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 (RODE) 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 expression may play a role in the pathogenesis of BD.

References

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 Behçet’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

P003 Elevated levels of serum immunoglobulin D in active mucocutaneous 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-
Hughes-Stovin syndrome in Behçet’s disease: 13 cases

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

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

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 antithrombotic agents under strict surveillance. 7 cases have been treated surgically.

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.

Cyclophosphamides, 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.

Hughes-Stovin Syndrome in Behçet’s disease: 13 cases

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P004

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


References
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**

**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, 20 post-treated patients, and age-matched healthy volunteers were collected for metabolomics and lipidomics profiling using UPLC-QTOFMS and UPLC-QTOFMS® 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 polysaturated 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 5.76x10^-3 and 1.02x10^-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**

**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 -80°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 (5.2%) AS patient, and in none of the healthy subjects. The mean number of IFX cycles was 19±4 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 S-160 Mucus Membrane Pemphigoid (OcMMP) are classical chronic 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 be distinguished by their CD15 expression in Granulocytic myeloid-derived suppressor cells (G-MDSCs) (CD66b+ CD33low) within the LDN and NDN population in BD and OcMMP patients. A significant (p=0.05) high percentage of LDN and NDN population in BD and OcMMP patients. 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+ HLA-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 neutrophils and as a result neutrophils display a heterogeneous population within BD and OcMMP patients which may contribute towards a disease state. **References**


**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 cells (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 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


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 aphthosis 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 aphrexa, a weight gain, the stop of the hemoptysis. The chest x-ray showed bilateral rounded pulmonary opacities. Chest angioscan showed multiple aneurysms of the pulmonary arteries.

Conclusion. Behçet’s disease is a vasculitis of unknown cause. It 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


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+ NK, NKT and T cell percentages discriminated between BD patients and HC. Moreover, there was a positive correlation between the BD Current Activity form (BDCF) scores and the frequencies of NKG2D+ NK and NKT cells. A higher frequency of NK cells expressing CD107a was induced in PBMC from BD patients than HC after interaction with K562 targets. Concentrations of IL-5, IL-10, IL-12 (p70), IL-13, IFN-γ and MIP-1β were higher in plasma of BD patients than HC.

Conclusion. Monitoring the frequencies of NKG2D+ lymphocytes, and CD107a+ NK cells after the degranulation assay could help the clinicians in BD patients management. The increased expression of NKG2D should be investigated in disease pathogenesis.

Reference

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 vitreous 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.
Clinical and Experimental Rheumatology 2018

**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 diarrhoea, abdominal pain, oligoarthritis and recurrent oral and genital ulcers. Laboratory studies revealed an iron deficiency anaemia and a biological inflammatory syndrome. The colonoscopy showed a diffuse ulcerative colitis. Histological examination of colonic 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, diarrhoea 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 colonic biopsies revealed crypt distortions, epitheloid 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, diarrhoea 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.

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**P016**

Alterations in the taxonomic 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. Mucocutaneous 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 signaling 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.

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Table P015.

<table>
<thead>
<tr>
<th>Author / Year</th>
<th>Age / Sex</th>
<th>Delay of the diagnosis between the two pathologies</th>
<th>Clinical signs</th>
<th>Gastro-intestinal involvement</th>
<th>Endoscopy</th>
<th>Histology</th>
<th>Other common manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldstein / 1978</td>
<td>30 / F</td>
<td>3 years</td>
<td>Diarrhoea - abdominal pain - perianal abscess</td>
<td>Stenosis - diffuse ulcerations</td>
<td>Granulomatous colitis</td>
<td>Bipolar aphthosis - erythema nodosum</td>
<td></td>
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<td>Yagita / 1978</td>
<td>39 / F</td>
<td>10 years</td>
<td>Abdominal pain</td>
<td>Irregular ileocecal ulcerations - polyp</td>
<td>Not specific</td>
<td>Bipolar aphthosis</td>
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<tr>
<td>Yagita / 1978</td>
<td>27 / F</td>
<td>Unspecified</td>
<td>Abdominal pain - right iliac fossa mass</td>
<td>Irregular ulceration of the ascending colon</td>
<td>Not specific</td>
<td>Bipolar aphthosis</td>
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<tr>
<td>Mif-Madjlessi / 1972</td>
<td>15 / F</td>
<td>15 years</td>
<td>Diarrhoea - abdominal pain - rectovaginal fistula</td>
<td>Diffuse irregular ulcerations - stenosis</td>
<td>Non-granulomatous transmural colitis</td>
<td>Bipolar aphthosis - erythema nodosum - thromboembolitis - neuro-behget - arthrits</td>
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<tr>
<td>Toca / 1989</td>
<td>15 / M</td>
<td>1 month</td>
<td>Abdominal pain - diarrhoea</td>
<td>Diffuse linear irregular ulcerations</td>
<td>Microgranulomas</td>
<td>Bipolar aphthosis - panuveitis - erythema nodosum - arthrits</td>
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<tr>
<td>Nagama / 2002</td>
<td>37 / F</td>
<td>Not specified</td>
<td>Abdominal pain - diarrhoea</td>
<td>Longitudinal diffuse ulcerations</td>
<td>Granulomatous colitis</td>
<td>Bipolar aphthosis - erythema nodosum</td>
<td></td>
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<tr>
<td>Kobashigawa / 2014</td>
<td>49 / M</td>
<td>Not specified</td>
<td>Bloody stools - anal fistula</td>
<td>Multiple ulcerations</td>
<td>Not specific</td>
<td>Arthralgia - bipolar aphthosis - erythema nodosum</td>
<td></td>
</tr>
<tr>
<td>Zekai / 2005</td>
<td>26 / M</td>
<td>3 months</td>
<td>Abdominal pain</td>
<td>Ulcerations</td>
<td>Granulomatous colitis</td>
<td>Bipolar aphthosis - pseudofolliculitis - arthritis</td>
<td></td>
</tr>
<tr>
<td>Berrada / 2017</td>
<td>41 / F</td>
<td>2 years</td>
<td>Diarrhoea</td>
<td>Ulcerated ileitis</td>
<td>Not specific</td>
<td>Bipolar aphthosis - anterior uveitis - arthritis</td>
<td></td>
</tr>
<tr>
<td>Our case / 2018</td>
<td>24 / F</td>
<td>2 years</td>
<td>Diarrhoea - abdominal pain</td>
<td>Diffuse ulcerative colitis</td>
<td>Cryptosis - epitheloid granulomas</td>
<td>Bipolar aphthosis - pseudofolliculitis - panuveitis - arthritis</td>
<td></td>
</tr>
</tbody>
</table>
P018
Primary gastrointestinal lymphoma in a patient with Behçet’s disease: a rare association and an exceptional cause of chronic diarrhea!
La Rabta, TUNIS, Tunisia.

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 cyclosporin. Six months later, she presented with abdominal pain and diarrhea which persisted despite stopping colchicine. The colonoscopy showed three ileocecal 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 hemicolecotomy 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 as our case. Corticosteroids and immunosuppressive 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 (hyperalbuminemia and low prothrombin time). As the heparin and the 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 antiangiogenic properties. 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 few papers (1, 3, 4).

Aims. The aim of our study was to investigate the mutational state of two IL-10 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 rs1800872 and rs1800872 were genotyped after a primer design bioinformatics step using NCBI Primer-Blaster 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 silico step was performed for the variant analysis using bioinformatics tools (BlustN 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-10 polymorphisms distribution between BS patients and control group. IL-10 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 statistically significant differences were observed when BS patients and controls and CC genotypes were compared. The heterozygote 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, heterozygote AG and mutant GG genotype frequencies of IL10 rs1800872 were compared.

Table 1. Genotype frequencies of IL-10 rs1800872 and rs1800872 in BS patients and controls.

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNP</th>
<th>Genotype</th>
<th>BS patients (n=40)</th>
<th>Controls (n=42)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10</td>
<td>rs1800872</td>
<td>AA</td>
<td>8 (20.00)</td>
<td>4 (9.52)</td>
<td>2.34 (1.04-5.12)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AC</td>
<td>7 (17.50)</td>
<td>17 (40.48)</td>
<td>6.01 (1.22-28.87)</td>
<td>0.012**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CC</td>
<td>25 (62.50)</td>
<td>21 (50.00)</td>
<td>1.87 (0.60-5.72)</td>
<td>NS</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNP</th>
<th>Genotype</th>
<th>BS patients (n=40)</th>
<th>Controls (n=42)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10</td>
<td>rs1800872</td>
<td>AA</td>
<td>10 (25.00)</td>
<td>9 (21.43)</td>
<td>1.04 (0.32-3.58)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AG</td>
<td>7 (17.50)</td>
<td>13 (30.95)</td>
<td>6.47 (1.77-21.33)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GG</td>
<td>13 (32.50)</td>
<td>10 (23.81)</td>
<td>1.52 (0.54-4.89)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: SNP, single nucleotide polymorphism; BS, Behçet syndrome; n, number of subjects; AA, allele; rs, single nucleotide; 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, while 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 needed to confirm this preliminary data and to explain the SNP role in BS pathogenesis.

References
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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 polymorphisms of IL-8 and IL-17A 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, episcleritis and central nervous involvement. However there were a higher tendency of IL-17A 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
Interleukin-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 pheno- types. 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 37.8±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.

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
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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 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.

Acknowledgements. This work was partly supported by the Health and Labour Sciences Research Grants (Research on Intractable Diseases) from the MHLW of Japan, and Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture of Japan.

P025

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

L. Chadwick, N. Goodson, R. Moots

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Introduction. Behçet’s syndrome (BS) exhibits significant heterogeneity in clinical manifestations, including orogenital ulceration, skin rash, arthralgia and ocular, venous, gastrointestinal and neurologic 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 yet 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 EQSD 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, 45% skin rash and 20% ocular, 7% neurologic, 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 1.35, 23.27) in comparison to patients with two manifestations in the multivariate model.

Conclusion. This study highlights 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


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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 disease in which the presence of ROU is one of the diagnostic signs of the 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 Group 1 (Gp1), and 80 BD patients (Gp2), who were diagnosed according to The International Study Group 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 a 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) and controls. IL-18 –607CC genotype (OR=2, CI=1.01-3.5) 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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2, South-Korea.

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=27,800) 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 bincentric 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=0.01) and neurological 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 aphthosis, genital ulcers and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Although BS pathology 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 tends 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 31st 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. A comparative study of clinical characteristics between males (group 1) and females (group 2) was performed.

Results. 324 BS patients were identified in our database. 39 (17 males and 22 females) were excluded because did not satisfy ISG criteria and 285 (168 males and 177 females) resulted eligible for the present study. Results are summarized in Table I. We found statistically significant differences in papulopustular lesions, posterior uveitis and deep venous thrombosis, which occur more frequently in males compared with females (83.3% versus 46.2%, 57% versus 18.8% and 8.3% versus 0.9% respectively, p<0.01).
2. HATEMI G, SEYAHI E, FRESKO I, TALARICO R, HAMURYUDAN V
3. PIPITONE N, BOIARDI L, OLIVIERI I, CANTINI F, SALVI F, MALATESTA R

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fovea centered 3 mm diameter area manually. The flow index was measured as detected flow signals within the

We measured foveal avascular zone area, vessel density in the parafoveal

control subjects (mean age 51.4; 46.7% female) were involved in the study.

A total of 23 patients with Behçet Disease without ocular involve

Methods.

To evaluate the OCTA features of patients with Behçet Disease.

Ankara University, Faculty of Medicine, ANKARA, Turkey.

Behçet disease

cohort of Italian BS patients the disease results slightly

more prevalent in males. Gender-related differences were observed for posterior uveitis, DVP and papulopustular lesions which are 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 (%) Male (%) Female (%) OR (95% CI) p-value

Gul Ulcers (OA) 287 (6.08%) 168 (6.04%) 119 (6.08%) 1.41 (0.69-2.81) NS

Oral Ulcers (OU) 171 (3.68%) 97 (3.68%) 74 (3.68%) 0.70 (0.38-1.34) NS

Eye Ulcers (OE) 139 (6.4%) 89 (6.41%) 50 (6.41%) 0.48 (0.34-0.70) 0.0027*

Feltersatio 36.0 (7.15) 32 (6.89) 18 (6.73) 1.29 (0.78-2.14) NS

Fingertip lesions 186 (3.68) 114 (3.68) 72 (3.68) 1.07 (0.59-2.06) NS

Tender-T 20.3 (4.15) 12.5 (4.15) 4.8 (4.15) 1.93 (0.62-6.48) NS

Perforating kerato 64 (6.25) 43 (6.25) 12 (6.25) 3.31 (1.44-7.5) 0.0019*

Atematic crises 31 (3.16) 20 (3.16) 11 (3.16) 0.90 (0.49-1.68) NS

Pain (ocular) 34 (6.48) 17 (6.48) 17 (6.48) 1.17 (0.74-1.43) NS

Episcleritis 2.13 2.13 0.70 0.89 (0.16-4.89) NS

Arthralgia 134 (6.95) 73 (6.95) 61 (6.95) 0.42 (0.24-0.74) 0.0065*

Arthritis 124 (6.28) 44 (6.28) 80 (6.28) 1.39 (0.86-2.27) NS

Deep venous thrombosis (DVT) 6 (1.41) 4 (1.41) 2 (1.41) 3.51 (1.37-9.31) 0.0047*

Suppurative venous thrombosis (SVT) 11 (2.21) 8 (2.21) 3 (2.21) 1.42 (0.69-2.94) NS

Uveitic involvement 15 (3.06) 9 (3.06) 6 (3.06) 1.07 (0.56-2.07) NS

Fever 4 (0.59) 1 (0.59) 0 (0.59) 0.0 (0.0-1.0) NS

Intestinal involvement 64 (3.49) 39 (3.49) 25 (3.49) 9.47 (2.43-8.81) 0.0008*

HLA-B5 positivity 156 (34.37) 114 (34.37) 42 (34.37) 1.02 (0.73-1.42) NS

Abbreviations: BS, Behçet syndrome; OA, number of subjects; OU, oral ulcer; OE, ocular ulcer. Confidence intervals. Notes: **statistically significant (p-value <0.01); ***statistically significant (p-value <0.001)

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 papulopustular 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


Poster Session 1

18th International Conference on Behçet’s Disease

**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: rs0000603, p=0.0496 in 3p12; p=0.000040, p=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 (p>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


3. YUASA T, FUJIOKA T, OHNO S, BAHRAM S, MIZUKI N: Genetics of Behçet disease 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).

**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 involve (mean age 45.7; 49.5% female) and 29 healthy age and sex matched control subjects (mean age 45.7; 49.5% female) and 29 healthy age and sex matched

Conclusion. These results show that macular vascular changes can be seen in Behçet patients.

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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 1, 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 1. Demographics and clinical manifestations of BS compared by gender (*statistically significant).

<table>
<thead>
<tr>
<th>Male (n=140)</th>
<th>Female (n=293)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, range) (y)</td>
<td>45.2 (12.0)</td>
<td>48.1 (14.6)</td>
</tr>
<tr>
<td>Recurrent oral aphthosis, n (%)</td>
<td>139 (99.3)</td>
<td>281 (98.9)</td>
</tr>
<tr>
<td>Genital aphthosis, n (%)</td>
<td>111 (78.6)</td>
<td>278 (94.9)</td>
</tr>
<tr>
<td>Papulopustular skin rash, n (%)</td>
<td>69 (49.3)</td>
<td>167 (16.1)</td>
</tr>
<tr>
<td>Erythema nodosum, n (%)</td>
<td>29 (20.7)</td>
<td>56 (19.1)</td>
</tr>
<tr>
<td>Scleritis, n (%)</td>
<td>7 (5.0)</td>
<td>8 (2.7)</td>
</tr>
<tr>
<td>Uveitis, n (%)</td>
<td>81 (57.9)</td>
<td>99 (33.8)</td>
</tr>
<tr>
<td>Retinal vasculitis, n (%)</td>
<td>39 (27.9)</td>
<td>34 (11.5)</td>
</tr>
<tr>
<td>Central nervous system involvement, n (%)</td>
<td>16 (11.4)</td>
<td>20 (6.8)</td>
</tr>
<tr>
<td>Large vein thrombosis, n (%)</td>
<td>22 (15.7)</td>
<td>19 (6.5)</td>
</tr>
<tr>
<td>Arterial thrombosis or aneurysm, n (%)</td>
<td>4 (2.9)</td>
<td>7 (2.4)</td>
</tr>
<tr>
<td>Thrombocytopenia, n (%)</td>
<td>10 (7.1)</td>
<td>5 (1.7)</td>
</tr>
<tr>
<td>Gastro-intestinal involvement, n (%)</td>
<td>8 (5.7)</td>
<td>25 (8.5)</td>
</tr>
<tr>
<td>Arthritis, n (%)</td>
<td>68 (48.6)</td>
<td>180 (61.4)</td>
</tr>
<tr>
<td>Ethnicity (British or White), n (%)</td>
<td>90 (64.3)</td>
<td>238 (85.9)</td>
</tr>
<tr>
<td>(n=286)</td>
<td>(n=377)</td>
<td></td>
</tr>
<tr>
<td>HLA-B51 positive, n (%)</td>
<td>14 (10.0)</td>
<td>27 (9.1)</td>
</tr>
</tbody>
</table>

Discussion. The differentiation of BD patients with different ethnic background. The aim for this study is to identify different genes involved in BD patients with different ethnic background.

Methods. We selected fifteen SNPs from six genes (STAT3, UBAC2, TGBFR3, PTPN22, GIMAP4 and IL10) which have been identified as high risk factors in BD patients in previous studies in other population along the same line. Then repeated the DNA genotyping in a case-control study in British cohort.

Results. Our current results showed two rs1301082 and rs2476601 polymorphism in PTPN22 was strongly associated with the susceptibility to BD in UK cohort, but have less effect in Turkish population as compare with health controls and even not existing in Han-Chinese BD patients. The rest thirteen SNPs(rs3825427, rs9517768, rs9517701 and rs7999348 in UBAC2 lous, rs1805110 in TGBFR3, rs1522596 in GIMAP4, rs6530695, rs2293152 in STAT3 and rs1518111, rs3024505 and rs3024490 in IL10) have no significant 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 CTTA 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, TGBFR3, GIMAP4, RS175602 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 interaction) definitely 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. The aim of this study 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 I² 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 (I²=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**


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Poster Session I

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 pre- 
dominance of female patients (64.80%). Ethnic and racial backgrounds differed between cohorts, with Stanford having the most diverse popula- 
tion 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, NYU, and/or Michigan. CNS- and GI involvement were similar 
between Stanford, NYU and NIH/NYU (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 NYU 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 dem- 
onstrated 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
5. KILIAN N, SAWALHA A. Eur J Rheumatol 2017; 4: 239-244.

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 re- 
view similar cases from previous reports.

Methods. A systematic literature review was performed in Japanese litera- 
ture database (Ichu-shi) using the keywords (Behçet’s disease) AND (my- 
elodysplastic 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, dyspea, loss of appetite and loss of 
weight (4kg/3weeks). She has been diagnosed as having intestinal 
Behçet’s disease over 11 years. She has presented with recurrent oral ul- 
cers, arthritis, folliculitis and intestinal ulcers. She has been treated with 
metrotexate, but not with colchicine, salazosulfapyridine and 5-aminosal- 
cyclic 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 
biposied specimen. Bone marrow biopsy showed morphologic changes in 
erthroid without the increase of blast cells. Further chromosomal analy- 
sis 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 amelio- 
rated the symptoms. The bone marrow transplantation for the treatment of 
MDS was not carried out because the patient had a past history of refrac- 
tory 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 alleles have been strongly implicated 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. On the other hand, 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 and 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 (Illunina).

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 SNPeHLA using the reference data collected by the Type1 Diabetes Genetic Consortium. Additional SNP genotypes from this region were also imputed using IMPUTE2 after phasing by SHAPEIT. For quality control, markers with MAF<0.01 and Hardy-Weinberg equilibrium p<0.001 were excluded. The concordance rate per allele in 2,186 samples for which HLA-B*51 was directly typed and 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=4).

Results. In 1,104 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 HLAAs showed the strongest association for HLA-B*51 (p=1.03×10^-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. In 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

P043
Documentation and follow-up in a multicenter Registry of Adamantiades-Behçet’s disease
A. Altenburg1, M. Lohan1, M.B. Abdel-Naser2, M. Augustin3, S.J. Rustenbach1, C. Sorbe4, M. Radke1, M. Schirmer4, L. Krause1, T. Stache1, C.C. Zouboulis1
1Dessau Medical Center, Brandenburg Medical School Theodor Fontane, DESSAU-ROSLAU, Germany. 2Ain Shams University Hospital, CAIRO, Egypt. 3University Medical Center Hamburg-Eppendorf, HAMBURG, Germany. 4University of Innsbruck, INNSBRUCK, Austria.

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 ophthalmological 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 explicitly 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-based analysis.

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 2011.

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 than those of the whole cohort. 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 than female, the male predominance disappeared in elderly. The similar pattern was found in elderly.
**P046**

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

N. Dilsen, M. Konice, O. Aral, L. Ocal, M. Inane, A. Gul

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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 diagnostic 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 develop multiple VOI together.

**Conclusion.** This study validated our previous findings, which is considered a problem. Some 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.

**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.

**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.

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**P047**

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


**Ibn Roch University Hospital, CASABLANCA, Morocco.**

**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 systems, 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%, oligoarthritis in 14.2% and monarthritis 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 aneurysms 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.

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**P048**

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


**Kitasato University School of Medicine, TOKYO, Japan.**

**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.

**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.
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-α 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 place-ments. 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 administered 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

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 (AAAs) 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 8 of 10 patients (80%) 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 predni-solone 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.

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 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 the open-label study VISUAL III completed the VISUAL I/II trials without TF, were eligible to enter the 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 17/22 (77.3%) of 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 1. Long-term efficacy of adalimumab in VISUAL III in patients with non-infectious uveitis associated with Behçet’s disease.

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 30</th>
<th>Week 54</th>
<th>Week 78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence, %</td>
<td>44.4</td>
<td>77.8</td>
<td>70.4</td>
<td>74.1</td>
</tr>
<tr>
<td>Non active inflammatory lesions, % (H S° CI)</td>
<td>66.7</td>
<td>85.2</td>
<td>77.8</td>
<td>77.8</td>
</tr>
<tr>
<td>Ac/cell grade ≤0.5+, % (H S° CI)</td>
<td>81.5</td>
<td>88.9</td>
<td>85.2</td>
<td>85.2</td>
</tr>
<tr>
<td>LogMAR BCVA, mean (SD)</td>
<td>0.16 (0.38)</td>
<td>0.11 (0.21)</td>
<td>0.15 (0.20)</td>
<td>0.11 (0.21)</td>
</tr>
</tbody>
</table>

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

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 effectiveness 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 was treated with 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 aphthosis. 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 he was being treated with alpha interferon and Corticosteroids for his uveitis, he had developed 2 giants Genital Ulcers: diameter superior to 1 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 combined 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 Behçet's uveitis

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Introduction. Behçet’s disease can cause sight threatening panuveitis. It is a relitively 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 uveitis 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 azathioprine + 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 inflection 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 azathioprine + 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 any 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 inflection 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 azathioprine + 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 months 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 knowledge, there isn’t study of Vitamin D and Behçet’s Disease (BD). In our country, there is high prevalence of hypovitamin D. In temic inflammatory diseases as Rheumatoid Arthritis and Gougerot Sjögren’s Syndrome. Vitamin D deficiency is highly prevalent in patients with systemic inflammatory diseases as Rheumatoid Arthritis and Gougerot Sjögren’s Syndrome. In our knowledge, there isn’t study of Vitamin D and Behçet’s Disease (BD).

Aims. 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 azathioprine + 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 inflection 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 azathioprine + 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 any 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 inflection 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 azathioprine + 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 switched to adalimumab 40mg/2wks because of insufficient response. He was stable for the last 6 months 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.

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 and 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 5, infections in 2, neurologic involvement in 2, ischmiac 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, azospermia, 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 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 were 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 46% 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. 71.4%, 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, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury) and 4 (3.9%) patients in the placebo group (diarrhea, OU flare, genital ulcer, arthralgia, soft tissue injury).

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.

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

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 5.2a±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).

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 Behçet’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 guidelines 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), colonoscopy, or brain imaging due to gastrointestinal symptoms. Mean age was 41.2 ± 7.9 years. Forty-four out of 755 (5.8%) patients had gastrointestinal involvement: 39 terminal ileum, and 5 esophagus. None of them had both esophageal and ileal ulcers. In all patients with esophageal BD, immunohistochecmical 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.

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 ophthalmological 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 ophthalmological 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 1. Table 1. Comparison of frequencies of previous 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.
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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 CS 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 or who had 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±18.8 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

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2. ALIBAZ-ONER F: Medicine (Baltimore) 2015.

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 lamivudine. 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 an 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 iritis 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 pulses 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 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.

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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 peres 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.**

**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 was 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/ 53 R) (72%) patients. 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/ 53 R) (72%) patients. Damage scores were graded from 0 to 5.

**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.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Vitreous opacity is present but there is no visible retinal structural change.</td>
</tr>
<tr>
<td>1</td>
<td>There is only vascular sheathing on the peripheral retina.</td>
</tr>
<tr>
<td>2</td>
<td>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.</td>
</tr>
<tr>
<td>3</td>
<td>There are widespread peripheral sheathing, macular atrophic pigment alterations, moderate optic disc atrophy and visible choroidal capillary changes.</td>
</tr>
<tr>
<td>4</td>
<td>There are total optic atrophy, extensive vaso-occlusive changes, diffuse pigment alterations along with atrophic changes in the choroidal capillary layer and in the ciliary body.</td>
</tr>
<tr>
<td>5</td>
<td>There is end stage structural damage in both anterior and posterior segments. Often, due to cataract and phthisis bulb, fundus examination could not be done.</td>
</tr>
</tbody>
</table>

**Table.** Uveitis damage score: definition of grades.

**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 (LEVY) 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 unsuccessful 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: Behçet OR Behçet’s OR Adanantimides-Beheçet AND surgery OR surgical OR intervention 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 thrombus cases resulted with re-occlusion. Antiagulant 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...
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.

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

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**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.

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**Table. P066**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Gender, age</th>
<th>Involved veins</th>
<th>Invasive procedure</th>
<th>Followup (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorell, 2015</td>
<td>F, 52</td>
<td>Subclavian, left brachiocephalic (SVCS), LEVT</td>
<td>SVC stent</td>
<td>12</td>
<td>Patient stent</td>
</tr>
<tr>
<td>Seinturier, 2014</td>
<td>F, 30</td>
<td>Right femoral, common iliac</td>
<td>Endovascular fibrinolysis, thrombectomy, thrombosis failure. At 1 year balloon dilatation, stent</td>
<td>30</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Li, 2014</td>
<td>2 patients*</td>
<td>LEVT*</td>
<td>IVC filter</td>
<td>24</td>
<td>Emboli resolution at 3 months, no relapse</td>
</tr>
<tr>
<td>Li, 2014</td>
<td>2 patients*</td>
<td>NA</td>
<td>IVC hepatic (BCS)</td>
<td>24</td>
<td>Recanalized</td>
</tr>
<tr>
<td>Celik, 2013</td>
<td>F, 32</td>
<td>SVC, bilateral jugular, brachiocephalic, SVCS</td>
<td>Local thrombolysis</td>
<td>24</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Geng, 2013</td>
<td>M, 40</td>
<td>Bilateral LEVT, IVC, PAA, left renal</td>
<td>IVC filter, PAA coil</td>
<td>9</td>
<td>No relapse</td>
</tr>
<tr>
<td>Jeong, 2013</td>
<td>F, 25</td>
<td>IVC, bilateral iliac</td>
<td>Thrombectomy, balloon angioplasty</td>
<td>1</td>
<td>No relapse</td>
</tr>
<tr>
<td>Yu, 2012</td>
<td>M, 36</td>
<td>SVC (No thrombosis), SVCS</td>
<td>SVC balloon angioplasty. At first week: SVC stent due to occlusion. 2 months later, excision and bypass due to stent thrombosis</td>
<td>12</td>
<td>No relapse</td>
</tr>
<tr>
<td>Tekbas, 2012</td>
<td>5 patients*</td>
<td>Iliofemoral (also IVC in 2 patients)</td>
<td>PTA and stents in 3 patients, second intervention at first month due to reocclusion; unsuccessful in other 2 patients</td>
<td>NA</td>
<td>Reocclusion</td>
</tr>
<tr>
<td>Tekbas, 2012</td>
<td>2 M patients*</td>
<td>NA</td>
<td>Bilateral subclavian, brachiocephalic, internal jugular, SVC</td>
<td>PTA and stents; second interventions at first week and eight month due to reocclusion</td>
<td>48 and 36</td>
</tr>
<tr>
<td>Tekbas, 2012</td>
<td>E, NA</td>
<td>NA</td>
<td>PTA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tekbas, 2012</td>
<td>2 E patients*</td>
<td>NA</td>
<td>Hepatic IVC stenosis (BCS), Iliofemoral</td>
<td>IVC stent, iliofemoral PTA</td>
<td>NA</td>
</tr>
<tr>
<td>Vanderheynst, 2008</td>
<td>M, 38</td>
<td>SVC (No thrombosis), SVCS</td>
<td>SVC angioplasty</td>
<td>36</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Han, 2004</td>
<td>M, 45</td>
<td>Hepatic, IVC (BCS)</td>
<td>IVC balloon angioplasty, stent</td>
<td>NA</td>
<td>Patent stents</td>
</tr>
<tr>
<td>Kuniyoshi, 2002</td>
<td>M, 24</td>
<td>IVC (BCS)</td>
<td>PTA failure for 3 times, 11 months later: resection, thrombectomy, IVC graft</td>
<td>60</td>
<td>HV IVC-reocclusion, resection, HV-right atrium bypass</td>
</tr>
<tr>
<td>Kuniyoshi, 2002</td>
<td>F, 58</td>
<td>HV, IVC (BCS)</td>
<td>At 6 months: resection, thrombectomy</td>
<td>5</td>
<td>Reus, MDF, exitus</td>
</tr>
<tr>
<td>Uthman, 2001</td>
<td>M, 27</td>
<td>Right subclavian</td>
<td>Local thrombolysis, balloon angioplasty. At first month: balloon dilatation and stent due to reocclusion</td>
<td>6</td>
<td>No relapse</td>
</tr>
<tr>
<td>Radke, 2001</td>
<td>F, 29</td>
<td>Right iliofemoral, IVC, right renal</td>
<td>IVC filter, excised 8 days later due to occlusion</td>
<td>12</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Sagdic, 1996</td>
<td>2 patients*</td>
<td>Iliofemoral</td>
<td>IVC filter in a patient; Palma op, Graft, AV fistula in other</td>
<td>28 and 31</td>
<td>No emboli in a patient; reocclusion at fifth month in other</td>
</tr>
<tr>
<td>Sagdic, 1996</td>
<td>NA</td>
<td>SVC</td>
<td>Right innominate vein-right atrium bypass</td>
<td>24</td>
<td>Collaterals</td>
</tr>
</tbody>
</table>
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-ct. 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-ct treatment, although Secukinumab 300 mg monthly resulted superior in inducing CR of both articular and mucocutaneous manifestations.

References

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=103) or placebo (n=104) 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 assessment 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.
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 the Fatouma Bourguiba University Hospital, 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%) showed a significant increase of sex ratio (M/F) from 1.59 to 3.16. Manifestations in 43.1%, neurological and vascular involvement were found in 10.7%. Ocular involvement was found in 38.2% of the cases, articular manifestations in 41.3%, 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 3.16 (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 involvement. 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.
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 of obstruction, recanalization, reflux, and collaterals.

Results. When vascular involvement developed, mean age was 32.7±8.6. Venous assessment was done after 6(±26) years first vascular event. During venous assessment, median disease duration was 9 (0-34) years. Eighty (84.2%) patients were under immunosuppressive (IS) treatment and 13 of these patients were under anticoagulation treatment in addition to ISs. Median IS time was 37.5 (1-256); anticoagulation time was 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 relapses. 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. Forty (47.6%) patients had both upper and lower leg vessel involvement. But we didn’t find any association 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 1).

**Table 1.** Clinical and venous assessment characteristics of patients with vascular Behçet disease.

<table>
<thead>
<tr>
<th>Post-thrombotic Syndrome</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>BSAS score (n=93)</strong></td>
<td></td>
</tr>
<tr>
<td>8.06±6.9</td>
<td>8.24±3.97</td>
</tr>
<tr>
<td><strong>VCSS score (n=85)</strong></td>
<td></td>
</tr>
<tr>
<td>2.27±1.64</td>
<td>6.54±4.09</td>
</tr>
<tr>
<td>18.50 (50%)</td>
<td>11.19 (33%)</td>
</tr>
<tr>
<td>15.61 (36%)</td>
<td>34.69 (59.6%)</td>
</tr>
<tr>
<td><strong>Veines QoL total score (n=93)</strong></td>
<td></td>
</tr>
<tr>
<td>97.19±17.8</td>
<td>77.75±17.3</td>
</tr>
<tr>
<td><strong>Veines symptom score</strong></td>
<td></td>
</tr>
<tr>
<td>43.3±9.9</td>
<td>35.2±9.1</td>
</tr>
<tr>
<td><strong>CEAP</strong></td>
<td></td>
</tr>
<tr>
<td>1.53±1.34</td>
<td>2.94±1.83</td>
</tr>
<tr>
<td><strong>DVT</strong></td>
<td></td>
</tr>
<tr>
<td>72.4(40%)</td>
<td>36(60%)</td>
</tr>
<tr>
<td>12 (21.2%)</td>
<td>21 (36.3%)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td></td>
</tr>
<tr>
<td>13 (39.4%)</td>
<td>20 (60.6%)</td>
</tr>
<tr>
<td>IS+AC</td>
<td></td>
</tr>
<tr>
<td>17 (36.2%)</td>
<td>30 (63.8%)</td>
</tr>
<tr>
<td><strong>Treatment duration</strong></td>
<td></td>
</tr>
<tr>
<td>(months)</td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td></td>
</tr>
<tr>
<td>39 (1-200)</td>
<td>36 (3-256)</td>
</tr>
<tr>
<td>IS+AC</td>
<td></td>
</tr>
<tr>
<td>12 (1-156)</td>
<td>12 (1-156)</td>
</tr>
<tr>
<td><strong>Duration of trombosis</strong></td>
<td></td>
</tr>
<tr>
<td>(years)</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td></td>
</tr>
<tr>
<td>15 (40.5%)</td>
<td>22 (59.3%)</td>
</tr>
<tr>
<td>&gt;5</td>
<td></td>
</tr>
<tr>
<td>20 (36.4%)</td>
<td>35 (63.6%)</td>
</tr>
<tr>
<td><strong>Compression stockings</strong></td>
<td></td>
</tr>
<tr>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>18 (42.5%)</td>
<td>24 (57.5%)</td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
<tr>
<td>12 (24.5%)</td>
<td>21 (75.5%)</td>
</tr>
</tbody>
</table>

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 specific 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 possible problem for physicians treating VBD in daily practice.

**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 pathergic 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-expression 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 (flagellin) driven pathogenesis of the pathergy phenomenon.

We believe our results indicate an exaggerated TLR-response drives the auto-inflammatory nature of BD.

**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 aphtous ulcers (ROU) is 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 and during 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.

**Conclusion.** We found that PTS develops in more than half of the patients with VBD 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 specific 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.
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 non-smoker 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 38.5±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.

**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.

**P077**

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

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1Erasmus MC, University Medical Center, ROTTERDAM, The Netherlands.

**Introduction.** Behçet’s disease (BD) is a vasculitis characterized by aphthous oral-genital ulcers, inflammatory skin changes and uveitis. Although treatment is mainly immunosuppressive, elevated endothelium-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 Behçet’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.
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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2 Queen Mary’s School of Medicine and Dentistry, LONDON, United Kingdom.  
3 University Hospital Aintree, LIVERPOOL, United Kingdom.  
4 Royal Hallamshire Hospital, SHEFFIELD, United Kingdom.  
5 University of Liverpool, LIVERPOOL, United Kingdom.  
6 Institute of Child Health, University College London, LONDON, United Kingdom.

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 (BSDP) 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 BSDP, 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%) 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 PEDBD criteria.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>ICBD confirmed cases (n=56)</th>
<th>ISG confirmed cases (n=53)</th>
<th>PEDBD confirmed cases (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral ulceration</td>
<td>16/56 (29%)</td>
<td>10/53 (19%)</td>
<td>8/25 (32%)</td>
</tr>
<tr>
<td>Genital or penile ulceration</td>
<td>8/56 (14%)</td>
<td>6/53 (11%)</td>
<td>2/25 (8%)</td>
</tr>
<tr>
<td>Skin involvement</td>
<td>30/56 (52%)</td>
<td>28/53 (52%)</td>
<td>13/25 (52%)</td>
</tr>
<tr>
<td>Pseudofolliculitis</td>
<td>13/56 (23%)</td>
<td>12/53 (23%)</td>
<td>4/25 (16%)</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>10/56 (18%)</td>
<td>10/53 (19%)</td>
<td>5/25 (20%)</td>
</tr>
<tr>
<td>Blaschka</td>
<td>12/56 (21%)</td>
<td>12/53 (23%)</td>
<td>6/25 (24%)</td>
</tr>
<tr>
<td>Eye involvement</td>
<td>14/56 (25%)</td>
<td>12/53 (23%)</td>
<td>4/25 (16%)</td>
</tr>
<tr>
<td>Anterior uveitis</td>
<td>8/28 (14%)</td>
<td>8/28 (14%)</td>
<td>4/25 (16%)</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>2/14 (14%)</td>
<td>2/14 (14%)</td>
<td>1/25 (4%)</td>
</tr>
<tr>
<td>Peripheral uveitis</td>
<td>0/0 (0%)</td>
<td>0/0 (0%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Retinal vasculitis</td>
<td>1/7 (14%)</td>
<td>1/7 (14%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Visual loss</td>
<td>1/7 (14%)</td>
<td>1/7 (14%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Neurological involvement</td>
<td>7/14 (50%)</td>
<td>6/14 (43%)</td>
<td>3/25 (12%)</td>
</tr>
<tr>
<td>Headaches</td>
<td>4/7 (57%)</td>
<td>4/7 (57%)</td>
<td>2/25 (8%)</td>
</tr>
<tr>
<td>Central Venous Thrombosis</td>
<td>1/7 (14%)</td>
<td>1/7 (14%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Sensorineural deafness</td>
<td>1/7 (14%)</td>
<td>1/7 (14%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Acute Meningo-</td>
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<td>0/0 (0%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Parenchymal involvement</td>
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<td>0/0 (0%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Other involvement</td>
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<td>22/7 (31%)</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>9/14 (64%)</td>
<td>8/14 (57%)</td>
<td>5/25 (20%)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>7/14 (50%)</td>
<td>6/14 (43%)</td>
<td>3/25 (12%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2/7 (29%)</td>
<td>2/7 (29%)</td>
<td>1/25 (4%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2/7 (29%)</td>
<td>2/7 (29%)</td>
<td>0/25 (0%)</td>
</tr>
<tr>
<td>Fever</td>
<td>2/7 (29%)</td>
<td>2/7 (29%)</td>
<td>0/25 (0%)</td>
</tr>
</tbody>
</table>

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. While thrombosis in Behçet’s Syndrome (BS) is considered to be mainly caused by inflammation in the vessel wall, several prothrombotic factors have been associated with and without thrombosis. Conflicts were solved by a third reviewer (GH). The pooled odds ratios (OR) 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.

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

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

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 associated with and without thrombosis. Conflicts were solved by a third reviewer (GH). The pooled odds ratios (OR) with 95% CI were calculated for binary outcomes and standardized mean differences (MD) were calculated for continuous outcomes by using RevMan 5.3.
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 autoimmune rather than autoimmunome, 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 colchicine 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 (improve- ment 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 (90%), colchicine in 3, azathioprine in 3, and cyclosporine 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% 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 autoimmune diseases (1). A prospective trial with higher dosages should be the next step.

References

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
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. 1/4 of the pts had isolated pulmonary artery thrombosis (IPTA); 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 64x4 courses, which was significantly shorter compared to the previous cohort. Twenty-three (49%) 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. SEVAK E. Medicine (Baltimore) 2012.

P086
New major organ involvement is lower in young male Behçet's patients 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 insufficiently 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. Immunsupressive (IS) treatment in the follow-up had significantly lower FMD at baseline compared to healthy 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.

Conclusions. 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.

P087
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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1Marmara University, Faculty of Health Sciences, ISTANBUL, Turkey.

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 (M₁) and (ii) tooth extraction (M₂) 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.

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**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-Amercia, 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-60) 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 fulminating course of the seizures treatment with corticosteroids were considered. This raises an issue as BD is not confirmed.

**Conclusion.** BD is a protein 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 importance 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.

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**P091**

Muucocutaneous 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 (EN) 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; 6.8±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.

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**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/
Clinical and Experimental Rheumatology 2018

P094

Pulmonary Hypertension in Behçet’s Disease


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Introduction. Behçet’s disease (BD) is a systemic vasculitis that involves 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 transhoracic echocardiography (TTE) for the presence of PH. BD patients were categorized according to the involved organs in 5 groups: group 1 mucocutaneous and articular, group 2 ocular, group 3 vascular, group 4 gastrointestinal and group 5 neurologic involvements. The presence of PH was defined as estimated sPAP ≥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.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients</th>
<th>pAPad(mmHg)</th>
<th>pAPad(mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=154)</td>
<td>(n=17)</td>
<td>(n=137)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>62 (40.3)</td>
<td>6 (35.3)</td>
<td>56 (40.9)</td>
</tr>
<tr>
<td>Age, median (min-max)</td>
<td>41 (18-73)</td>
<td>44 (26-72)</td>
<td>40 (18-73)</td>
</tr>
<tr>
<td>Disease duration (months), median (min-max)</td>
<td>126 (6-540)</td>
<td>188 (12-540)</td>
<td>120 (6-480)</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>9 (5.8)</td>
<td>1 (5.9)</td>
<td>8 (5.8)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>26 (16.9)</td>
<td>5 (23.4)</td>
<td>21 (15.3)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>76 (49.4)</td>
<td>7 (41.2)</td>
<td>69 (50.4)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>47 (30.5)</td>
<td>5 (23.4)</td>
<td>42 (30.7)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>31 (20.1)</td>
<td>5 (23.4)</td>
<td>26 (19.0)</td>
</tr>
<tr>
<td>Oral ulcer, n (%)</td>
<td>154 (100)</td>
<td>17 (100)</td>
<td>137 (100)</td>
</tr>
<tr>
<td>Genital ulcer, n (%)</td>
<td>104 (67.5)</td>
<td>11 (64.7)</td>
<td>93 (69.7)</td>
</tr>
<tr>
<td>Erythema nodosum, n (%)</td>
<td>64 (41.6)</td>
<td>7 (41.2)</td>
<td>57 (41.6)</td>
</tr>
<tr>
<td>Papulo-pustular lesion, n (%)</td>
<td>35 (22.7)</td>
<td>3 (17.6)</td>
<td>32 (23.4)</td>
</tr>
<tr>
<td>Acneiform lesions, n (%)</td>
<td>105 (68.8)</td>
<td>8 (47.1)*</td>
<td>97 (70.8)*</td>
</tr>
<tr>
<td>Articular involvement, n (%)</td>
<td>35 (22.7)</td>
<td>4 (23.5)</td>
<td>31 (22.6)</td>
</tr>
<tr>
<td>Uveitis, n (%)</td>
<td>75 (48.7)</td>
<td>9 (51.2)</td>
<td>66 (48.2)</td>
</tr>
<tr>
<td>Pathergy, n (%)</td>
<td>40 (26)</td>
<td>6 (33.3)</td>
<td>34 (24.8)</td>
</tr>
<tr>
<td>Pulmonary arterial involvement, n (%)</td>
<td>19 (12.7)</td>
<td>2 (11.8)</td>
<td>17 (11.7)</td>
</tr>
<tr>
<td>Gastrointestinal involvement, n (%)</td>
<td>12 (7.8)</td>
<td>1 (5.9)</td>
<td>11 (8.0)</td>
</tr>
</tbody>
</table>

*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 ≥2). 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 compared to patients without PH (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 implicate 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 between 1976-2000 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 overall prevalence 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.

Discussion. The reasons for death were infections in 5, related to ESRD in 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts 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 10 (71%) of these 14 pts and 10 (37%) are still alive after a median follow up of 16 (IQR: 10-23) years.
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.

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

<table>
<thead>
<tr>
<th>Severity and form of the disease</th>
<th>N=12(%)</th>
<th>Miscarriage, undelivered pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light</td>
<td>5(41.7)</td>
<td>3</td>
</tr>
<tr>
<td>Medium</td>
<td>1(8.3)</td>
<td>-</td>
</tr>
<tr>
<td>Severe</td>
<td>6(50)</td>
<td>2</td>
</tr>
</tbody>
</table>

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


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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 of 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.
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 two 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°C fever with cardiopulmonary auscultation without abnormalities. Dermatologic examination revealed painful, raised, erythematous papules, plaques, and nodules 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 9,140/mm³); CRP elevated to 70 mg/L. Histopathologic examination of the skin biopsy taken from the erythematous plaque found on his arms showed an abundant edema of the papillary dermis, 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°C 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 10,140/mm³); 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 patient’s biopsy, no fibrinoid necrosis was observed.

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 symptoms and pathergy test positivity 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, biaxial 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 biaxial 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


Fig. 1. Odds ratios and 95% confidence intervals from the logistic regression model predicting ISG+ status.
Clinical characteristics of parenchymal neuro-Beḥcet’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-Beḥcet’s Disease (p-NBD) accounts for the majority of BD cases.

Aims. The aim of the study is to investigate the clinical characteristics of parenchymal neuro-Beḥcet’s Disease.

Methods. We retrospectively reviewed all the medical records of BD patients admitted to Peking Union Medical College Hospital from 2000 to 2016. The diagnosis of neurological involvement was based on the criteria of 2014 International Consensus on NBD. 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%) (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.

Conclusion. p-NBD is a disabling and life-threatening complication despite its rarityness 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

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 unsatisfactorily 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-immunosuppressive (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<3), CI≤6 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±3.1 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 (1.4±0.9 vs 2.0±0.1) 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.

Outcome of short-term Infliximab treatment for sight-threaten

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Introduction. Previous recommendations on the use of anti-TNF agents in HD 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 drugregimen (Sifakis 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 uveal involvement (Sifakis PP et al. Arthritis Rheumatol 2018).

P104 Outcome of short-term Infliximab treatment for sight-threaten

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S-195
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=9) 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±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 on 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 subsequently feed into future clearer guidance for other non-oral medicine specialists 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 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 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
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.

**P108 Cardiac involvement in Behçet disease in a Tunisian cohort**

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**Introduction.** Cardiac involvement in behçet disease (BD) is rare account in adults or children.

**Aims.** We aimed in this work to describe clinical manifestations and therapeutical 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 aphthosis (100%), genital aphthosis (83.3%), necrotic pseudofolliculitis (83.3%), erythema nodosum (16.7%) and ophthalmic 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.

**P109 The assessment of work productivity and activity impairment in patients with Behçet’s disease: a multi-national study**

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1Marmara University, Faculty of Health Sciences, ISTANBUL, Turkey.

**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±3,7 vs 9±7,4 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=0.011) 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%) (p:0.4 p=0.001 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.

**P110 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 aphthosis was observed in 100%. Genital aphthosis 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.
P111
A case of the Behçet’s disease revealed by the panniculitis

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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 histopathology remains unclear. Few cases of Behçet’s disease revealed by panniculitis were described in the literature.

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 aphthosis and a positive pathergy test and demorphypeddermal nodules sensitive, touching two legs and taking blue contusiform aspects. The neurological examination revealed a bilateral cerebellar syndrome and a pyramidal syndrome. In biology he had a biological inflammatory syndrome. Haemogram showed leukocytosis at 13400 / mm3. 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.

P112
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 impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments. They can be difficult to manage and cause disability leading to unemployment and severe impairments.

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 lower extremity vein thrombosis. 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 (15/24) and the anterior surface of the tibia (14/24). 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. Hofrost 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 (5 [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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>24</td>
<td>23 (M)/1 (F)</td>
</tr>
<tr>
<td>Age at disease onset (yrs)</td>
<td></td>
<td>27.5±7.1</td>
</tr>
<tr>
<td>Median time interval between disease onset and ulcer development (yrs)</td>
<td>4.0 [2.5-11.5]</td>
<td></td>
</tr>
<tr>
<td>Median follow-up duration (yrs)</td>
<td>7.8 [2.9-14.2]</td>
<td></td>
</tr>
<tr>
<td>Unemployment due to the leg ulcers (%)</td>
<td>11 (46)</td>
<td></td>
</tr>
<tr>
<td>Eye disease, n (%)</td>
<td>7 (29)</td>
<td></td>
</tr>
<tr>
<td>Large vessel involvement (%)</td>
<td>9 (38)</td>
<td></td>
</tr>
<tr>
<td>Dural sinus thrombosis (%)</td>
<td>3 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Vena cava superior vein thrombosis (%)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery involvement (%)</td>
<td>5 (21)</td>
<td></td>
</tr>
<tr>
<td>Other arterial involvement (%)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Lower extremity vein thrombosis (%)</td>
<td>20 (83)</td>
<td></td>
</tr>
<tr>
<td>Bilateral (%)</td>
<td>15 (62.5)</td>
<td></td>
</tr>
<tr>
<td>Femoral vein (%)</td>
<td>20 (83)</td>
<td></td>
</tr>
<tr>
<td>Popliteal vein (%)</td>
<td>14 (58)</td>
<td></td>
</tr>
<tr>
<td>Superficial vein (%)</td>
<td>7 (29)</td>
<td></td>
</tr>
<tr>
<td>No venous thrombosis or insufficiency (%)</td>
<td>4 (17)</td>
<td></td>
</tr>
<tr>
<td>Pts with a solitary ulcer (%)</td>
<td>12 (50)</td>
<td></td>
</tr>
<tr>
<td>Pts with more than 1 ulcer (&gt;1) (%)</td>
<td>12 (50)</td>
<td></td>
</tr>
<tr>
<td>Pts with healed ulcers (%)</td>
<td>15 (63)</td>
<td></td>
</tr>
<tr>
<td>Pts with active ulcers (%)</td>
<td>13 (54)</td>
<td></td>
</tr>
<tr>
<td>Anatomical localization (total n =54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial malleolus (%)</td>
<td>15 (44%)</td>
<td></td>
</tr>
<tr>
<td>Anterior surface of the tibia (%)</td>
<td>14 (45%)</td>
<td></td>
</tr>
<tr>
<td>Other (%)</td>
<td>5 (19%)</td>
<td></td>
</tr>
</tbody>
</table>

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.

P113
Retrospective analysis of initial presentation findings of Behçet’s syndrome throughout 4 decades

Istanbul University Cerrahpasa Medical School, ISTANBUL, Turkey.

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
Table. Initial demographic and clinical characteristics of cohorts.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979-81 cohort n=211</td>
<td>1990-99 cohort n=130</td>
<td>2000 cohort n=225</td>
<td>2001 cohort n=270</td>
</tr>
</tbody>
</table>

- **Male/Female**
  - Male: 149/61
  - Female: 110/60

- **Mean age at disease onset**
  - 35.5 ± 18.3

- **Median disease duration**
  - 2.5 (1.0-4.0) y

<table>
<thead>
<tr>
<th>Macroscopic inv., %</th>
<th>Microscopic inv., %</th>
<th>Clinical inv., %</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**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**

**P115**

**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 conducted a retrospective study of 296 patients who were followed for BD in our department, between October 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 cutaneous-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 68.9%. Monarthropathy, polyarthropathy, and oligoarthropathy were observed in 7.4%, 10.7%, and 14.87%, respectively, most of them occurring intermittently (70.24%). Knees (n=87) and ankles (n=65) were the most affected joints. A pelvi-axial involvement was noted in 19.8% (n=24). Inflammatory arthralgia was the most common manifestation and observed in 19.8% (n=24). Inflammatory arthralgia was the most common manifestation and observed in 68.9%. Monarthropathy, polyarthropathy, and oligoarthropathy were observed in 7.4%, 10.7%, and 14.87%, respectively, most of them occurring intermittently (70.24%). Knees (n=87) and ankles (n=65) were the most affected joints. A pelvi-axial involvement was noted in 19.8% (n=24). Inflammatory arthralgia was the most common manifestation and observed in 68.9%. Monarthropathy, polyarthropathy, and oligoarthropathy were observed in 7.4%, 10.7%, and 14.87%, respectively, most of them occurring intermittently (70.24%). Knees (n=87) and ankles (n=65) were the most affected joints. A pelvi-axial involvement was noted in 19.8% (n=24). Inflammatory arthralgia was the most common manifestatio
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 RVTED 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=0.002) 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 the risk factor evaluation 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 extremities in patients without BD (95.2%), but without significant differences concerning venous network and extent of these thrombosis. Frequencies of pulmonary embolism and other thrombotic localizations were similar between 2 groups. Comparison of frequencies of the use of different therapeutic means and frequencies of different complications are presented in Table I.

Conclusion. The fact that endohepatology is the main pathophysiological basis of thrombosis during BD explain that RVTED were less recurrent in patients with BD than in those without BD.

P117

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

A. Gokturk, S.N. Esatoglu, Y. Ozguler, E. Atahan, B. Musellim, V. Hamuryudan, H. Yazici, E. Seyahi

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 malignant conditions, SVCS in BS usually has a benign course, complicated rarely by hemoptysis, pleural effusion and a chylous reflux. 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.

Reference


Table I.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (BS patients with SVCS)</th>
<th>Group 2 (BS patients with vascular involvement)</th>
<th>Group 3 (BS patients with no vascular involvement)</th>
<th>Group 4 (Healthy controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>28</td>
<td>80</td>
<td>59</td>
<td>80</td>
</tr>
<tr>
<td>Age, mean ± SD, years</td>
<td>44.3 ± 9.7</td>
<td>42.1 ± 7.8</td>
<td>41.9 ± 5.9</td>
<td>42.7 ± 9.7</td>
</tr>
<tr>
<td>Disease duration, mean ± SD, years</td>
<td>18.7 ± 9.4</td>
<td>14.6 ± 7.7</td>
<td>12.5 ± 6.5</td>
<td>12.5 ± 6.5</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>4 (14.3)</td>
<td>6 (7.5)</td>
<td>2 (4.0)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>26.8 ± 4.7</td>
<td>26.4 ± 3.9</td>
<td>26.2 ± 3.3</td>
<td>27.0 ± 3.5</td>
</tr>
<tr>
<td>High-risk for OSA, n (%)</td>
<td>16 (57.1)</td>
<td>12 (15)</td>
<td>5 (8.5)</td>
<td>9 (11.3)</td>
</tr>
</tbody>
</table>

P118

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

W. Madanat1, S. Khasawneh2, F. Madanat3

1Rheumatology Clinic, AMMAN, Jordan. 2Gastroenterology clinic, AMMAN, Jordan. 3Hematology, Oncology clinic, AMMAN, Jordan.

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 present 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 Cyclophosphamide IV for 6 doses then maintained on AZA 100mg/day and colchicine 1mg/day. In addition he was on daily oral molecular weight heparin.

Methods. On evaluation, the patient was alert. No jaundice or lymphadenopathy. An abdominal examination revealed hepatosplenomegaly, 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, (lo 12-64), alkaline phosphatase 140U/L, (lo 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 the 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 ascitic fluid aspirated which consisted of mesothelial cells and was negative for malignancy.

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Lever biopsy showed Nodular areas devoid of fibrous tissue and portal tracts are seen in one core suggestive of NRH. Upper endoscopy was planned. Heparin and AZA was discontinued, dose of prednisolone was increased to 1mg/kg, plus diuretics. Mycophenolate mofetil 500mg x 1 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 TMTT 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.

**References**

**P120**
Patients with (suspected) Behçet syndrome: clinical presentation of 101 patients

**FG. Kerstens. S.S. Mohamed, A.E. van der Hoeven, F. Turkstra Read, Jan van Breezen Research institute, AMSTERDAM, The Netherlands.**

**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 lesions 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 considered no BS was present.

**Conclusion.** 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%). Colchicine, 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 Dapson were prescribed in 10, 6 and 4 patients, respectively. Thalidomide was given to both (two 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 was 13.0 mm/hour (ranging from 1 to 51).

**Table I.** Disease duration and VWT.

<table>
<thead>
<tr>
<th>Disease duration and VWT.</th>
<th>BS without vascular involvement</th>
<th>Non vascular involvement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISG criteria positives</td>
<td>AR, N=101</td>
<td>ISG criteria positive, N=37</td>
<td></td>
</tr>
<tr>
<td>Oral ulcerate</td>
<td>95 (94)</td>
<td>37 (100)</td>
<td></td>
</tr>
<tr>
<td>Genital ulcerate</td>
<td>57 (56)</td>
<td>33 (89)</td>
<td></td>
</tr>
<tr>
<td>Skin involvement</td>
<td>37 (37)</td>
<td>27 (71)</td>
<td></td>
</tr>
<tr>
<td>Eye involvement</td>
<td>27 (27)</td>
<td>16 (46)</td>
<td></td>
</tr>
<tr>
<td>Loss of Visual Acuity</td>
<td>5 (19)</td>
<td>1 (19)</td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>5 (15)</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>11 (11)</td>
<td>7 (19)</td>
<td></td>
</tr>
<tr>
<td>Articular involvement</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>CNS vasculitis</td>
<td>8 (8)</td>
<td>5 (15)</td>
<td></td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>18 (18)</td>
<td>9 (24)</td>
<td></td>
</tr>
<tr>
<td>involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>30 (30)</td>
<td>16 (43)</td>
<td></td>
</tr>
<tr>
<td>Erythoderm</td>
<td>7 (7)*</td>
<td>2 (2)*</td>
<td></td>
</tr>
<tr>
<td>Positive pathergy test</td>
<td>17 (17)</td>
<td>15 (15)</td>
<td></td>
</tr>
<tr>
<td>% of patients with eye involvement % of male patients</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 others. 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**
The relationship between Behçet’s disease flare up and menstruation in an Irish cohort

W.L. Ng1, F. Adeb2, J. Devlin1, A. Fraser2
1University Hospital Limerick, LIMERICK, Ireland

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. 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).

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 (22.2%) patients in our cohort were menopausal. 9 (50%) of the patients reported that the occurrence of BD flare ups was correlated to the menstrual cycle. The types of disease activity flare experienced include oral aphthosis (88.9%), arthralgia (55.6%), 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.

Table Characteristics of the included subjects.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>BD with eye disease</th>
<th>BD with vascular disease</th>
<th>BD with neurologic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>M:F</td>
<td>M:F</td>
<td>M:F</td>
</tr>
<tr>
<td>Mean age</td>
<td>36.8</td>
<td>35.3</td>
<td>37.5</td>
<td>38.8</td>
</tr>
<tr>
<td>Mean disease duration</td>
<td>8.2±5.6</td>
<td>8.3±5.6</td>
<td>8.1±5.7</td>
<td>8.3±5.7</td>
</tr>
<tr>
<td>Mean WIS score</td>
<td>12.2±9.8</td>
<td>11.4±5.6</td>
<td>10.9±8.1</td>
<td>11.7±7.0</td>
</tr>
<tr>
<td>Mean WPAI-presenteeism score</td>
<td>3.7±0.9</td>
<td>3.1±0.7</td>
<td>3.4±1.7</td>
<td>3.3±1.5</td>
</tr>
<tr>
<td>Mean WPAI-absenteeism score</td>
<td>4.2±1.0</td>
<td>4.1±0.9</td>
<td>3.8±1.0</td>
<td>3.8±1.0</td>
</tr>
<tr>
<td>Mean BDCAFL score</td>
<td>4.3±2.7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Mean BAS (mean±SD)</td>
<td>28.2±7.9</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Mean BASQI score</td>
<td>17.6±8.2</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Mean BASFI (mean±SD)</td>
<td>3.6±1.7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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

Poster Session 2
18th International Conference on Behçet’s Disease

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 involvement are among the most serious and challenging manifestations of the disease.

Aims. To assess the efficacy of biological therapy in refractory ocular and neurologic 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, 5 mg/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 adult and working years, thus affecting productivity. Work disability is needed to specify their use in the upcoming new guidelines.

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.

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 by at least 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 (26.0% 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.

P123
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 (22.2%) 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 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. Detailed studies involving larger cohorts should be performed to further support and strengthen this evidence.

References

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/neo-ro-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 papillodema; 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-aphtous 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-aphtous 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.

P126
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.

P127

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 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 oculair pathology that may cause a decrease in the BCVA macula or optic disc 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 74.4±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

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.


Results. A 54 years old patient with history of muco-cutaneous Behçet’s disease was admitted for acute abdominal pain, diarrhea, rectal syndrome and a giant genital ulcers, skin lesions in the forearm consisting with cutaneous vasculitis. Laboratory data showed an important inflammatory syndrome. 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 inflammation 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.

Clinical and Experimental Rheumatology 2018
Clinical characteristics of older age-onset Behçet syndrome patients

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Introduction. The usual onset of Behçet syndrome (BS) is in the 3rd 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 1. 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 classic-onset BS pts (Males/ Females)

<table>
<thead>
<tr>
<th>Age at ISG criteria is fulfilling yrs</th>
<th>Older onset males (n=70)</th>
<th>Classical onset males (n=65)</th>
<th>P</th>
<th>Older onset females (n=54)</th>
<th>Classical onset females (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral ulcer, n (%)</td>
<td>60 (90)</td>
<td>167 (100)</td>
<td>-</td>
<td>64 (100)</td>
<td>105 (100)</td>
</tr>
<tr>
<td>Genital ulcer, n (%)</td>
<td>60 (90)</td>
<td>137 (84)</td>
<td>0.845</td>
<td>51 (80)</td>
<td>90 (160)</td>
</tr>
<tr>
<td>Papulopustular lesion, n (%)</td>
<td>49 (70)</td>
<td>133 (82)</td>
<td>0.050</td>
<td>39 (61)</td>
<td>71 (60)</td>
</tr>
<tr>
<td>Nodular lesion, n (%)</td>
<td>13 (21)</td>
<td>76 (74)</td>
<td>0.000</td>
<td>29 (45)</td>
<td>60 (157)</td>
</tr>
<tr>
<td>Arthritis, n (%)</td>
<td>10 (15)</td>
<td>45 (28)</td>
<td>0.028</td>
<td>13 (20)</td>
<td>23 (24)</td>
</tr>
<tr>
<td>Eye involvement, n (%)</td>
<td>24 (39)</td>
<td>88 (50)</td>
<td>0.006</td>
<td>26 (41)</td>
<td>41 (39)</td>
</tr>
<tr>
<td>Only ulcers, cell n (n*°)</td>
<td>2 (3)</td>
<td>25 (28)</td>
<td>0.008</td>
<td>7 (27)</td>
<td>14 (34)</td>
</tr>
<tr>
<td>VIH – -1 in either or both eye</td>
<td>8 (33)</td>
<td>27 (33)</td>
<td>0.941</td>
<td>4 (15)</td>
<td>9 (23)</td>
</tr>
<tr>
<td>Vascular involvement, n (%)</td>
<td>13 (19)</td>
<td>27 (17)</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pathergy positivity, n (n*°)</td>
<td>39 (56)</td>
<td>94 (58)</td>
<td>0.876</td>
<td>34 (53)</td>
<td>49 (47)</td>
</tr>
<tr>
<td>OMS involvement, n (%)</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>GIS involvement, n (%)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

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

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 and seen a Rheumatologist, Ophthalmologist, Oral Medicine Specialist and Clinical Psychologist on more than one occasion were included. At each visit Disease activity (BDAAI) 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. BDAAI 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 BDAAI. BDAAI 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 BDAAI, 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 BDAAI also corresponded with an increase in 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.
Adalimumab provides long lasting clinical improvement in refractory mucocutaneous Behçet’s Disease without formation of antidrug antibodies

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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 long-term 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 (BDCF) within 6 months. Secondary endpoints included serum cytokines and the long-term formation of anti-adalimumab antibodies.

Results. BDCF 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 elevated in five patients and decreased upon treatment (p=0.017). Adalimumab was safe 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.

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 disease activity.

Aims. Whole genome sequencing (WGS) was performed in a family with Behçet’s disease.

Methods. WGS (software version 2.5.0.37) was performed in 3 patients with BD 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_000222.exon4:c.A251G:p.G84C) was found.

Conclusion. ADA gene in affected family members was found. Exac reveals a very low frequency; 8.24x10^{-5}.

References
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-ophthalmology 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 immunosuppressive medications and/or corticosteroids. Prognosis was favorable 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. Immunosuppressants should be given along with corticosteroids.
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 1990s. 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 retrolubar 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 retrolubar neuritis, its clinical course and treatment modalities, in patients with behçet disease.

**Methods.** A retrospective study of 287 patients with neurobehçet over a period from 1981 to December 2017, we collected 8 cases of retrolubar 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 lost in 1/10 in 37.6% of eyes. The retrolubar optic neuritis was associated with other ocular lesions in 4 cases (1 vasculartis and 3 uveitis) and 1 patient had a venous thrombosis of the upper longitudinal sinus. 7 patients received high dose IV corticosteroids 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 retrolubar neuritis is a rare neurological involvement in Behçet’s disease. The association of optic retrolubar 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.