Disease Quality of Life: BDQoL; Behçet's Disease Current Activity Index (BDCAI); Behçet's Syndrome Activity Score (BSAS)

Results. The mean age of BS patients was 36±7.8 and the mean disease duration was 8.2±5.6 years. 35 of BS patients with only mucocutaneous, 40 with eye, 28 with vascular and 22 with neurologic involvement were included. Among BS patients 42% reported missing work days (mean 1.8 days/mo), and 48% reported that their productivity was reduced at least by half (mean 4.3 days/mo). The mean WIS score was 12.2 (9.8) in BS patients. 59 BS patients had moderate and 18 BS patients had high work instability. Patients with BS had significantly higher absenteeism (10.0% vs. 1.7%), presenteeism (37.0% vs. 9.3%), and daily activity impairment (26.4% vs. 8.6%) than HCs (p<0.001) assessed by WPAI. Scores were similar between BS and AS patients. WIS and WPS scores were also similar between BS and AS patients and worse than healthy controls. Work impairment was more pronounced in patients with eye involvement compared to mucocutaneous involvement (p=0.04) and there were no differences between other BS groups. The WPAI presenteeism score was moderately correlated with Behçet Disease Quality of Life scale score (r=-0.57). Multivariate analysis showed that QoL (OR=0.77, 95% CI=0.66-0.88) and disease activity (OR=1.66, 95% CI=1.01-2.50) were related with WPAI-presenteeism.
Conclusion. Work productivity is impaired in BS patients, especially among those with eye involvement. Work instability is frequent and correlated with disease activity and quality of life.

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The relationship between Behçet's disease flare up and menstruation in an Irish cohort

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Introduction. Behçet's disease, which is a poorly understood autoinflammatory condition is commonly diagnosed during the reproductive years. Literature showed antiinflammatory properties in both progesterone and oestrogen hormones (1). There has been interest to determine the link between Behçet's Disease (BD) and menstruation. A Korean study also showed evidence of BD flare ups following the precipitous decline of progesterone at the onset of menstruation and after delivery (2).
Aims. This study was aimed to determine the effect of menstruation in triggering exacerbations of Behçet's disease in an Irish cohort.
Methods. A total of 18 female patients from a regional rheumatology centre fulfilling the International Study Group for Behçet's Disease (ISGBD) criteria were recruited. Telephone interviews were conducted to establish whether the occurrence of BD flare ups was correlated to the menstrual cycle.
Results. All 18 patients took part in the telephone interview, with the mean age of 38.8 years and mean age of menarche of 13 years. Four (22.22%) patients in our cohort were menopausal. 9(50%) of the patients reported that their BD flare ups were correlated to their menstrual cycle. The types of disease flare experienced include oral aphthosis (88.9%), arthralgia (55.6%), genital ulcerations (44.4%), lethargy (44.4%), skin lesions (11.1%) and

headaches (11.1%). Six of the seven patients (86%) from our cohort who were on contraception were on a progesterone containing contraception. Four out of nine (44%) who did not notice any flare ups during menstruation stated that they were on progesterone containing contraceptives. It is of note that 10 patients (55.56%) had previous pregnancies while 3 patients had an episode of miscarriage and 1 had a stillbirth.

Conclusion. The results from our study demonstrated that the disease activity in BD is related to the menstrual cycle, which is contributed by the female sex hormones. This study supports previous hypothesis that the abrupt decline in progesterone during onset of menstruation is associated with exacerbation of BD.[2] Detailed studies involving larger cohorts should be performed to further support and strengthen this evidence.

References

1. SZEKERES-BARTHO J, BARAKONYI A, PAR G *et al*.: Progesterone as an immunomodulatory molecule. *Int J Immunopharmacol* 2001; 1: 1037-48.
2. BANG D, CHUN YS, HAAM IB *et al*.: The influence of pregnancy on Behçet's disease. *Yonsei Med J* 1997; 38: 437-43.

P124

Pseudotumor cerebri syndrome without cerebral venous sinus thrombosis in Behçet's disease

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Introduction. Pseudotumor cerebri (PTC) syndrome is one of the common forms of neurological involvement in Behçet's disease (BD) which is generally due to cerebral venous sinus thrombosis (CVST) involving the transverse or superior sagittal sinuses. However some BD patients with PTC appear not to have had CVST, with patent venous sinuses.

Aims. Here we aim to review retrospectively BD-PTC patients without any evidence of CVST, seen in three Turkish university neurology/neuro-ophthalmology departments.

Methods. Records of neuro-Behçet and neuro-ophthalmology outpatient clinics of 3 Turkish universities were reviewed retrospectively. Essential criteria for the diagnosis of PTC were: 1. bilateral papilledema; 2. lumbar CSF pressure >250mmH2O; 3. no mass lesion or hydrocephalus on brain imaging. We searched for BD-PTC patients whose MRI and MRV with contrast did not show any CVST. These images were then reviewed by all the authors including a neuro-radiologist, to confirm that each of the studies was technically adequate to exclude CVST. Patients with technically inadequate scans were excluded.

Results. There were 8 patients with BD and PTC without any demonstrable CVST. They were aged 26-57 years, 3 were male, 5 were female. In 4 patients PTC was the presenting syndrome of BD; in these the diagnosis of BD was made when it became apparent that the patient also had symptoms and signs of systemic BD, particularly recurrent oro-genital ulceration. Cerebrospinal fluid examination showed that only 2 patients had >5 white cells in the CSF (all lymphocytes) and the protein levels were in normal range. In 4 patients PTC occurred in the course of known BD. One of these had been misdiagnosed as dural sinus thrombosis; however when the scans were re-evaluated they were found to show transverse sinus stenosis, rather than thrombosis.

Conclusion. In areas with a high prevalence for BD, it should be kept in mind in the differential diagnosis of patients presenting with PTC, especially when the patient is male. It should also be noted that PTC may occasionally occur in patients with BD without sinus thrombosis. A very common mistake is to consider a congenitally stenotic sinus as a sinus thrombosis. Therefore scans should be carefully evaluated in such cases.

P125

Non-aphthous beginning as an independent risk factor for the prognosis of Behçet's disease

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Introduction. Behçet disease (BD) is a multisystem inflammatory disorder characterized by recurrent manifestations in mucocutaneous tissues, eyes, joints, blood vessels, intestines and brain. Since there is no pathognomonic clinical and laboratory finding, diagnosis of BD relies on constellation of a group of manifestations. Recurrent oral aphthous ulcers (ROU) are the commonest manifestation, and widely used International Study Group (ISG) diagnostic criteria require ROU in all patients. However, some patients may not develop ROU at disease onset, which may cause a challenge in the diagnosis of BD.

Aims. This study aimed to investigate the disease course and appearance of the manifestations in those patients with or without ROU at the disease onset.

Methods. The study group consisted of 570 patients with a follow-up record between 1976 and 2016, and 449 of them fulfilled the ISG diagnostic criteria. All patients interviewed personally for their disease course and their medical records were investigated retrospectively. Differences in the disease course were analyzed according to the type of manifestations at the disease onset, sequence of appearance of other manifestations.

Results. Non-aphthous beginning (NAB) at the disease onset was found in 13.6% of patients, and it was more frequent among smokers compared to non-smokers (18.4% vs 6.8% in males, p=0.019; 22.9% vs 9.7% in females, p=0.038). Frequency of uveitis (54.1% vs 30.2%, p<0.001) and cardiovascular involvement (39.3% vs 24.2%, p=0.019) was higher in patients with NAB compared to the patients with ROU at onset. Both NAB group and ROU at onset group fulfilled the ISG diagnostic criteria within similar disease duration (median 48 vs 54 months). However, a 3-month delay was noted after the fulfillment of ISG criteria in patients with ROU at onset despite a 5.3-month delay in NAB group (p=0.003). Overall, the most frequent manifestations developing at the onset of BD were ROU, genital ulcers, and uveitis; and the latest manifestation during the course was pulmonary parenchymal involvement. Erythema nodosum-like lesions as initial findings were more frequent in females (11.3% vs 5.1%, p=0.024), and deep-vein thrombosis (DVT) was more frequent in males (4.6% vs 0.9%, p=0.04). NAB was identified as an independent risk factor for the development of uveitis (OR=2.06) and DVT (OR=2.25) by logistic regression analysis. None of the BD patients had arterial aneurysms or thrombosis, pulmonary parenchymal, gastrointestinal or genitourinary involvement as initial manifestations.

Conclusion. This retrospective study revealed that 13.6% of BD patients may not have ROU at onset, and those patients with NAB may have different features in their disease course. NAB may be considered as an independent prognostic factor for a more severe disease because of increased frequency of uveitis and cardiovascular involvement in those patients.

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The OMERACT core set of domains for outcomes measures in Behçet's syndrome

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Introduction. There is an unmet need for reliable, validated, and widely-accepted outcome measures for randomized clinical trials (RCTs) in Behçet's syndrome (BS). The Outcome Measures in Rheumatology Clinical Trials (OMERACT) Behçet's Syndrome Working Group has worked to advance the creation of a Core Set of data-driven outcome measures for use in all clinical trials.

Aims. To develop a core set of domains for all clinical trials investigating the various forms of Behçets syndrome.

Methods. The Core Domain Set was developed through a comprehensive, iterative multi-stage multi-year project that followed the methodologically rigorous processes and standards set forth by OMERACT: i) a systematic review; ii) a survey among experts in BS; iii) an outcome measures interest group meeting during the International Conference on Behçet's Disease; iv) qualitative patient interviews; v) a three-round modified Delphi exercise involving both patients with BS and a multidisciplinary set of physicians expert in BS, focused on obtaining consensus on the domains of illness necessary in the study of BS; and vi) utilization of the data, insight, and feedback generated by the outlined processes to develop a final Core Domain Set. The final Core Set was presented and put up for a vote of endorsement at the 2018 OMERACT meeting.
Results. All steps in the process outlined were completed. The systematic review clearly demonstrated the substantial variability in the domains studied in clinical trials of BS and a lack availability of validated outcome measures in BS. The survey of physicians, the in-person meeting of experts, and the qualitative research with patients all helped generate an extensive list of candidate domains and sub-domains to consider for use in RCTs. It also become clear that there was a need and strong interest in delineating domains across the several major organ systems involved in this disease and in recognizing that RCTs in BS often focus on specific manifestations and not the disease in its entirety. The Delphi involved 74 physician experts in BS from 21 countries and from within a wide range of specialties, and 64 patients from 10 countries. The Delphi utilized both ratings and rankings to prioritize 56 domains and sub-domains originally under consideration.
The final proposed Core Set included 5 sub-domains mandatory for study in all trials in BS, with additional sub-domains mandatory for study of specific organ-systems when that system is the focus of a trial: mucocutaneous (2 additional sub-domains), ocular (4), central nervous system (3), musculoskeletal (2), vascular (4), and gastrointestinal (2). The final Core Set was endorsed at the 2018 OMERACT meeting.
Conclusion. Multiple disease-related domains in BS have been identified by physicians and patients as important to address in clinical trials, leading to the development and endorsement of a final Core Set of Domains for use in clinical trials in BS. The Core Set provides the foundation through which the international research community, including clinical investigators, patients, the biopharmaceutical industry, and government regulatory bodies can harmonize the study of this complex disease, compare findings across studies, and advance development of effective agents.

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Investigation of clinical profile of Behçet's disease related versus idiopathic branched retinal vein occlusion

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Introduction. To compare the clinical features of branch retinal vein occlusion between Behçet's Disease related and idiopathic type.
Aims. To compare the long term results of the patients with branched retinal vein occlusion (BRVO) secondary to Behçet's disease with the patients with unknown etiology.
Methods. Medical records and optical coherence tomography (OCT) imaging results of the patients with BRVO secondary to Behçet's disease and with unknown etiology were reviewed retrospectively at a single center. Best corrected visual acuity (BCVA) at the diagnosis and the last visit were determined as logMar equivalents. The presence of injection, application of laser photocoagulation, involvement of the macula or optic disc, the anatomical location of BRVO were evaluated
Results. Sixteen eyes of 14 patients with idiopathic BRVO and 28 eyes of 23 patients with BRVO secondary to Behçet's disease were included in the study. The patients with coexisting ocular pathology that may cause a decrease in the BCVA, macula and optic disc anatomy were excluded. While Female:Male ratio was 7:7 in the control group, it was 4:19 in the study group. The mean duration of follow up after the development of BRVO was 74.6±57.4 months in the study group and 69.0±59.9 months in the control group (p=0.77). The rate of bilaterality in the study group (21.7%) was not significantly different from the control group (14.3%) (p=0.68). While the most common location of BRVO in the control group was superotemporal quadrant (50%), it was inferotemporal quadrant (25%) in the study group. No significant difference was detected between the study and control group in terms of the application of laser photocoagulation and involvement of macula (p=1.0 and 0.61 respectively). However the rate of need for injection was significantly lower in the patients with BRVO secondary to Behçet's disease in comparison to the patients with unknown etiology (p=0.008). Despite effective treatment in both groups, final BCVA was not significantly different from the onset of BRVO (p=0.16 for the study group, p=0.2 for the control group).
Conclusion. Although the treatment of BRVO is laser photocoagulation and intravitreal injection of anti-VEGF agents or dexamethasone implant, the patients with Behçet's disease might respond very well to systemic immunomodulatory agents in case of BRVO. Thus, rearrangement of the immunomodulatory treatment before starting intravitreal injections should be considered in the patients with BRVO secondary to Behçet's disease.
References

1. ÖZDAL PC, ORTAC S, TAŞKINTUNA I, & FIRAT E: Posterior segment involvement in ocular Behçet's disease. *European journal of ophthalmology* 2002; 12(5): 424-431.
2. YAHIA SB, KAHLOUN R, JELLITI B, & KHAIRALLAH M: Branch retinal artery occlusion associated with Behçet disease. *Ocular immunology and inflammation* 2011; 19(4): 293-295.
3. CHEN Y, STANFORD MR, WALLACE GR, VAUGHAN RW, KONDEATIS E, & FORTUNE F: Factor V Leiden mutation does not correlate with retinal vascular occlusion in white patients with Behçet's disease. *British journal of ophthalmology* 2003; 87(8): 1048-1049.
4. JAULIM A, AHMED B, KHANAM T, & CHATZIRALLI IP: Branch retinal vein occlusion: epidemiology, pathogenesis, risk factors, clinical features, diagnosis, and complications. An update of the literature. *Retina* 2013; 33(5): 901-910.

P128

Entero-Behçet: a deadly case

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Introduction. Behçet's disease is a chronic systemic disease, although it is classically known by a triad oral and genital ulcerations and uveitis, it can affect every organ system. Gastro-intestinal involvement is rare with a poor prognosis and can be very challenging.
Aims. The present report is a reminder of an important clinical lesson for clinicians, many of whom do not have experience with such deadly complications from BD. We report a new case of a severe intestinal involvement in BD.
Methods. A retrospective case report of an intestinal complications in Behçet's disease.
Results. A 54 years old patient with history of muco-cutaneous Behçet's disease was admitted for acute abdominal pain, diarrhea, rectal syndrome and intestinal bleed (hematemesis and melena). The patient had fevers, anorexia and 30 kg weight loss in 6 months. This was concomitant to an oral and a giant genital ulcers, skin lesions in the forearm consisting with cutaneous vasculitis.
Laboratory data showed an important inflammatory syndrome. the colonoscopy showed diffuse ulcerated lesions in the ileum and the colon. The biopsy revealed a subacute segmental ulcerative colitis.
During his hospital stay the patient developed an intestinal occlusion with air-fluid levels on x rays, confirmed at an abdominal CT scan wich showed a diffuse ileal wall infiltration and intestinal obstruction in the left iliac fossa requiring an urgent surgical intervention .
The patient received high dose intra-venous corticosteroid before and after surgery. Unfortunately, He died 4 weeks after by an intestinal perforation.
Conclusion. Intestinal Behçet's disease rarely requires a surgical treatment and has a high recurrence rate. The patients who achieved a complete remission with medical treatment, who had no history of intestinal perforation, and who received azathioprine after operation showed better clinical courses. Resection of a short segment of bowel would be a more appropriate surgical procedure.

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Clinical characteristics of older age-onset Behçet syndrome patients

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Introduction. The usual onset of Behçet syndrome (BS) is in the 3. decade. Older age-onset defined as fulfilling the International Study Group (ISG) criteria after 40 years of age is rare and our knowledge about it is limited. One early study again from our center had reported the severity of eye disease was not different between early onset (≤24 years) and late onset (≥25 years) group, while the total clinical activity scores were smaller in the late onset group (1). While there is ambiguity in the definition of the older onset, a few case series (2-4) coming mostly from ophthalmology or dermatology settings describe a similar or less severe clinical picture among late onset patients (pts) compared to that seen in the early onset.
Aims. The aim of this retrospective study was to evaluate clinical characteristics of pts with older onset BS pts and to compare them with a group of classic onset BS pts.
Methods. The charts of 3335 BS pts who were registered between January 2000 and December 2010 were reviewed retrospectively. Pts who fulfilled the ISG criteria for BS after 40 years of age (≥40) were defined as older onset, while those who fulfilled the criteria before 30 years of age as classic onset. For each older onset chart, 2 consecutively registered early onset charts were selected. Only clinical manifestations at initial presentation were recorded. A clinical activity index (1) was modified and calculated for each pt.
Results. There were only 134(70 M/64 F) pts with older onset BS, which gave a prevalence of 4% in the whole cohort. Age of onset was 40-44 years of age in 54 pts, 45-49 years in 47 and 50+ in the remaining 32. As controls 268 (163 M/105 F) classic onset pts were selected. Demographic and clinical characteristics among older and classic onset pts are described for males and females separately, in Table I. The frequency of skin manifestations, arthritis and eye disease as well as the mean clinical activity scores were significantly higher among male classic onset pts compared to older onset male pts. Interestingly, the frequency of those with positive pathergy test, vascular involvement and severe eye involvement did not seem to be different among older onset and classic onset male pts. On the other hand, clinical characteristics and total activity scores were similar between the older onset and classic onset groups among females (Table). The main limitation is that the information was based solely on patient's charts and outcome information was not available.

Table I. Clinical characteristics of older age-onset and classical-onset BS pts (Males/Females).

	Older onset males (n=70)	Classical onset males (n=163)	P	Older onset females (n=64)	Classical onset females (n=105)
Age at ISG criteria fulfilling, yrs	47.0 ± 6.0	24.2 ± 4.5		46.6 ± 5.7	23.1± 4.4
Oral ulcer, n (%)	69 (99)	163 (100)	-	64 (100)	105 (100)
Genital ulcer, n (%)	60 (86)	137 (84)	0.845	51 (80)	90 (86)
Papulopustular lesions, n (%)	49 (70)	133 (82)	0.050	39 (61)	71 (68)
Nodular lesions, n (%)	15 (21)	76 (47)	0.0001	29 (45)	60 (57)
Arthritis, n (%)	10 (14)	45 (28)	0.028	13 (20)	25 (24)
Eye involvement, n (%)	24 (34)	88 (54)	0.006	26 (41)	41 (39)
Only vitreus cell (+), n (%)*	2 (8)	25 (28)	0.058	7 (27)	14 (34)
VA: <0.1 on either or both eye*	8 (33)	27 (33)	0.941	4 (15)	9 (23)
Vascular involvement, n (%)	13 (19)	27 (17)	0.710	2	0
Pathergy positivity, n (%)**	39 (56)	94 (58)	0.876	34 (53)	49 (47)
CNS Involvement, n (%)	3	3	-	2	2
GIS Involvement, n (%)	1	1	-	0	1
Activity score, mean ± SD	5.60 ± 3.36	6.38 ± 3.15	0.020	5.20 ± 2.21	4.79 ± 2.39

*: Calculations are made only among those with eye involvement.
**: Pathergy test was made only in 70 older onset and 163 younger onset male pts, 64 older onset and 105 younger onset female pts. VA: visual acuity

Conclusion. Compared to classic onset pts, males tend to be less frequent in the older cohort. At presentation, older onset male pts had significantly less frequent skin, joint, eye disease, and significantly lower total activity scores compared with classic onset pts. There was no difference between the classic and older onset group, among females.

References

1. YAZICI H *et al.*: *Ann Rheum Dis* 1984.
2. TSAI J *et al.*: *J Eur Acad Dermatol Venereol* 2008.
3. HAMZAOUI A *et al.*: *Acta Medica Iranica* 2014.
4. CITIRIK M *et al.*: *Ophthalmologica* 2011.

P130

Longitudinal study investigating the relationship between disease activity and psychological status of patients with Behçet's disease

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Introduction. Behçet's disease (BD) is a chronic, relapsing, systemic inflammatory disease with a wide range of clinical manifestations, most commonly oro-genital ulcers, skin lesions and potentially blinding intraocular inflammation. It is well recognised that BD also has a profound psychological effect on patients. Previous research has examined patients' quality of life including a number of psychological conditions, such as anxiety, depression, fatigue and compared these to disease activity. Most studies have assessed patients at only one-time point, so it is unclear whether over time any change in disease activity reflects a corresponding change in psychological health status.
Aims. To determine the longitudinal relationship between disease activity and psychological status in BD patients.
Methods. Patients attending the Birmingham National Centre of Excellence between January 2016 – December 2017 who fulfilled the ISG criteria for BD and seen a Rheumatologist, Ophthalmologist, Oral Medicine Specialist and Clinical Psychologist on more than one occasion were included. At each visit Disease activity (BDAI) including clinician and patient perception of disease was documented and patients completed a number of validated quality of life instruments: EQ-5D and Visual Analogue scale (EQ-VAS), work and social adjustment scale (WSAS), degree of depression using the patient health questionnaire (PHQ-9), degree of anxiety using the general anxiety disorder questionnaire (GAD-7), and the Warwickshire-Edinburgh Mental Wellbeing Scale (WEMWBS). Data was entered into a REDCap database and analyses included a linear mixed model and linear regression, highlighted by a number of example case-studies.
Results. A total of 102 BD patients (65 females, 35 males; mean age 42 years) who made 378 visits (mean 3.7 visits) were included. BDAI weakly correlated with EQ-5D, PHQ-9, GAD-7 and WEMWBS. Clinician and patient perceptions were strongly correlated with each other (r=0.848) and were significantly correlated with scores for all the psychological questionnaires, unlike BDAI. BDAI positively correlated with patient's perception of disease activity, indicating that as the number of symptoms increased the patient's perception of their disease activity worsened and the same was shown for clinician's perception (r=0.350). Case-study analyses showed that between patients the influence of disease activity on psychological status varies over time.
Conclusion. In BD patients, clinician and patient perception are more closely related to psychological questionnaire scores than BDAI, according to regression and linear mixed model analyses. As the clinician or patient perception of disease activity improves there is a slight increase in quality of life (EQ-5D) and wellbeing (WEMWBS) and an improvement in depression (PHQ-9), anxiety (GAD-7) and work and social adjustment (WSAS). A decrease in BDAI also corresponded with an increase in quality of life and wellbeing and an improvement in depression and anxiety. However, changes in BDAI accounted for only a small proportion of changes in psychological status where intra-patient variation appears largely responsible.

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Adalimumab provides long lasting clinical improvement in refractory mucocutaneous Behçet's Disease without formation of antidrug antibodies

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, Not applicable.

Introduction. The TNF-blocker adalimumab can be effective in Behçet's disease (BD), a multisystem auto-inflammatory disorder. Unfortunately, the therapeutic efficacy of TNF-blockers can be hampered by the formation of anti-drug antibodies. We present an observational study of adalimumab in refractory BD with measurement of anti-drug antibodies.
Aims. To investigate safety and longterm effects of adalimumab in Behçet's disease patients and to evaluate formation of anti-adalimumab antibodies.
Methods. The effect of fortnightly 40mg adalimumab in nine patients with therapy refractory mucocutaneous, non-ocular or organ threatening BD was studied up to 60 months. Primary endpoint was a decrease in disease activity, measured by the BD Current Activity Form (BDCAF) within 6 months. Secondary endpoints included serum cytokines and the long-term formation of anti-adalimumab antibodies.
Results. BDCAF improved significantly in all nine patients from 5.4 (SD=1.4) to 2.4 (SD=1.4) (p=0.007) within one month up to 6 months and after prolonged follow up of 5 years. All patients could either taper or stop concomitant therapy. Symptoms of mucocutaneous lesions, erythema nodosum and joint involvement decreased or disappeared. Serum TNF-alpha levels were elevates in five patients and decreased upon treatment (p=0.017). Adalimumab was save and none of the patients experienced therapy failure or antibodies against adalimumab.
Conclusion. We present an observational study on patients with BD treated with adalimumab and provide a basis for long-term use in refractory mucocutaneous BD. These findings show that adalimumab can safely be administered yielding sustainable clinical effects in refractory BD patients with mucocutaneous disease without formation of anti-adalimumab antibodies, even after long follow up.

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A rare adenosine deaminase (ADA) variant in a family with Behçet's disease

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Introduction. Behçet's disease (BD) is genetically associated to variants in HLA, like HLA-B51, and non-HLA genes such as IL-23, IL-12 and IL10 as detected by genome wide associated studies (GWAS). Moreover, a recent mutation in the NFκB regulatory protein TNFAIP3 (A20) was reported in an autoinflammatory syndrome with Behçet-like disease. Various molecular biomarkers were reported in BD including ADA. Patients with BD have significant higher serum ADA levels than controls and these levels correlate with active disease.
Aims. Whole genome sequencing (WGS) in a family with BD.
Methods. WGS (software version 2.5.0.37) was performed in 3 patients with BD disease and 2 healthy family members as described by Drmanac (1). Analysis of the massive parallel sequencing data was performed using Complete Genomics analysis tools (cga tools version 1.8.0 build 1; http://www.completegenomics.com/sequence-data/cgatools/) and TIBCO/ Spotfire version 7.0.1 (http://spotfire.tibco.com/).
Variants were identified using a custom made Python script called "multiple genome analysis" using the Complete Genomics' cgatools script 'listvariants' and 'testvariants'. Variants were filtered for a dominant inheritance.
Results. In this family three members suffered from BD according to BD criteria set including recurrent oral stomatitis, uveitis, skin disease and positive pathergy test. Patients are HLA-B51 negative. Mapped sequence of samples varied between 158 and 165 Gigabytes. Confident genome coverage could be made for 97% of the reference genome in all samples. 42 dominant variants were detected. After linking the variants to vasculitis a probably damaging variant (NM_000022:exon4:c.A251G:p.Y84C) in the in ADA gene in affected family members was found. Exac reveals a very low frequency; $8.24x10^{-6}$.
Conclusion. ADA is an enzyme that catalyzes the hydrolysis from adenosine to inosine. ADA. Increased ADA levels are linked to autoimmune hemolytic anemia and BD activity. We speculate that ADA mutations may contribute to the BD phenotype. Functional studies are under investigation.
References
1. DRMANAC R *et al.*: Human genome sequencing using unchained base reads on self-assembling DNA nanoarrays. *Science* 2010; 327: 78-81.

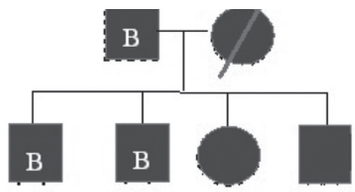

Fig. 1.

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Ocular involvement during Behçet's disease: about a Tunisian series

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Introduction. Ocular involvement of Behçet's disease (MB) is frequent, it occurs in 30 to 80% of cases, and can be inaugural in 10 to 20% of. It usually occurs during the first two years following diagnosis and often moves towards bi lateralization. Uveitis during MB is typically recurrent and conditions functional prognosis. Blindness remains the most formidable complication with a rate approaching 25%.
Aims. We report a series of Tunisian patients with MB in order to specify the particularities of ocular involvement in MB and compare patients with and without ocular involvement in MB.
Methods. We conducted a comparative study between the results of two groups divided according to the existence (group 1) or not (group 2) of uveitis or retinal vasculitis in a department of internal medicine during a period of 15 years.
Results. We collected 85 patients including 67 men and 18 women and (gender-ratio 3.7). Group 1 consisted of 33 patients; Group 2 consisted of 52 patients. The mean age at diagnosis of ocular involvement was 35.3 years (range: de 21 à 67 years). The 33 patients with ocular involvement were divided into 28 men and 5 women with a gender-ratio M/F of 56. Ocular involvement was inaugural in 11 cases (12%) %). The mean time to onset of ocular involvement in the diagnosis of BD was 3.8 years (range 2 months to 16 years). The average time to diagnosis of ocular involvement was 14.5 months (range 1 to 178 months). Twenty-one patients (63.6%) had panuveitis, 7 (21.2%) isolated posterior uveitis, and 3 (9.1%) had anterior uveitis. In 26 cases (78.8%) the attack was bilateral. Seven patients (21.2%) had unilateral involvement. Retinal vasculitis was found in 19 cases (57.5%). It was associated with uveitis in 17 cases (51.5%) and isolated in two cases. The comparison between the two groups did not show any significant difference with respect to age, gender, mucocutaneous, articular and vascular involvement. NeuroBehçet was more associated with ocular involvement (21.2% vs. 5.8%) with a significant difference (p=0,03). All patients had received corticosteroid treatment. Intravenous lipids of methylprednisolone for 3 consecutive days, followed by oral corticosteroid therapy at a dose of 1 mg/kg/day of prednisone, were prescribed in 27 patients (81.8%) with posterior uveitis, pan uveitis or retinal. Twenty-eight patients (84.8%) received immunosuppressive therapy: cyclophosphamide (71.4%), azathioprine (17.9%) and cyclosporine (10.7%). Seven patients were on TNF-α antagonist therapy. The outcome was favorable in 19 patients (57.6%) and 8 patients (24.2%) were stable.
Conclusion. Ocular involvement during BM conditions prognosis of the disease. This last can be improved by early management and regular clinical and angiographic follow-up.

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Blindness in patients with Behçet disease: population-based cohort study

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Introduction. Severe cases of Behçet's uveitis can cause permanent loss of vision although earlier and more aggressive immunosuppressive treatment has improved the visual prognosis.
Aims. To investigate the risk of blindness in uveitis patients with or without Behçet disease (BD).
Methods. The data were from the population-based cohort containing national health insurance claims from 2002 to 2013. We washed out first one year (2002) for newly detected cases. Operational definition of new incidence of uveitis was first claim with diagnostic code with uveitis (H20 or H30) and prescription code of systemic/topical steroids or systemic immunosuppressive agents to treat uveitis. In study period, the diagnostic codes for BD were also identified. Legal blindness was defined as best-corrected visual acuity in the worse-eyeing eye of <20/400. Cox proportional hazard regression analyses were performed to identify hazard associated with blindness.
Results. Of 14408 patient of new incident uveitis, 161 cases of BD was identified. Legal blindness occurred in 3.7% of uveitis patient with BD whereas 1.0% of uveitis patient without BD experienced blindness. BD was associated with an increased risk of blindness occurrence (hazard ratio [HR], 3.50; 95% confidence interval [95% CI], 1.54—7.94). Old age (over 50 year) and low income were also associated with the risk of legal blindness (HR, 4.17 and 1.62; 95% CI, 1.83—9.47 and 1.16—2.27, respectively).
Conclusion. BD and low income were significantly associated with subsequent legal blindness in uveitis patients. The findings of our study will help in the assessment of the blindness-related socioeconomic burden in uveitis patients and in healthcare planning.

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Optical coherence tomography (OCT) findings in Behçet uveitis

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Introduction. The optical coherence tomography (OCT) is a valuable device for diagnosing and monitoring macular pathology. Only a few studies have evaluated the macula changes with OCT in Behçet uveitis (1, 2).
Aims. To evaluate the macular changes, detected by optical coherence tomography (OCT), during active and remission periods in patients with Behçet uveitis and to investigate if there is a relationship between macular edema and development of macular damage.
Methods. The patients with Behçet disease who were followed at Ankara University Department of Ophthalmolgy and had posterior uveitis or panuveitis were retrospectively reviewed. Best corrected visual acuity (BCVA), central macular thickness (CMT) and OCT findings of the patients during active and remission periods were recorded. We compared these findings between active and remission periods in patients who had OCT images in both active and remission periods.
Results. Eighty-eight eyes of 48 patients were included in the study. Thirteen of the patients were female, 35 were male and the mean age was 35.7±10.7. In active uveitis period, 32.1% of the eyes were normal and 67.9% of the eyes had any kind of macular pathology on OCT scans. There was macular edema in 39.7% of eyes with active uveitis (51.6% cystoid macular edema, 32.2% diffuse macular edema, 25.8% serous retinal detachments). In remission period, OCT findings included epiretinal membrane (ERM) in 50.6%, ellipsoid zone damage in 18.2%, external limiting membrane damage in 13%, retinal nerve fiber layer damage in 14.3% and 9.1% macular atrophy. Best corrected visual acuity (logMAR) of the eyes in the active period (0.666±0.80) was significantly lower than that in the remission period (0.366±0.76) (p<0.001). Central macular thickness in the period of remission (163.26±38.25μm) was significantly lower than in the active period (262.29±159.81 μm) (p<0.001). However, no statistically significant correlation was found between macular edema in the active uveitis period and macular damage in the remission period.
Conclusion. The most common macular pathology detected by OCT was macular edema during the active period and ERM during the remission period. Macular thickness of patients with Behçet uveitis in remission period was found to be lower than in the active period.

References

1. TAKEUCHI M, IWASAKI T, KEZUKA T, USUI Y, OKUNUKI Y, SAKAI J *et al*.: Functional and morphological changes in the eyes of Behçet's patients with uveitis. *Acta Ophthalmol* 2010; 88(2): 257-62.
2. UNOKI N, NISHIJIMA K, KITA M, HAYASHI R, YOSHIMURA N: Structural changes of fovea during remission of Behçet's disease as imaged by spectral domain optical coherence tomography. *Eye* (Lond) 2010; 24(6): 969-5.

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Optic neuritis in Behçet's disease

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Introduction. Optic neuropathy (ON) has rarely been reported in Behçet's disease (BD). We are presenting a multicenter study of patients who presented with optic neuropathy associated with BD.
Aims. Our aim was to define the timing of optic nerve involvement in BD, its association with other clinical features and relevant laboratory and neuro-imaging findings.
Methods. Data from neuro-Behçet and neuro-opthalmology outpatient clinics of four Turkish university hospitals were reviewed. Patients whose optic neuropathy seemed to be unrelated to Behçet's Disease, or were secondary to other causes such as intracranial hypertension, were excluded. The cohort was divided into two groups; those who had already been diagnosed as BD when ON developed (BD-ON Group), and those who were given a diagnosis of BD during further evaluation of the etiologic factors underlying ON (ON-BD Group). Two groups were compared in terms of demographics, clinical findings, laboratory and neuro-imaging findings, treatment and prognosis.
Results. Twenty-five patients whose optic neuritis were related to Behçet's Disease were included; 13 men and 12 women, aged 16-55 years (mean 35.64). Twelve patients (48%) were in BD-ON Group, whereas 13 (52%) were in ON-BD Group. Patients in BD-ON Group were significantly older. Bilateral involvement of optic nerve was observed in 3 patients of BD-ON Group and 5 patients of ON-BD Group. Disc edema was seen in 13 of the patients, 10 of which were in ON-BD Group. 14 patients also had uveitis. Neurological involvement other than optic neuritis was detected in 8 patients, 5 with an MS-like presentation, 4 of which belonged to BD-ON Group. All patients except one received immunsuppressive medications and/or corticosteroids. Prognosis was favourable in most of the patients. Improvement was observed in 80% of the patients and was more frequently observed in patients receiving combined therapies.
Conclusion. BD may be diagnosed earlier if it is considered and investigated during the assessment of ON. Prognosis of ON related with BD might not be as poor as the prognosis of uveitis. Immunsuppressants should be given along with corticosteroids.

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Behçet uveitis: comparison of patients presented in 1990s and 2000s.

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Introduction. Behçet's uveitis is characterized by recurrent inflammatory attacks which may cause to significant damage and severe visual loss. The course and severity of disease show regional and individual variations. Although the visual prognosis is improving since the 1990s, the disease has still a guarded prognosis.
Aims. To compare the epidemiological and clinical characteristics of Turkish patients with Behçet uveitis (BU) presented in 3 different time period.
Methods. A total of 436 patients (784 eyes) presented between 1993-1999 (Group 1), 2000-2009 (Group 2) and 2010-2017 (Group 3) and followed-up

for at least 6 months were included to the study. Age at presentation, sex, laterality, anatomical classification of uveitis, visual acuity (VA) at presentation and the last visit, complication rates and medications were compared between the groups.
Results. Group 1 consisted of 94 patients (21.6%), Group 2; 239 patients (54.8%) and Group 3; 103 patients (23.6%). 76.8% of patients were male and the mean age at presentation was 31.6±9.56 years. Male ratio and the mean age at presentation were similar in all groups. The disease was bilateral in 79.8% of patients and the rate of bilaterality was higher in Group 1 (89.4%, *p*:0.009). The frequency of posterior segment involvement did not show significant difference. Having a VA ≤0.1 at presentation has been observed in 30.9% of eyes and this rate was similar in all groups. However, the frequency of having a final VA ≤ 0.1 was significantly less in Group 2 (27.3%) and Group 3 (29%) compared to Group 1 (42.6%) ($p<0.001$). The use of azathioprine (AZA) and cyclosporine-A (CS-A) increased significantly with time. Although not statistically significant, the use of combination therapy (AZA+CS-A) was also increased over time. The rate of patients using a biologic treatment increased significantly from 6.4% (Group 1) to 12.1% (Group 2) and 38.8% (Group 3) ($p<0.001$).
Conclusion. Behçet uveitis is still a disease affecting mostly the young males. Visual prognosis of BU showed an improvement in 2000s compared to 1900s. This improvement seems to associate with the more intensive use of immunosuppressive and biologic agents rather than a milder disease course.

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Optic retrobulbar neuritis in Behçet disease about 8 cases

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Introduction. Optic neuritis is rarely encountered in the course of the Behçet's disease (BD), it can occur as an isolated neurological involvement or be a part of more extensive uveitis or neuro-Behçet.
Aims. To describe the epidemiological and clinical aspects of optic retrobulbar neuritis, its clinical course and treatment modalities, in patients with behcet disease.
Methods. A retrospective study of 287 patients with neurobehcet over a period from 1981 to December 2017, we collected 8 cases of retrobulbar optic neuritis, all patients met the international criteria for Behçet's disease (ICBD, 2014). They were treated at a tertiary internal medicine department in Casablanca, Morocco.
Results. 6 male and 2 female (sex-ratio of 3:1), mean age at disease onset was 25.4 years. Disease duration at diagnosis was 15 months. All our patients had bilateral involvement, the vision was less than 1/10 in 37.6% of eyes. The retrobulbar optic neuritis was associated with other ocular lesions in 4 cases (1 vascularitis and 3 uveitis) ,and 1 patient had a venous thrombosis of the upper longitudinal sinus. 7 patients received high dose IV cortisteroids and one patient had prednisone at 1 mg per Kg and rapid taper dosing. 4 patients went into full remission, 3 patients has stable course and one patient fail to respond
Conclusion. The optic retrobulbar neuritis is a rare neurological involvement in Behçet's disease.The association of optic retrobulbar neuritis with other ocular lesions could be responsible for a diagnostic delay. Its treatment relies essentially on systemic corticosteroids.The evolution depends on the early onset of symptomatic treatment.

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Oculo-Behçet, a Moroccan experience, 300 cases

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Introduction. Behçet's disease (BD) is a chronic systemic inflammatory disorder of unknown etiology. It is characterized by recurrent oral and genital aphthosis. Ocular involvement has been described since Hippocrates antic era. Prevalence varies across different ethnic groups and geographical locations. Outcome depends on appropriate health care services and prompt multidisciplinary management
Aims. The aim of this study is to describe the epidemiological and clinical characteristics in Moroccan patients with ocular BD.
Methods. It's a retrospective monocentric study on 300 patients presenting ocular BD and treated at a tertiary internal medicine department in Morocco over a period of 17 years, January 2000 to December 2017. The diagnosis was established according to the revised International Criteria for BD (ICBD, 2010). Outcome measures were the degree of anterior and posterior chamber inflammation, visual acuity improvement assessed by the Monoyer decimal scale .Retinal angiography and optical coherence tomography were performed when deemed necessary.
Results. Out of 300 patients, 220 were male and 80 were female. The sex-ratio was 2.7. Ocular disease was inaugural in 17%. The mean duration to diagnosis was 5 years. About half of our patients presented with advanced disease with visual acuity of less than 3/10. 75% of the patients had panuveitis and 23% had retinal vasculitis. All the patients received high dose oral corticosteroids, cyclophosphamide was indicated in 43%, and eleven patients was prescribes TNF alpha antagonists. 50% of the patients had good outcome and went into sustained remission, unfortunately 30% ended-up with near vision loss, essentially due to delayed diagnosis.
Conclusion. Ocular BD can lead to irreversible loss of vision if not treated in a timely manner. Early and systematic eye exam and follow ups should be stressed in the management of BD patients.