O1.

SERUM CYTOKINE PROFILE IN PATIENTS WITH BEHÇET'S DISEASE

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Introduction. Behçet's disease (BD) is a multi-systemic disorder characterized by relapsing oral–genital ulcers, uveitis, and involvement of vascular, gastrointestinal, neurological and musculoskeletal system. Although BD aetiology is not fully understood, several data showed that impaired immune response observed in BD patients is characterized by enhanced serum cytokines levels that might provide diagnostic or activity markers for the disease.
Objectives. The aim of the study was to investigate the serum levels of a panel of twenty-five cytokines in patients with Behçet's disease (BD) compared with Healthy Controls (HC) and to correlate their concentration with the status of disease activity.
Materials & Methods. 54 serum samples from 46 BD patients (17 males, 29 females, mean age 45,5±11,3 years) and 19 age- and sex- matched HC were recruited. A panel of twenty-five serum cytokines (APRIL/TNFS13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IFNb, sIL-6Ra, IL-10, IL-11, IL-19, IL-20, IL-26, IL-27 (p28), IL-28A/IFN-lambda2, IL-29/IFN-lambda1, IL-32, IL-34, IL-35, LIGHT/TNFSF-14, Pentraxin-3, sTNF-R1, sTNF-R2, TSLP and TWEAK/TNFSF-12) were simultaneously quantified using a Bio-Rad cytokine bead arrays. BD patients were included in active-BD group when they had at least two of the following clinical findings: uveitis, oral aphthosis, genital aphthosis, cutaneous disease, central nervous system involvement, vascular involvement, gastrointestinal involvement. Statistical approaches included Mann-Whitney test or Student's t-test, one-way analysis of variance (ANOVA) and correlations were calculated using Spearman's correlation (two-tailed p-value) as well as Pearson's correlation test when required.
Results. The results revealed that serum concentrations of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1, sTNF-R2 were significantly higher than in HC. Moreover, Spearman's rho's test showed moderate positive correlations between sTNF-R1, sTNF-R2 and gp130/sIL-6Rb (Spearman rho 0.706 and 0.783 respectively) and between sTNF-R1 and sTNF-R2 (Spearman rho 0.7308). Additionally, based on BD disease activity, serum levels of sTNF-R1 ($p<0.01$) and sTNF-R2 ($p<0.01$) resulted higher in both active- and inactive-BD than HC, while Chitinase3-like1 ($p<0.05$) and gp130/sIL-6Rb ($p<0.01$) serum levels were significantly higher in inactive-BD and IL-26 ($p<0.01$) in active-BD than HC.
Conclusions. Our findings support a key role for IL-6 as well as TNF cell activation in BD pathogenesis, in particular as a feature of inactive disease patients. Moreover, in active-BD patients enhanced IL-26 serum levels were found, supporting the potential involvement of Th17 activation pathway in the disease activity.

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O2.

OCULAR DISEASE PHENOTYPING FROM MULTIPARAMETER CELL ANALYSIS BY MACHINE LEARNING ALGORITHMS

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Background. Current analysis of cell populations in body fluids from patients with ocular diseases relies strongly on cytometry, which measures the expression of markers on each cell. However, cell heterogeneity can be a difficult challenge for current single-cell biology, and it can be difficult to distinguish between complex ocular diseases. A recent study1 combined multiparameter single cell analysis with machine learning classification to accurately predict patients with Behçet's Disease (BD) and patients with sarcoidosis on the basis of five markers on CD8+ cells. We have now extended the numbers of patients analysed and incorporated patients with other ocular diseases.
Methods. Peripheral blood mononuclear cells (PBMC) was isolated from patients with BD (n=-100), sarcoidosis (n=15) isolated idiopathic uveitis (n=15) and birdshot uveitis (BU; n=15) and healthy controls (n=45). PBMC were labelled with a 15-colour antibody panel and the data was collected using flow cytometry and subsequently compensated using FlowJo. Compensated data was then analysed by two machine learning algorithms, Supercell, which randomly allocates multiple single cells into a supercell and calculates a single score value for all parameters which are then compared between patient groups to identify differences; and quantile-based analysis which compares each parameter against all others to identify the most significant phenotype which can discriminate between patient groups.
Results. The results show that all disease groups can be distinguished from healthy controls via supercell and quantile-based analysis. In patients with BD this was based on markers including IL22, TNF-α and IL-23R supporting previous findings by protein and genomic studies. Patients with ocular BD could be distinguished from patients without eye involvement by markers such as TNF-α,IL23R and IL17. Between diseases patients with BD could be distinguished from patients with Birdshot uveitis IL22 and CCR7.
Conclusions. Flow cytometry has been a hugely influential technique in advancing our understanding of the cellular basis of ocular disease. Novel machine learning algorithms increase the range of analysis to distinguish between diseases with a similar aetiology. The ability to apply such techniques to include other parameters such as gender, genetics and therapy have exciting potential.

Reference

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O3.

EXPRESSION OF HOMING MAKERS ON PERIPHERAL BLOOD LYMPHOCYTES IN BEHÇET'S DISEASE PATIENTS AND HEALTHY CONTROLS

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Background. Behçet's Disease (BD) is characterised by significant mucosal pathologies including recurrent oral aphthous ulcerations, genital ulcers and ocular inflammation as well as skin involvement. Some of the sites of pathology (ocular, oral and genital mucosa) are considered as immune privileged sites so that disregulation of homeostatic process must contribute to the symptoms experienced by patients, including recruitment of inflammatory cells into the tissues initiating the inflammatory profile characteristic of the disease.
In recent years the role of the unconventional γδ T cell population has been re-examined in many diseases. While these cells represent only a small proportion of circulating lymphocytes their role in maintaining both homeostasis and driving inflammatory processes warrants careful scrutiny in the context of BD.
Vγ9Vδ2(+) (Vδ2) T cells proliferate and accumulate in mucosal tissues following microbial activation and these cells have been demonstrated in the ulcer bed of oral ulcers in BD patients. Vδ2T cells produce proinflammatory cytokines in response to bacterial species, especially to those capable of producing phosphoantigens, many of which are resident in the oral microflora. We hypothesized that circulating Vδ2T cells can home to mucosal tissue (and /or skin) and contribute to inflammation. We have hypothesized that oral mucosal sites have homing receptors for β7 and CLA which may be responsible for the homing (tropism) of γδ T cells to oral mucosa (or skin) and drive the inflammatory processes in BD.
Methods. Peripheral Blood Mononuclear Cells were stimulated with IL-2, and the microbial phosphoantigen (1-hydroxy-2-methyl-2-buten-4-yl 4-diphosphate [HDMAPP]) and medium alone for seven days. Flow cytometry was performed to detect the expression of β7 and CLA by Vδ2+ and αβ T cells. Data obtained by flow cytometry was analysed using Flow Jo software.
Peripheral blood lymphocytes were also investigated for their binding to mucosal addressin cell adhesion molecule-1 (MadCam-1) in vitro.
Results. Both unstimulated Vδ2+ and αβ T cells from BD showed greater expression of β7 and CLA compared to HC revealing the potential for homing to mucosa and skin. The stimulated Vδ2+ and αβ T cells from both BD and HC exhibited increased β7 (up to 80%) but CLA was down-regulated in stimulated BD samples. Stimulated HC appeared to segregated into two distinct populations; one showing high CLA expression and other with lower expression of CLA.
Conclusion. Stimulation of PBMCs with HDMAPP upregulated the expression of β7 by Vδ2+ and αβ T cells in both BD and HC. However, the mean expression of β7 in BD was higher than HC suggesting that the cells were already primed in BD for migration to the mucosal site. CLA was down regulated in stimulated BD but inconsistent results obtained for HC reveals there might be some ethnic background involvement.

O4.

DENSE GENOTYPING OF IMMUNE-RELATED LOCI IMPLICATES HOST RESPONSES TO MICROBIAL EXPOSURE IN BEHÇET'S DISEASE SUSCEPTIBILITY

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Background. Recent genetic studies have identified multiple susceptibility loci exceeding genome-wide significance. However, these genetic factors do not fully explain the apparent disease heritability. Pathogenic and opportunistic infections have been proposed as important environmental factors contributing to both the development and exacerbation of Behçet's disease. The purpose of this study was to densely genotype loci associated with immune-related diseases to identify novel susceptibility loci for Behçet's disease.
Methods. 1,900 Turkish Behçet's disease patients and 1,779 controls were genotyped using the Immunochip. After strict quality control, we performed association tests. For novel loci with association test $p<5\times10\text{-}5$, additional SNPs in the region were imputed using 1000 Genomes Project data as a reference. For replication, the lead SNP genotyped by the Immunochip in each novel locus with $p<5\times10\text{-}5$ in the Turkish population was genotyped in 982 cases and 826 controls from Iran. We also replicated disease associations with imputed previous GWAS data from 608 Japanese cases and 737 controls.
Results. HLA-B*51 was the strongest associated marker and rs1050502 the strongest associated SNP. rs1050502 is located in exon 2 of HLA-B and the risk allele T is a tag SNP for HLA-B*51. Outside of the MHC region, we identified 4 novel loci, IL1A-IL1B, ADO-EGR2, IRF8, and CEBPB-PTPN1, which exceeded genome-wide significance in Turks. In addition, we confirmed four previously reported loci, IL10, CCR1, IL12A, and FUT2. Genotyping Iranian samples and meta-analysis with Turkish data replicated associations of three loci, ADO-EGR2, IRF8 and CEBPB-PTPN1. Comprehensive meta-analysis of the regional imputed genotype data of Turks and Japanese replicated two loci, ADO-EGR2 and IRF8, and revealed two additional novel loci, RIPK2 and LACC1. The lead SNP, rs4402765, for IL1A-IL1B is also the most significantly IL1A expression-associated variant in a lymphoblastoid cell eQTL database. The eQTL database also showed decreased expression of RIPK2 and CEBPB associated with the risk allele of the lead SNP for each locus. Homozygosity for ancestry specific FUT2 non-secretor alleles, rs601338 (p.Trp143Ter) in Turks and Iranians and rs1047781 (p.Ile129Phe) in Japanese, showed strong disease association. The non-secretor genotype has been associated with Crohn's disease and gut microbiome composition.
Conclusion. Here, we conducted an Immunochip study in the largest Behçet's disease discovery cohort ever with multiple populations for replication. This study provided robust evidence for HLA-B*51 as the primary source of the strong disease association in the HLA region and identified 6 novel loci (IL1A-IL1B, RIPK2, ADO-EGR2, LACC1, IRF8, and CEBPB-PTPN1) with genome-wide significance for Behçet's disease. Our findings that the disease-associated alleles of IL1A, RIPK2 and CEBPB are associated with decreased gene expression and that disease-associated FUT2 structural variants are hypofunctional suggest that an impaired host response to the microbiome may contribute to Behçet's disease susceptibility

O5.

GENOME-WIDE SCREENING OF LOCI ASSOCIATED WITH CLINICAL MANIFESTATIONS OF BEHÇET'S DISEASE

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Objective. Behçet's disease (BD) is a chronic systemic inflammatory disorder characterized by four major symptoms: recurrent ocular symptoms, oral ulcers, genital ulcers, and skin lesions. BD is occasionally associated with inflammation in other tissues, such as joints, the vascular system, the gastrointestinal tract, the central nervous system, and epididymis. The etiology of BD is still uncertain, but the disease 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. Recent genome-wide association studies (GWASs) have reported several susceptibility loci/genes for BD, including UBAC2, HLA-A*26, IL10, IL23R-IL12RB2, ERAP1, CCR1, KLRC4, STAT4, and GIMAP. The purpose of this study was to identify loci specifically associated with clinical manifestations of BD using a GWAS.
Materials and Methods. We used previous GWAS data with a Japanese population (612 BD patients and 740 healthy controls) using Affymetrix GeneChip Human Mapping 500K Array Set (500,568 SNPs) (Nat Genet 2010;42(8):703-6.). After sample and SNP quality control, a total of 309,362 autosomal SNPs from 611 patients and 737 controls were used for statistical analyses to identify loci affecting specific disease manifestations (oral ulcer, skin lesion, ocular lesion, genital ulcer, arthritis, epididymitis, gastrointestinal lesion, vascular lesion, and central nervous system lesion). In order to be considered a candidate, we required SNPs to have $p<00001$ and OR ≥1.40 in patients with a specific disease manifestation but $p>0.05$ and OR <1.1 in patients without the manifestation.
Results. We identified 40, 25, 36, and 31 candidate risk loci for oral ulcer, skin lesion, ocular lesion, and genital ulcer, respectively. We also identified 28, 37, 36, 35, and 89 candidate risk loci for arthritis, epididymitis, gastrointestinal lesion, vascular lesion, and central nervous system lesion, respectively. The candidate loci for each major symptom include some HLA loci, whereas no HLA loci were associated with minor symptoms.
Conclusions: Preliminary results of the ongoing study point out to risk loci for clinical manifestations of BD. To confirm the findings, future validation studies with other independent populations are needed.

O6.

HOMOZYGOSITY FOR A SINGLE ERAP1 ALLOTYPE GREATLY INCREASES BEHÇET'S DISEASE RISK IN HLA-B*51 CARRIERS

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Background. Endoplasmic reticulum aminopeptidase-1 (ERAP1) trims intracellular proteasome-processed peptides, a step required for efficient loading of many peptides onto HLA class I molecules prior to transport to the surface of nearly all cell types. These HLA-peptide complexes play important roles in immune surveillance through their interactions with cytotoxic T cells and natural killer cells. The class I HLA type, HLA-B*51, has been identified in multiple populations as the most significant genetic risk factor for Behçet's disease and several ERAP1 gene variants have been found to interact with this factor. The ERAP1 protein has numerous missense variants that collectively influence its peptide specificity and enzymatic activity. In this study we determined the haplotypes of ERAP1 variants and the encoded ERAP1 allotypes found in the Turkish population and determined their association with Behçet's disease risk.
Methods. Ten ERAP1 missense variants, 8 directly genotyped on the Immunochip and 2 imputed from the ERAP1 region genotypes using Impute2 and 1000 genomes phase I reference haplotypes, were determined in 1876 individuals with Behçet's disease and 1761 controls from Turkey. HLA-B*51 types were imputed with Immunochip HLA region genotypes using SNP2HLA and 10,450 reference HLA marker and classical HLA type haplotypes as reference. Haplotypes and Pearson chi squared disease association tests were determined with SNP Variation Suite 8.4.

Results. The 10 ERAP1 missense variants with minor allele frequency greater than 1% defined 8 haplotypes or protein allotypes with greater than 1% frequency in the Turkish population. One allotype with 5 non-ancestral amino acids was recessively associated with disease (p=3.13 x 10-6, odds ratio 2.55, 95% CI 1.70 to 3.82). This association was enhanced in individuals who carry HLA-B*51 (p=4.58 x 10-8, odds ratio 3.05, 95% CI 1.64 to 5.66) and absent in individuals who did not carry HLA-B*51 (p=0.82). Individuals who carry HLA-B*51 and are also homozygous for the ERAP1 haplotype had substantially increased disease odds compared with those with neither risk factor (p=4.8 x 10-20, odds ratio 10.96, 95% CI 5.91 to 20.32).
Conclusion. The disease-associated ERAP1 allotype likely contributes to Behçet's disease susceptibility by altering its peptidase activity and or substrate specificity, suggesting that either an over production of ERAP1 allotype specific disease promoting peptides or inadequate production of disease-protective peptides contributes to disease susceptibility. Identifying the nature and source of such peptides, for example, are they self-derived or do they originate in pathogenic or commensal organisms, would be an important step towards elucidating the mechanism by which HLA-B*51 contributes to Behçet's disease risk.

O7.

POST-THROMBOTIC SYNDROME IS INCREASED AND VENOUS DISEASE SPESIFIC QUALITY OF LIFE IS IMPAIRED IN PATIENTS WITH VASCULAR BEHÇET'S DISEASE WITH NO BENEFIT OF ANTICOAGULANT USE

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Objective. Deep venous thrombosis (DVT) is the most common form of vascular involvement in Behçet's disease (BD). Chronic post-thrombotic syndrome (PTS) develops in up to one-half of patients with DVT and is associated with impaired quality of life (QoL). We aimed to evaluate PTS, venous disease spesific QoL and the associated factors in patients with VBD.
Method. This study included 94 patients (Male/Female:75/19) with VBD and 29 age and gender-matched individuals, (Male/Female: 18/11) with DVT associated with non-BD causes. Villalta scale was used to assess of PTS. Venous Disability Score (VDS) and 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 questionnaire (VEINES-QoL/Sym). Behçet Syndrom Activity Score (BSAS) questionnaire was used to assess disease activity.
Results. A high presence of PTS (61.7%) was observed in VBD (Table 1). The rate of anticoagulant usage was significantly lower (63% vs 100%, p=0.001), and the number of DVT attacks were significantly higher in VBD (1.6 vs 1.3, p=0.001) compared to non-BD. When VBD patients with PTS were compared to VBD patients without PTS, VEINES-QoL and VEINES-Sym VCSS were significantly worse in VBD with PTS. BSAS was also significantly higher in patients with PTS. An inverse correlation was observed between VEINES-QoL and BSAS in multivariate analysis. There were no differences between anticoagulant users and non-users regarding the presence of PTS and scores of all venous assessment tools in VBD.

Table I. Venous assessment and quality of life parameters in studi groups.

	Vascular Behçet Disease (n=94)	Non-Behçet group (n=29)	P value
PTS, n (%)	58 (% 61.7)	21 (%84)	0.036
VEINES-QoL	87,80±16,55	72,31±19,67	0.001
VEINES-Sym	38,83±8,95	32,72±10,32	0.002
VCSS	4,74±4,33	6,43±4,53	0.015
CEAP	2,09±1,68	2,25±1,51	0.468
VDS	1,04±0,59	1,48±0,58	0,001

PTS:Post-thrombotic syndrome, VEINES-QoL/Sym: Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire, VCSS: Venous Clinical Severity Score, CEAP:Clinical, Etiologic, Anatomic, Pathophysiologic) classification, VDS: Venous Disability Score

Conclusion. A high presence of PTS and impaired venous disease spesific QoL, symptom severity and venous disability scores was observed in VBD in our study. Venous disease spesific QoL negatively correlated with general disease activity. Any additional benefit of anticoagulant treatment on development of PTS and venous QoL was present. Our results suggest that successful control of disease activity might decrease development of PTS, improve venouse disease spesific QoL as well as preventing the relapses in VBD.

O8.

AN OUTCOME SURVEY OF 100 PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS DUE TO BEHÇET'S SYNDROME FOLLOWED UP AT A SINGLE, DEDICATED CENTER

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Background and objectives. Behçet's syndrome (BS) is a well-recognized cause of cerebral venous sinus thrombosis (CVST). We assessed the outcome of a large cohort of patients with CVST due to BS attending a single dedicated center.
Methods. We identified 100 (81 M/19 F) BS patients out of 8000 who were diagnosed as having CVST. Their outcome was evaluated between Feb and Dec 2015. All contacted were called back to the outpatient clinic for a clinical, neurological and ophthalmological examination and cranial MRI /MR venography.
Results. The mean age of the patients at the onset of the symptoms was 28±10 years. A total of 48 patients developed CVST before or at the onset of ISG fulfillment, while 52 developed CVST after a median 3 [2-8] years of ISG fulfillment. Detailed radiological information was not available in 3 patients. Cranial MRI did not show any abnormality in 8 patients, although all had symptoms of acute onset of intracranial hypertension with bilateral papilledema. In the remaining, superior sagittal (n=47) and transverse sinuses (n=46) were most commonly involved followed by sigmoid sinus (n=26) and jugular vein thrombosis (n=15).
A total of 59 (53 M/ 6 F) patients had vascular involvement in addition to CVST. In about half (32/59), CVST preceded any type of additional vascular involvement. Eye involvement was seen in 37 patients, parenchymal CNS involvement in 8 (all later than CVST) and gastrointestinal involvement in 5.
Seven patients died, due to causes unrelated with CVST such as hepatic encephalopathy due to Budd-Chiari syndrome (n=3), pulmonary artery involvement PAI (n=2), sepsis and suicide (n=1). Six patients were lost to follow-up after a single visit. By the end of the study, all remaining 87 patients were alive and contacted with a median follow-up time of 11 [IQR: 6-15] years. Only 6 patients had a relapsing CVST course. A total of 81 (95 %) patients received immunosuppressive treatment and 5 underwent shunting surgery/or embolization.
By the end of Dec 2015, a total of 50 patients were re-evaluated at the clinic. None had symptoms of intracranial hypertension. Ophthalmological examination showed that 17 patients had complications such as bilateral optic atrophy (n= 3), bilateral papilledema (n= 5), bilateral optic disc pallor (n=4) and fibrotic scars around optic disc (n= 5). Sensorineural type hearing loss was detected in 4 patients. Neurological examination was found to be normal among 43 patients with isolated CSVT, whereas abnormal in the remaining 7 patients with concomitant parenchymal CNS involvement.
Cranial MR/MR venographies were abnormal in 36 (72 %) patients showing occlusion/ irregularity/ hypoplasia or collaterals in the sagittal or transverse sinus. In the remaining 14, these were found to be normal.
Conclusions. CVST due to BS is closely associated with vascular involvement elsewhere in the body and may be considered as a risk factor for future vascular involvement. CVST relapses are rare; however, the course is not uneventful: visual acuity or field may be impaired totally or partially because of optic disc atrophy; in addition hearing deficits may occur.

O9.

A LOW BALANCE BETWEEN MICROPARTICLES EXPRESSING TISSUE FACTOR PATHWAY INHIBITOR AND TISSUE FACTOR IS ASSOCIATED WITH THROMBOSIS IN BEHÇET'S SYNDROME

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Background. Thrombosis is common in Behçet's Syndrome (BS), and there is a need for an understanding of causation and for better biomarkers to enable thrombotic risk assessment.
Objectives. We investigated whether plasma microparticles expressing Tissue Factor (TF) are increased in BS and how TF positive MPs relate to numbers of MP expressing Tissue Factor Pathway Inhibitor (TFPI).

Methods. This was a case-control study comparing 88 BS patients with 72 healthy controls. The BS group contained 21 patients with a thrombosis history (Th+) and 67 patients without (Th-). MPs were identified by size and annexin V binding using flow cytometry, and were further analyzed with antibodies to surface antigens.
Results. Total MP numbers were increased in BS compared to HC, as were MPs expressing TF and TFPI (all $p<0.0001$). Amongst BS patients, the Th+ group had increased total and TF positive MP numbers (both $p<0.0002$) compared to the Th- group, but had a lower proportion of TFPI positive MPs ($p<0.05$). Consequently, the ratio of TFPI to TF MP counts (TFPI/TF) was significantly lower in Th+ versus Th- BS patients ($p=0.0002$), and no patient with a TFPI/TF MP ratio >0.7 had a history of clinical thrombosis.
Conclusions. We conclude that MP expressing TF are increased in BS and more so in patients with a history of thrombosis. An imbalance between microparticulate TF and TFPI may be pathophysiologically important for thrombosis in BS and may contribute to improved identification and appropriate treatment of thrombotic risk.

O10.

EARLIER USE OF INFLIXIMAB FOR THE UVEITIS OF BEHÇET'S SYNDROME APPEARS TO BE ASSOCIATED WITH BETTER OUTCOME

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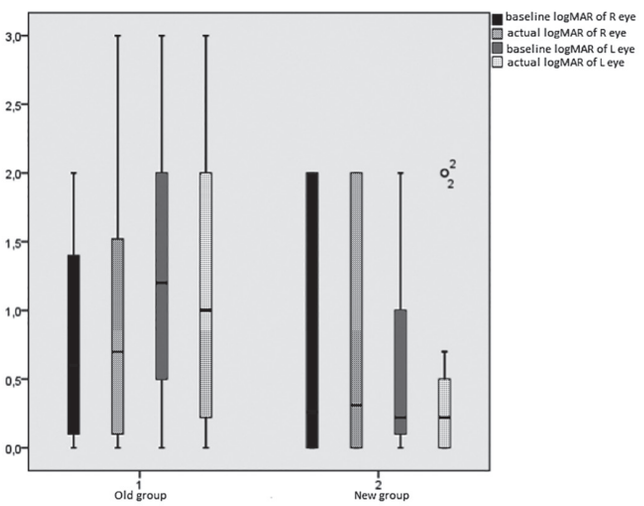
Background. New data suggest a better visual outcome for Behçet's Syndrome (BS) compared to earlier reports (1,2). This improvement may have resulted from the introduction of more effective therapeutic agents like anti-TNFs, but perhaps also from their more efficacious use. However, whether the disease characteristics and treatment responses of BS patients starting specifically anti-TNF therapy for uveitis have changed over time is not known.
Objective. To compare the clinical characteristics and treatment responses of BS patients who started infliximab (IFX) for uveitis before and after 2013.
Methods. The charts of 17 patients (15 men, 2 women; age at the initation of IFX: 33.8±7.5 SD years) receiving IFX (5 mg/kg) for uveitis at our centre after 2013 (New Group) were reviewed retrospectively. The data were compared with those of 43 patients starting IFX before 2013 (Old Group) (3).
Results. Similar to the patients in the old group, the patients in the new group also had severe, sight-threatening posterior uveitis that was refractory to previous treatment with conventional immunosuppressives (azathioprine=15, cyclosporin A=15, interferon alfa=13, cyclophosphamide=2 and steroids). The duration of previous immunosuppressive treatment was significantly shorter (median: 26 months; IQR: 10-53 months) in the new group compared to that of the old group (median: 60 months; IQR: 25-84 months; $p=0.012$). The duration of uveitis until the initiation of IFX was also shorter in the new group (median: 39 months; IQR: 16-94 months) than the old group (median: 72 months; IQR: 45-132 months) but this did not reach statistical significance ($p=0.075$). There was no significant difference between groups regarding the baseline visual acuity (VA) at the time of initation of IFX in the right eye (Median LogMAR for new group: 0.3, for old group: 0.7; $p=0.8$) but the baseline VA of the left eye of the new group (median LogMAR: 0.22; IQR: 0.05-1) was significantly better compared to that of the old group (median LogMAR: 1.2; IQR: 0.5-2; $p=0.005$). The percentage of patients with no useful vision (LogMAR>1) in at least one eye was 47% in the new group and 67% in the old group ($p=0.23$). Information on outcome was available for 14 patients in the new group. The duration of IFX treatment was 13.8±7.9 SD months (median 11.5 months). Ten patients (71%) had at least one attack in the right, left or both eyes before IFX, while all patients except one (93%) became attack free under IFX. The mean VA of the left eye improved significantly with IFX (Figure 1).



Discussion. Earlier use of IFX for BS uveitis appears to be associated with better outcome.

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O11.

EVALUATION OF OCULAR DISEASE ACTIVITY USING BEHÇET'S DISEASE OCULAR ATTACK SCORE 24

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Background. ocular involvement in Behçet's disease (BD) is reported to range from 47 to 69% and is characterized by recurrent attacks of intraocular inflammation, including anterior and more often posterior uveitis or panuveitis. Evaluation of ocular inflammatory activity is difficult and usually based on frequency of ocular attacks, best-corrected visual acuity, location of inflammation. BD ocular attack score 24 (BOS24) – the new easily used objective scoring system for quantitative evaluation of disease activity related to ocular BD proposed by Japanese ophthalmologists (1).
Objective. to evaluate of ocular disease activity using BOS24 scoring system
Methods. 124 BD patients were enrolled in the study. All the patients met the criteria of the International Study Group for BD (1990). The disease activity was assessed by scoring system BDCAF. All the patients were examined by an ophthalmologist. 81 (65,3%) of these BD patients had ocular involvement. 61 (75,3%) BD patients with ocular involvement were men with mean age (M±m) 33,6±1,11 years. An ocular attack was defined as acute aggravation of intraocular inflammation with subjective symptoms of uveitis (conjunctival ciliary injection, floaters, blurred visions, etc.) and objective signs observed by slit-lamp microscopy and fundoscopy. For evaluation of ocular disease activity BOS24 scoring system used. The BOS24 consists of a total 24 points summarized from 6 objective parameters of ocular inflammatory symptoms, including anterior chamber cells, vitreous opacity peripheral fundus lesions, posterior pole lesions, subfoveal lesions and optic disc lesions. Simultaneous bilateral attacks (attacks in both eyes) were considered to be 2 attacks, 1 attack for each eye, and BOS24 was separately determined for each eye.
Results. 31 from 81 (38,3%) BD patients with ocular involvement had current ocular attack. Total amount of ocular attacks (eyes with intraocular inflammation) was 56. 25 (81%) patients with current ocular attacks had panuveitis and 6 (19%) – posterior uveitis. Total BOS24 was done for all BD patients with ocular attack. The average score BOS24 for the 56 ocular attacks before treatment was (M±m) 9,10±0,95 (from 2 to 19). All the BD patients were treated by systemic anti-inflammatory/ immunosuppressive drugs such as systemic corticosteroid

(100%), cyclosporine (53%), azathioprine (47%). The average score BOS24 significantly decreased to 2,67±1,40 (from 0 to 6) (p<0,001) after 8,92±3,47 (M±m) months treatment. The BOS24 before the treatment was positive correlated with number of ocular attacks during current year (R=0,89), severity of BD (R=0,37), skin (R=0,46) and vascular (R=0,28) involvement and was negative correlated with duration of ocular involvement (R=-0,37).
Conclusion. BOS24 is useful objective scoring system for quantitative evaluation of ocular BD activities and the efficacy of treatment.

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O12.

CELLULAR IMMUNE RESPONSES IN BEHÇET'S DISEASE PATIENTS WITH UVEITIS DURING INFLIXIMAB TREATMENT

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Purpose. Infliximab is a chimeric IgG1 monoclonal antibody that blocks binding of TNF-α to its receptor, and various studies have shown remarkably beneficial effects of infliximab in the treatment of Behçet's disease (BD)-associated uveitis. However, recurrent uveitis was observed in some BD patients after initiation of infliximab treatment. It has been found that peripheral blood mononuclear cells (PBMCs) obtained from BD patients produce proinflammatory cytokines, and Th1-, Th2-, and Th17-related cytokines when stimulated with interphotoreceptor retinoid-binding protein (IRBP) that is one of retinal self-antigen. In this study, we examined the quantitative changes of proinflammatory cytokines, and Th1-, Th2-, and Th17-related cytokines produced by PBMCs from BD patients with uveitis before and after treatment with infliximab when stimulated with IRBP. Furthermore, we compared cytokine production between BD patients with recurrent uveitis during infliximab treatment and those in whom recurrent uveitis was not observed after initiation of infliximab treatment.
Methods. Eight BD patients who were treated with infliximab more than 1 year were enrolled in this study. BD patients were also classified into a group with recurrent uveitis (BD-recurrent uveitis group) in which recurrence of uveitis was occasionally observed even after initiation of infliximab treatment and a group with remitted uveitis (BD-remitted uveitis group) in which uveitis did not recur after initiation of infliximab treatment. Ten healthy subjects were enrolled as controls. PBMC were collected from BD patients before and one week after infliximab infusion, and from healthy controls at any time. PBMCs were cultured in vitro with various concentrations of IRBP, and levels of proinflammatory (IL-1β, IL-6, and TNF-α), Th1- (IFN-γ and soluble CD40 ligand: sCD40L), Th2- (IL-4, IL-10, and IL-31), and Th17- (IL-17A, IL-17F, IL-21, and IL-22) cytokines in cultures were measured by Bio-Plex kit® (Bio-Rad Laboratories Inc.)., IL-10, IL-17F, and IL-22 were reduced after infliximab infusion in BD-remitted uveitis group but not in BD-recurrent uveitis group. α, TNFγ.
Results. All these cytokines except for sCD40L were higher in BD patients before infliximab infusion than in healthy subjects, and decreased in BD patients after infliximab infusion, but were still higher than in healthy subjects except for IL-4 and IL-10. In BD patients, all cytokines except for IL-6 were higher in BD-recurrent uveitis group compared with BD-remitted uveitis group before infliximab infusion, and decreased after infliximab infusion to a greater extent in BD-remitted uveitis group than in BD-recurrent uveitis group. Especially, IFN-.
Conclusions. Th1-, Th-2, and Th17-related cytokines by PBMCs upon IRBP stimulation were suppressed after infliximab infusion preferentially in BD patients without recurrent uveitis. Measurement of these cytokines by IRBP-stimulated PBMCs would be a clue to evaluate quantitatively the efficacy of infliximab treatment for uveitis in BD patients.

O13.

COGNITIVE IMPAIRMENT IN CHRONIC PROGRESSIVE NEURO- BEHÇET'S DISEASE: COMPARATIVE STUDY OF BRAINSTEM AND HIPPOCAMPUS REGION USING BRAIN MAGNETIC RESONANCE IMAGING

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Background/Purpose. 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 NB (ANB) and chronic progressive NB (CPNB) based upon differences in the clinical course and response to corticosteroid treatment. Brainstem atrophy is significantly more frequently observed in CPNB than in ANB. It is also noteworthy that cognitive dysfunction, in addition to truncal ataxia, is frequently observed in CPNB, and this cannot be accounted for by brainstem atrophy. In the present study, we examined volumes of the hippocampus in order to identify the responsible lesions for neurobehavioral changes in CPNB.
Methods. The subjects were 32 patients, including 13 with CPNB (11 males and 2 females, age 51.2±12.1 years old [mean ± SD]), 13 with Behçet's disease without NB (non-NB) (10 males and 3 females, age 54.4±11.4 years old), and 6 with Alzheimer's Disease (AD) (5 males and 1 female, age 78.8±7.5 years old). All patients with BD satisfied the international classification criteria for Behçet's disease. CPNB was defined as intractable, slowly progressive neurobehavioral changes and/or ataxia accompanied by persistent elevation of interleukin-6 of >20 pg/mL in cerebrospinal fluid on two different occasions at an interval of at least 2 weeks. All patients with AD satisfied the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria. Sagittal sections of T1-weighted images on brain magnetic resonance imaging (MRI) were obtained from each subject. The areas of the midbrain tegmentum and pons were measured on mid-sagittal sections of T1-weighted images using image analysis software (Image J ver.1.45: NIH, USA). Severity of gray matter loss in the hippocampal region and whole brain were investigated using Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD) software (Eisai Co., Ltd) to determine the degrees of hippocampal region atrophy (Z score) and whole-brain atrophy (WBAI).
Results. The brainstem area was significantly decreased in CPNB (461.8±87.3 [mean ± SD]) compared with those in AD (661.9±56.1) and non-NB (666.1±50.6) (Figure 1, A). VSRAD analysis showed that Z score was significantly increased in CPNB (1.46±0.70) and AD (3.13±1.21) compared with non-NB (0.77±0.40) (Figure 1, B). All patients with CPNB showed brainstem atrophy, but there was no significant correlation between the area of brainstem atrophy and Z score. Neither Z score nor WBAI was correlated with age in CPNB.
Conclusion. These results indicate that the hippocampus, in addition to the brainstem, is a common site for lesions in CPNB, accounting for the progressive cognitive dysfunction in this disease. The lack of correlation between brainstem atrophy and hippocampal atrophy suggests that predisposing factors might determine the lesion site in CPNB.

O14.

BEHÇET'S SYNDROME AND PSYCHIATRIC INVOLVEMENT: IS IT A PRIMARY OR SECONDARY FEATURE OF THE DISEASE?

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Background. Frequency of psychiatric disorders in Behçet's syndrome (BS) is a debated issue: while some experts attribute their presence to the chronicity of the illness, others think that they may be imputable to disease activity or to intrinsic features of the disease.
Objectives. The primary aims were to determine the frequency of psychiatric disorders in BS patients, both with neurological involvement or without; the secondary aims were: to investigate a possible association between disease activity/organ involvement and psychiatric profile of the BS patients and to compare the distribution of psychiatric disorders of patients with BS with those in patients with other chronic diseases.
Methods. One hundred and seven BS patients with a diagnosis of BS according the ISG criteria were studied. Demographic profile of the cohort studied are summarised in Table I. Psychiatric disorders evaluated were: bipolar disorder, obsessive-compulsive disorder, depression and sleep disorder. Age and sex

matched disease controls of systemic lupus erythematosus (SLE) and chronic arterial hypertension were included.
Results. Prevalence of psychiatric disorders are shown in Table II. No correlations were found between the presence of psychiatric disorders and disease activity/organ involvement. Moreover, the frequency of bipolar disorder resulted significantly higher than in disease controls (p<0.001).

Table I. Demographic profile.

	Neuro-BS (n)	BS without neurological involvement (n)
Number of patients	44	63
M/F	36/8	41/22
Mean age ± SD (min-max) (years)	43±7 (15-68)	42±8 (18-71)
Mean disease duration ± SD (min-max) (years)	9±2 (2-28)	10±2 (3-28)

Table II. Prevalence of psychiatric disorders.

	Neuro-BS n (%)	BS without neurological involvement n (%)
bipolar disorder	41 *(65)*	28 *(64)*
obsessive-compulsive disorder	29 *(46)*	20 *(43)*
depression	20 *(32)*	16 *(36)*
sleep disorder	5 *(11)*	10 *(16)*

Conclusions. Our results show a high frequency of psychiatric disorders in BS patients. This elevated prevalence both in BS patient with or without neurological involvement, in presence or absence of disease activity and in a higher frequency than in disease controls, strongly suggest that BS patients are characterised by a specific psychiatric profile.

O15.

THE COCHLEAR INVOLVEMENT IN BEHÇET'S DISEASE: CROSS SECTIONAL STUDY

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Introduction. The cochlear damage was a common symptom of Behçet Disease (B D) esteemed between 9 and 80% of cases. It was ranked second or third after cutaneous and ocular damage according to most studies.
Objective. To determine the frequency of cochlear involvement (CI) during BD and Identify their demographic, clinical and paraclinical particularities.
Patient and methods. We conducted a cross-sectional study including 55 patients with BD fulfilled the diagnostic criteria of the International Study Group on the BD, followed at Medicine Interne Department of the Hospital of Fattouma Bourguiba Monastir. All patients underwent clinical examination and cochleovestibular investigations. We compared the group with CI and its sub-groups to the control group consisted of patients with BD but without CI.
Results. The CI was objectified in 17 cases (31%). It was isolated in 12 cases (70.5%) and associated with vestibular dysfunction in 5 cases (29.4%). Deafness was bilateral and symmetric in 76.5% of cases, light in 70.6% of cases and focusing on high frequencies in 88.2% of cases. THE majority had sensorineural hearing loss (94.1%), classified deafness endocohléaire in 13 cases (81.25%) and retrocochlear in 3 cases (18.75%). Patients with CI were significantly older (p=0.048) with a late onset of BD compared to control patients (p=0.013). However, the duration of BD was longer in the group of sensorineural hearing loss compared to the control group without being statistically significant. The vascular injury was significantly less frequent in patients with CI and particularly those with sensorineural hearing loss. The frequency of the pseudofolliculitis necrotic was significantly higher in the group with sensorineural hearing loss (p=0.034).
Conclusion. CI is prevalent in BD, but remains underestimated. Therefore, all Behçet's patients should be regulary subjected to cochlear investigations to detect inner ear involvement.

O16.

PREDICTIVE VALUE OF BONE SCINTIGRAPHY FOR THE DETECTION OF JOINT INVOLVEMENT IN BEHÇET'S DISEASE: DERMATOLOGISTS' PERSPECTIVES

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Background. Behçet's disease (BD) is a chronic multi-organ inflammatory disease with joint involvement. It is very common for physicians in different clinical settings to experience BD patients with joint symptoms. Because non-specific arthralgia without objective signs of arthritis, such as swelling or effusion is frequent in patients with BD, an accurate diagnosis of joint involvement is often challenging, especially for non-rheumatologists. Considering the high frequency of BD-associated arthritis and the importance of early detection, finding a useful and simple imaging technique for detecting articular involvement is a high priority for physicians in many fields.
Objectives. The aims of this study were to analyse the correlation between bone scintigraphy findings and clinical symptoms and to validate the diagnostic specificity achievable in this context by supplementing the dermatologist's clinical examination with bone scintigraphy.
Materials and methods. This study included 211 patients with BD (mean age 49.0±10.8 yr; M/F 53/158). The prevalence of joint complaints, based on clinical evaluations and positive bone scintigraphy results, was estimated for each of anatomic sites, and agreement between bone scintigraphy findings and clinically evaluated joint complaints was assessed using Cohen's kappa (κ) statistic. Furthermore, a patient subset (n=104) whose joint complaints and scintigraphy findings were mutually compatible was re-evaluated by a rheumatologist to determine the level on diagnostic specificity attained by combining bone scintigraphy with clinical examinations of dermatologists.
Results. The total kappa value (211 patients) was 0.604, indicating fair agreement between joint complaints and scintigraphy results. Individual analysis of eleven joint categories revealed that there were statistically significant correlations in wrist (κ=0.677), shoulder (κ=0.661), and foot joints (κ=0.618). Of the 104 cases referred to a rheumatologist, 95 (91.34%) were confirmed as having BD-associated articular involvement. Joints acral areas (*e.g.*, foot, hand, wrist, and shoulder) that had the highest kappa value correlations also ranked highest in diagnostic specificity.
Conclusion. Bone scintigraphy is simple to perform and may be useful to assess joint involvement in BD patients, especially for specific anatomic sites. By improving diagnostic specificity in BD-associated arthritis, the capacities of physicians in various fields to effectively manage this unique and chronic inflammatory disease is heightened, allowing proper control of joint symptoms and prevention of destructive arthritis through early detection.

O17.

DIETARY AND NON-DIETARY TRIGGERS OF ORAL ULCER RECURRENCES IN BEHÇET'S DISEASE

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Background. Recurrent oral ulcers (OU) are a highly consistent feature of Behçet's disease (BD), but their pathophysiology is not well understood. Certain foods or other external factors admittedly play a role in BD-related OU recurrences. However, the proportion of patients among whom we can identify a specific triggering factor of their OU recurrences and the nature of these factors remain unknown.
Objectives. To study the role of dietary and non-dietary factors as triggers of BD-related OU recurrences.
Methods. A 23-item self-reporting questionnaire was given to in- and outpatients with BD who attended 7 French hospital departments of internal medicine over 12 months. Patients were enrolled if they agreed to participate and if they had a history of OU that had not definitively abated to ensure patients' ability to provide accurate information. The questionnaire consisted of 13 questions collecting general information (e.g., demographic characteristics, dietary habits, age at onset and severity of OU). Six open-ended, dichotomous (Yes or No) or scaled questions (Yes, I am sure, Yes, that's possible, No, that's highly unlikely, or I

don't know) collected information on potential OU-triggering factors. In particular, the questionnaire evaluated the effect of 6 general triggering situations (i.e., fatigue/stress, dental care, tooth brushing, menstruation, infection, and food), 24 selected food items, of 8 physicochemical properties of food (*i.e.*, salty, sweet, bitter, sour, astringent, hard, hot, cold), and of fast eating. The results are given as proportion of positive responses; for scaled questions, the response Yes, I am sure was considered positive.

Results. Among 101 questionnaires distributed, 87 were returned and 81 were usable. Among the 81 patients (mean age 41 years, 62% male), 79 (96%) fulfilled the ICBD classification criteria, 75% had a non-French origin and 83% consumed European-style food. The mean time since OU onset was 19 years; 53 patients (65%) reported >50 OU lifetime attacks and 42 (52%) qualified their OU recurrences during the previous 12 months as "very discomforting" or "discomforting". Among the 6 general situations suggested, 50 patients (62%) recognized ≥1 as a "sure" trigger of OU recurrence: fatigue/stress (37%) and food (32%) were the most frequent triggers. Among the 24 suggested foodstuffs, walnuts (48%), pineapple (42%), peanuts (32%), Emmental cheese (30%), almonds (24%), lemon (22%), and other cheeses (21%) were the most frequently reported. Sourness was the most frequently reported "sure" physicochemical OU-triggering food characteristic (13%). The corresponding open-text responses and subgroup analyses of the patients with >50 OU lifetime episodes or with "very discomforting" or "discomforting" OUs over the previous 12 months were highly consistent.

Conclusion. Most patients can identify triggering factors for their BD-related OUs, with fatigue/stress and food representing the most frequent triggers. The management of OU must take into account such external factors. The histamine-rich or histamine-liberating properties of the commonly cited OU-triggering foods suggest a hypersensitivity mechanism.

O18.

ORAL HEALTH CAN BE IMPROVED BY ORAL HYGIENE EDUCATION IN BEHÇET'S DISEASE: A LONG-TERM FOLLOW-UP STUDY

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Objective. The aim of the study was to evaluate factors associated with the oral health of patients with Behçet's disease (BD) in long-term follow-up.

Materials and methods. In this retrospective study, non-selected 143 BD patients (F/M: 87/56, mean age:33.4_7.1 years) followed by clinical and laboratory assessments were included. Among them, 93 patients (F/M:57/36, mean age: 31.9_6.9 years) were followed with dental and periodontal indices and oral hygiene education in each visit regularly (Regular follow-up (RF) group), whereas 50 patients (F/M:20/30, mean age:37.3_6.7years) were not under regular oral hygiene control (comparative (CP) group). The mean follow-up periods were similar between the groups (RF: 5.2±2.9 years vs CP: 4.4±2.3 years, p=0.18).

Results. Although no significant differences were observed in periodontal indices between RF group and the comparative group at baseline (p>0.05), scores of plaque index, gingival index and sulcus bleeding index were found to be higher in the CP group (1.9±0.9; 1.8±1.1 and 2.2±0.9) than the RF group (1.2±1.03; 1.5±1.1; 1.6±1.2, respectively) at the end of current follow-up (p>0.05).

When groups are analysed separately, in the RF group, scores of dental and periodontal indices were similar at baseline (plaque index:1.1±0.9; gingival index:1.5±0.9; sulcus bleeding index: 1.5±1.01) and follow-up (p>0.05).

In contrast, indices were worse at follow-up (plaque index:1.9±0.9; gingival index: 1.9±1.1; sulcus bleeding index: 2.2±0.9) than baseline (1.3±0.9; 1.6±1.01; 1.8±1.1, respectively) at the CP group (p<0.05).

Morover, the number of natural teeth was decreased at follow-up (16.5±8.8) compared to that of baseline (21.8±5.7) at the CP group (p=0.005) whereas was almost the same at baseline (19.9±8.1) and follow-up (19.7±8.7) at the RF group (p=0.94).

The utilisation of dental services for emergency care were higher in the CP group (61.2%) than the RF group (41.9%) (p=0.02). As expected, the frequency of tooth brushing was higher in RF group (1.3±0.8) than the CP (0.4± 0.5) (p=0.000) at follow-up.

Conclusion. A stability in oral health was accomplished in BD patients by oral hygiene motivation and education in long-term follow-up. As oral ulcers affect oral health poorly, a more aggressive approach for better oral health should be aimed in all BD patients to eliminate microbial factors which are a part of pathogenic processes.

Key words. Oral health, oral hygiene and Behçet's disease.

O19.

PAPULOPUSTULAR LESIONS ACCORDING TO AGE, SEX AND BODY PARTS IN BEHÇET'S SYNDROME PATIENTS COMPARED HEALTH POPULATIONS AND DISEASED CONTROL

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Objective. To assess whether papulopustular lesions are different in Behçet's syndrome (BS) according to site, age, sex and medications when compared to rheumatoid arthritis (RA) and apparently healthy population (HP) subjects.

Methods. 209 consecutive BS patients who were routinely followed-up in our dedicated BS center were studied. Patients with RA (n=146) who were followed up in the rheumatology outpatient clinic of the same unit and HP (n=149) were used as controls. All subjects were clinically evaluated by the same dermatologist and all skin lesions (papules, pustules, comedones, folliculitis, cysts, nodules) on the face, trunk and legs were separately counted. Information regarding the demographic and clinical features of primary disease and medications were obtained from patients' charts.

Results. Demographic features and mean number of papulopustular lesions according to site of body were summarized in Table I. Mean number of total papulopustular lesions were similar between BS and HP and significantly higher than in RA (F: 21.7, p:0.0001). Results were similar when subgroups of men and women and age groups (<30, 31-50, >50) were analyzed separately. In all 3 groups the mean total number of papulopustular lesions were significantly lower in older ages (F:95.8, p:0.0001). Corticosteroid use did not impact the results. When we analyzed the number of papulopustular lesions on the legs separately we observed that BS patients had significantly more lesions on the legs when compared to the RA and HP (F:12.2, p:0.0001) due to the high number of pustules and folliculitis on the legs of BS patients. When leg lesions were analyzed according to age, this difference persisted in age groups 31-50 and >50 (age 31-50, F:9.8 p:0.0001; age >50, F:6.2 p:0.002) but not in age group <30 (F: 0.8 p:0.45).

Table I.

	Behçet's syndrome	Rheumatoid arthritis	General population
Mean age (SD)	41±11	52±13	41± 15
Male/Female	78/131	21/125	74/75
Patients with steroid (n)	32 (15 M/17 F)	85 (13 M/72F)	-
N of patents with at least 1 papulopustular lesion	156/209	57/146	101/149
Mean n of total papulopustular lesion (SD)	5.9±7.8	1.5±3.0	6.6 ±9.0
Mean n of papulopustular lesions on the legs (SD)	0.6 ±1.4	0.05±0.6	0.3 ±1.1
Mean n of papulopustular lesions on the face (SD)	2.3 ± 3.4	0.8 ± 1.9	3.2 ± 4.6
Mean n of papulopustular lesions on the back (SD)	3 ± 5	0.7±1.5	3.1 ± 4.9
Mean total n of papulopustular lesion in males (SD)	7.8 ± 9.2	2.8 ± 5	6.3 ± 9.7
Mean n of papulopustular lesions on the legs in males (SD)	1.1 ± 1.8	0.3 ± 1.5	0.3 ± 1.2
Mean total n of papulopustular lesion in females (SD)	4.8± 6.5	1.3 ± 2.5	6.7 ± 8.4
Mean n of papulopustular lesions on the legs in females (SD)	1.2	0.01 ±0.9	0.2 ± 0.9

Conclusions. As had been sporadically observed in the past and now confirmed in a controlled in a study among healthy and diseased controls in a sizeable study BS patients have significantly more papulopustular lesions on the legs when compared to HP and RA. Number of papulopustular lesions tend to decrease as the patient ages in BS similar to RA and HP but it is still higher on the legs among BS even when the patients are over the age of 50. We may consider including only the papulopustular lesions on the legs in future classification/diagnostic criteria for BS.

O20.

FECAL CALPROTECTIN AS A NON-INVASIVE BIOMARKER FOR INTESTINAL INVOLVEMENT OF BEHÇET'S DISEASE

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Background. The diagnostic and prognostic values of fecal calprotectin levels in patients with inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, have been proven. However, little is known about the usefulness of fecal calprotectin (FC) measurement in predicting intestinal involvement of Behçet's disease (BD).
Methods. Forty-four consecutive patients with systemic BD who underwent colonoscopy for the evaluation of gastrointestinal symptoms were prospectively enrolled between November 2012 and March 2014 in a single tertiary medical center. Fecal specimens from the patients were obtained the day before bowel cleansing and 3 months after colonoscopy.
Results. Twenty-five patients showed intestinal ulcerations on colonoscopy (12 [48.0%) typical and 13 [48.0%) atypical ulcerations]. The median FC level in the intestinal BD group was significantly higher than that in the non-diagnostic group (112.53 [6.86-1604.39] vs. 31.64 [5.46-347.60] μg/g, respectively, p<0.001). Moreover, the typical ulceration group showed a significantly higher median FC level than the atypical ulceration group in patients with intestinal BD (435.995 [75.65-1604.39] vs. 71.42 [6.86-476.94] μg/g, respectively, p=0.003). Multivariate analysis revealed higher FC as an independent predictor of intestinal BD (OR=1.020; 95% CI=1.002-1.038; p=0.026). The cut-off level of FC for predicting intestinal BD was 68.89 μg/g (76% sensitivity and 79% specificity). The absolute changes between fecal calprotectin levels and the disease activity index of intestinal BD from initial diagnosis of intestinal BD to 3 months after diagnosis were significantly correlated (Pearson's correlation coefficient=0.470, p=0.027).
Conclusion. The FC level might serve as a non-invasive surrogate marker of intestinal involvement of BD.

O21.

BEHÇET DISEASE IN THE PEDIATRIC AGE: DATA ON 129 PATIENTS COLLECTED FROM AN ITALIAN COHORT

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Behçet's disease (BD) most often affects young adults, but occasionally can have its onset in childhood. Large series describing the disease in the pediatric age are scarce. The aim of our study was to collect information on clinical characteristics and treatment in pediatric patients (pts.) with BD in Italy. Demographic, clinical and therapy data from pediatric pts. with BD, enrolled in the Eurofever registry by Italian Pediatric Rheumatology Centers, have been analyzed. Patients enrolled met the international criteria (Lancet 1990) or were diagnosed by specialists as affected by Behçet's disease. 129 pts. were included in our study: 73 were males and 56 females. In about half of cases (n=64) a follow-up visit was also recorded, in addition to the baseline. Ethnicity was Caucasian for almost all (125/129). Mean age at disease onset was 9 years, mean age at diagnosis 13 years. A positive family history of BD was reported in 14 cases. At the baseline visit 94.3 % had muco-cutaneous symptoms; 41.5% ocular involvement; 35.9% musculoskeletal symptoms; 34.8% gastro-intestinal manifestations; 31.4% constitutional symptoms; 23.5% neurologic involvement. The most common mucocutaneous symptoms were recurrent oral aphtosis (93%); genital ulcers (27%), pseudo-follicolitis (17%), maculopapular rash (16%), erythema nodosum (13%), acneic or papulo-pustular lesions (12% each). Pathergy test was positive in 9 pts., negative in 68, not done in 7. Ocular involvement occurred in 37 pts.: 14 had anterior uveitis, 4 posterior uveitis 5 panuveitis, 8 retinal vasculitis, 5 papilledema, 5 papillitis, 3 episcleritis, 1 band keratopathy and keratitis. The most common musculoskeletal symptom was arthralgia (n=30), followed by myalgia (n=16), oligoarthritis (n=6), polyarthritis (n=5), and monoarthritis (n=2). Abdominal pain (n=30) and diarrhea (n=11) were the most common gastrointestinal symptoms (GI), followed by GI ulcers (n=4), and anal ulcers (n=2); 5 pts. had GI bleeding, one patient presented aseptic peritonitis and 2 patients gut perforation. Constitutional symptoms included recurrent fever in 22 patients, fatigue and malaise in 14. Headache was the most common neurologic symptom (n=17); 7 pts. had cranial nerve palsies, 3 presented vertigo, 1 optic neuritis and 1 aseptic meningitis. Moreover, 1 patient had ataxia and 1 presented hemiplegia and abnormal behavior. Venous thrombosis occurred in 3 pts. (thrombosis of transverse sinus in one of them). HLA-B51 was present in 39 pts., not done in 12. The main treatment used was systemic corticosteroids, followed by colchicine (n=31) and other immunosuppressants, ie azathioprine (n=6), metothrexate (n=5), cyclosporine (n=3), thalidomide (n=2), and cyclophosphamide (n=1). Infliximab was also used in one patient. During follow-up, other biologic agents were also used, ie Adalimumab (n=9) and Anakinra (n=1). This is one of the largest pediatric BD cohorts reported so far. Our data are similar to those of other pediatric series. The performance of the new Ped-BD criteria in our series is currently being evaluated, as well as possible correlations between clinical signs or symptoms at onset with immunosuppressive treatment.

O22.

IMPAIRED QUALITY OF LIFE IN PATIENTS WITH BEHÇET'S DISEASE IS ONLY IN PART RELATED TO DISEASE ACTIVITY.

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Background/Purpose. Behçet's disease (BD) has a chronic-relapsing course, could be debilitating and potentially life-threatening, and it has been associated with impaired quality of life (QoL). The objective of this study was to evaluate, through the Short Form 36 Questionnaire V2 (SF-36V2), the perception of health related QoL (HRQoL) in patients affected with BD and to identify major factors associated with its impairment.
Methods. Sixty-one patients (24 males, mean age 47.3±12.0 years and mean disease duration 14.0 ± 9.5 years) fulfilling the International Study Group (ISG) criteria for BD were enrolled. Patients with primary psychiatric illness were excluded. Each patient underwent clinical examination and completed the SF-36V2. The search for factors independently associated with impaired quality of life (defined as low results in the SF-36V2 domains) included univariate analyses and stepwise multiple regression models. Explanatory baseline variables were age, gender, disease duration, disease activity (Behçet's Disease Current Activity Form –BDCAF-, Physician and Patient Visual Analogic Scale – Phy-VAS and P-VAS, respectively-) and active clinical manifestations (categorized as present/absent). Sixty healthy subjects, 90 patients with Systemic Lupus Erythematosus and 50 patients with Rheumatoid Arthritis were enrolled and served as controls. P values less than 0.05 were considered significant.

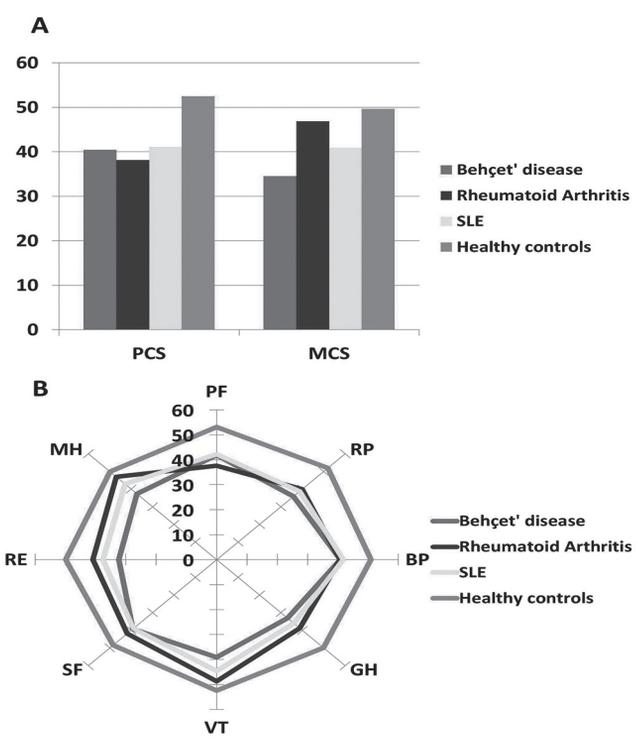

Fig. 1. A-B

Results. Patients with BD showed lower results in the mental component summary (MCS) scale and physical component summary (PCS) scale of the SF36V2 when compared with healthy controls (p<0.01). No differences were revealed comparing PCS score in BD patients (40.4±11.0) with PCS score in SLE (41.0±11.5) and RA (38.2±10.7) patients, whereas MCS score in BD patients (34.5±12.2) was lower than in SLE (40.9±12.0; p<0.01) and RA (46.8±12.9; p<0.01) patients (Figure 1A). This difference was explained by lower results in the mental health (MH), vitality (VT), role emotional (RE) and general health (GH) domains (figure 1B). The low results in PCS were independently associated with higher BDCAF results (p<0.001) whereas no factors independently associated with low MCS results were identified among those investigated.
Conclusions. Patients affected with BD reported of low QoL by means of SF36V2 compared with normal subjects and patients with other chronic systemic diseases. The low results in SF36V2 PCS were associated with high disease activity whereas causes of low results in MCS were not identified. Further studies are needed in order to identify major reasons for impaired mental quality of life in BD and to implement strategy to cope with that.

O23.

CORRELATION OF ESR, CRP, AND THE IRAN BEHÇET'S DISEASE DYNAMIC ACTIVITY MEASURE (IBDDAM) IN THE MAJOR MANIFESTATIONS OF BEHÇET'S DISEASE

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There is a correlation of ESR, CRP, and one of the Disease Activity Measures of Behçet's Disease, the Behçet's Disease Current Activity form (BDCAF), as shown by Melikoglu and TopKarci in Turkish patients.
The aim. of this study is to look for the same in Iranian patients, but with the IBDDAM instead of BDCAF.
Materials and methods. Patients (135) were selected as consecutive patients seen at the Behçet's Unit of the Rheumatology Research Center, Tehran University of Medical Sciences. ESR, CRP, and IBDDAM were calculated for patients having with the active manifestation of the day the patient was seen, and compared with the patients having the same manifestation in the past but not at the day of the evaluation. The t-test was used for the comparison. The number of cases (active and inactive), the mean, and the standard deviation (SD) is given. Then, items were compared by Mann-Whithney U Test and the p value is given. If the null hypothesis was rejected the figure was specified by *.
Results. Number of patients, active cases (AC), the mean and SD for ESR – CRP – IBDDAM were in oral aphthosis (OA): 59 (24.25, 22.4–13.3, 19.0–13.3, 15.5), and for inactive cases (IC) 76 (18.1, 20.3–8.4, 15.9–21.0, 27.0), p was 0.06, 0.03*, 0.5. In genital aphthosis (GA): AC 14 (34.1, 21.6–19.2, 18.0–6.5, 9.4), IC 73 (20.5, 10.5–17.5, 15.4–15.4, 22.2), p was 0.02*, 0.009*, 0.001*. Skin (Sk): AC 12 (30.7, 25.4–19.2, 25.1–14.7, 35.4), IC 23 (19.9, 16.5–9.8, 11.5–11.6, 13.9), p was 0.33, 0.46, 0.38. Pseudofolliculitis (PF): AC 6 (25.8, 21.0–15.3, 25.1–26.0, 49.4), IC 29 (23.1, 20.5–12.6, 16.2–9.9, 12.8), p was 0.36, 0.25, 0.22. Erythema nodosum (EN): AC 8 (37.0, 25.9–27.1, 27.8–3.4, 1.8), IC 27 (19.7, 17.0–8.9, 10.8–15.4, 25.7), p was 0.13, 0.12, 0.10*. Pathergy test (PT): AC 19 (20.95, 14.7–15.8, 23.6–20.6, 29.4), IC 49 (25.6, 27.1–11.6, 19.2–13.7, 17.5), p was 0.2, 0.09, 0.07. Eye Involvement (EI): AC 68 (11.9, 9.9–6.7, 13.6–31.7, 24.1), IC 24 (20.9, 25.4–12.6, 20.1–4.4, 6.7), p was 0.3, 0.5, 0.000*. Anterior uveitis (AU): AC 16 (16.4, 12.9–15.5, 23.3–44.4, 36.8), IC 52 (10.6, 8.4–3.9, 7.2–27.8, 17.5), p was 0.000, 0.000, 0.000. Posterior uveitis (PU): AC 60 (11.4, 9.3–6.1, 13.6–32.6, 24.8), IC 8 (15.7, 13.6–10.5, 14.4–25.0, 17.4), p was 0.000*, 0.06, 0.000* . Retinal Vasculitis (RV): AC 45 (10.2, 8.0–6.6, 15.5–38.8, 25.7), IC 23 (15.3, 12.2–6.7, 9.4–17.8, 11.8), p was 0.000*, 0.05, 0.000*. Vascular manifestations (VM): AC 10 (59, 28.1–38.8, 20.1–5.1, 3.6), IC 3 (21.3, 18.3–10, 17.3–3.0, 2.6), p was 0.05*, 0.11, 0.29. Joint Manifestation (JM): AC 17 (46.2, 21.8–20.2, 21.1–5.3, 5.6), IC 9 (19.0, 20.8–14.3, 22.0–5.9, 7.9), p was 0.001*, 0.43, 0.56. Neurological Manifestations (NM): AC 2 (18.0, 4.2–2.0, 2.8–6.5, 0.7), IC 1 (7–3–42), p was 1, 1, 1.
Conclusion. ESR and/or CRP were significantly higher in active cases of OA, GA, AU, PU, RV, VM, JM, and NM. IBDDAM was higher in OA, GA, EI, AU, PU, and RV.

O24.

EFFECT OF INFLIXIMAB IN CHRONIC PROGRESSIVE BEHÇET'S DISEASE: INFLUENCES OF TIME OF INTRODUCTION ON THE OUTCOME OF THE PATIENTS

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Objectives. Chronic progressive neuro-Behçet's disease (CPNBD) is characterized by progressive deterioration leading to disability and death. It has been appreciated that methotrexate is effective for CPNBD. In addition, recent studies have demonstrated that infliximab is effective for patients with recalcitrant CPNBD who had inadequate responses to methotrexate. However, the appropriate timing for introduction of infliximab remains unclear. We therefore explored the effects of intervals before introduction of infliximab on the outcome of patients with chronic progressive NBD.
Methods. Eleven patients (8 males, 3 females, ages 35.2±9.3 [mean±SD]), who met the international classification criteria for BD with CPNBD and received infliximab, were followed up until October 2015. The functional disability of the patients was rated by Steinbrocker functional classification as used in rheumatoid arthritis. Correlation between the patients' outcome and the intervals before the introduction of infliximab was analyzed by Spearman's rank correlation test.
Results. All the 11 patients had received methotrexate prior to infliximab. The intervals from the onset to the introduction of infliximab and the follow-up periods were 26.6±35.1 months and 65.2±43.6 months [mean±SD], respectively. Among the 11 patients, 9 patients did not show progression after the introduction of infliximab, whereas 2 patients progressed. In the latter 2 patients, infliximab had been discontinued before the final follow-up. The functional disability grades of the patients after the introduction of infliximab were significantly correlated with the intervals from the onset of CPNBD to the introduction of infliximab (r=0.6177, p=0.0476).
Conclusion. The results indicate that the delay of the introduction of infliximab leads to the irreversible functional disability of the patients with CPNBD. Thus, it is recommended that infliximab should be administered as soon as possible for the patients with CPNBD who do not respond to methotrexate adequately.

O25.

INFLIXIMAB THERAPY FOR NEUROLOGICAL, VASCULAR, AND INTESTINAL INVOLVEMENT IN BEHÇET'S DISEASE: EFFICACY, SAFETY, AND PHARMACOKINETICS IN A MULTICENTER, PROSPECTIVE, OPEN-LABEL, SINGLE-ARM PHASE 3 STUDY

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Background. Behçet's disease (BD) is a multisystem disease characterized by mucocutaneous, ocular, neurologic, vascular, or gastrointestinal manifestations. Involvement of the nervous system (neurological BD [NBD]), the vascular system (vascular BD [VBD]), and the intestinal tract (intestinal BD) is rare, although such cases tend to have a poor prognosis.
Objectives. We conducted a multicenter, prospective, open-label, single-arm phase 3 study to determine the efficacy, safety, and pharmacokinetics of infliximab (IFX) in BD patients with these serious complications who had displayed poor response or intolerance to conventional therapy (ClinicalTrials.gov, NCT01532570).
Methods. IFX at 5 mg/kg was administered to 18 patients (3 NBD [2 acute and 1 chronic progressive], 4 VBD, and 11 intestinal BD) at Weeks 0, 2, and 6 and every 8 weeks thereafter until Week 46. In patients who showed inadequate responses to IFX after Week 30, the dose was increased to 10 mg/kg. We then calculated the percentage of complete responders according to the predefined criteria depending on the symptoms and results of examinations (ileocolonoscopy, brain magnetic resonance imaging, computed tomography angiography, positron emission tomography, cerebrospinal fluid, or serum inflammatory markers), exploring the percentage of complete responders at Week 30 as the primary endpoint.

Results. The percentage of complete responders was 61% (11/18) at both Weeks 14 and 30 and remained the same until Week 54. By BD type, the percentage of complete responders at Week 30 was 33% (1/3) among NBD patients, 100% (4/4) among VBD patients, and 55% (6/11) among intestinal BD patients. In acute NBD patients, IFX lowered the cell count and interleukin-6 concentrations in the cerebrospinal fluid and inhibited the onset of attacks. In a chronic progressive NBD patient, IFX lowered cerebrospinal fluid interleukin-6 concentrations along with inhibition of progression of clinical symptoms and brainstem atrophy. VBD patients showed improvement in clinical symptoms at an early stage (Week 2) with reductions in serum C-reactive protein (CRP) levels and erythrocyte sedimentation rate. Imaging findings showed reversal of inflammatory changes in three of the four VBD patients. Intestinal BD patients showed improvement in clinical symptoms along with decrease in serum CRP levels after Week 2. Consistently, scarring or healing of the principal ulcers was found in more than 80% of these patients after Week 14. Irrespective of the type of BD, all patients achieved improvement in quality of life, leading to the dose reduction or withdrawal of steroids. IFX dose was increased to 10 mg/kg in three intestinal BD patients, resulting in improvement of clinical symptoms, CRP levels, and visual analogue scale score. Safety and pharmacokinetics profiles were comparable to those in patients with rheumatoid arthritis or Crohn's disease.
Conclusions. IFX is effective and well tolerated in the treatment of NBD, VBD, and intestinal BD with poor response or intolerance to conventional therapy. IFX may therefore represent a promising new therapeutic option for use in BD patients with these serious complications.

O26.

EFFICACY AND SAFETY PROFILE OF ANTI-INTERLEUKIN-1 TREATMENT IN BEHÇET'S DISEASE

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Growing data have provided encouraging results on the use of interleukin (IL)-1 inhibitors in Behçet's disease (BD). This study was aimed at reporting the largest experience with anti-IL-1 agents in BD patients. We evaluated 30 BD patients receiving treatment with anti-IL-1 agents. The primary aims of the study were to evaluate the efficacy of anakinra (ANA) and canakinumab (CAN) in a cohort of BD. The secondary aims were to evaluate the overall safety profile of the treatments, explore the timing of response to therapy and any adjustment of dosage and frequency of drugs studied, and investigate predictive factors of response to therapy. The frequency of first line therapy was 90 % with ANA and 10 % with CAN. The overall number of subjects in complete remission after 12 months of therapy with anti-IL-1 drugs was 13: 6 maintained the initial therapy regimen, 1 maintained the same initial anti-IL-1 drug with further therapeutic adjustments, and the remaining 6 shifted from ANA to CAN. Among them, 3 used CAN for at least 12 months without therapeutic adjustments, 1 had therapeutic adjustments, and 3 had an overall history of a 12-month complete remission. Adverse events (AEs) were reported in 15 % patients who received ANA, represented in all cases by local cutaneous reactions, while no AE were observed in patients who received CAN; we did not observe any serious AEs (SAEs) during the follow-up period. Our data have confirmed that the use of anti-IL-1β drugs is efficacious and safe with an overall acceptable retention on treatment.