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±13.1 years) and 19 age- and sex-matched HC were recruited. A panel of twenty-five serum cytokines (APRIL/TNFSF13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IFNβ, sIL-6Ra, IL-10, IL-11, IL-19, IL-20, IL-27 (p28), IL-28A/IFN-lambdα, IL-29/IFN-lambdα, IL-32, IL-34, LIGHT/TNFSF14, Pentraxin-3, sTNF-R1, sTNF-R2, TSLP and TWEAK/TNFSF12) were simultaneously quantified using a Bio-Rad cytokine bead array. 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 in inactive-BD and IL-26 (p<0.01) in active-BD than 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=0.08) 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.

References

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 study combined multiparameter single cell analysis with machine learning, which has shown impressive predictive power 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 disease patients with BD could be distinguished from patients with Birdshot uveitis H22 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

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 processes might 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. γδV9Vδ2 (+) V(82) 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. Vδ2 T cells produce pro-inflammatory cytokines in response to bacterial species, especially those capable of producing phosphoantigens, many of which are resident in the oral microflora. We hypothesized that circulating Vδ2 T cells can home to mucosal tissue (and/or skin) and contribute to inflammation. We have hypothesized that oral mucosal sites have homing receptors for γδ T and CLA which may be responsible for the homing (tropism) of γδ T cells to mucosa (or skin) and drive the inflammatory processes in BD.

Methods. Peripheral Blood Mononuclear Cells were stimulated with IL-2, and the microbial phosphoantigens (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 γδ T and CLA by Vδ2+ and γδ+ T cells. Data obtained by flow cytometry was analysed using FlowJo 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 γδ+ T cells from BD showed greater expression of γδ T and CLA compared to HC revealing the potential for homing to mucosa and skin. The stimulated Vδ2+ and γδ+ T cells from both BD and HC exhibited increased γδ T (up to 80%) but CLA was down-regulated in stimulated BD compared to all others to identify the most significant phenotype which can discriminate between γδ T cells (or skin) and drive the inflammatory processes in BD.

Conclusion. Stimulation of PBMCs with HDMAPP upregulated the expression of γδ T by Vδ2+ and γδ+ T cells in both BD and HC. However, the mean expression of γδ T in BD was higher than HC suggesting that the cells were already primed 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 tests p < 5 x 10^-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 x 10^-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 Turkish samples and meta-analysis with Turkish data replicated associations of three loci, ADO-EGR2, IRF8 and CEBPB-PTPN1. Comprehensive meta-analysis of the regional imputation 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 < 0.0001 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, 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.

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 oral 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 < 0.0001 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, 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 alleles 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 1 reference haplotypes, were determined in 1876 individuals with Behçet’s disease and 1761 controls from Turkey. HLA-B*51 types were imputed with Imputation HLA region genotypes using SNP2HLA and 10,450 reference HLA marker and classical HLA type haplotypes as reference. Haplotype 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 alootypes with greater than 1% frequency in the Turkish population. One alootype 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 allele likely contributes to Behçet’s disease susceptibility by altering its peptide activity and or substrate specificity, suggesting that either an over production of ERAP1 alloype specific disease promoting peptides or inadequate production of disease-protective peptides contribute 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 SPECIFIC 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 specific 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 a validated tool for venous QoL in VBD.

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, VENEIS-QoL and VENEIS-Sym VCSS were significantly worse in VBD with PTS. BSAS was also significantly higher in patients with PTS. An inverse correlation was observed between VENEIS-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 1. Venous assessment and quality of life parameters in study groups.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Vascular Behçet Disease</th>
<th>Non-Behçet Disease</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTS n (%)</td>
<td>58 (96.6)</td>
<td>21 (764)</td>
<td>0.016</td>
</tr>
<tr>
<td>VENEIS-QoL</td>
<td>87,9016,15,55</td>
<td>72,3113,19,67</td>
<td>0.001</td>
</tr>
<tr>
<td>VENEIS-Sym</td>
<td>38,8318,95</td>
<td>32,7712,03,32</td>
<td>0.002</td>
</tr>
<tr>
<td>VCSS</td>
<td>4,7413,33</td>
<td>6,4334,53</td>
<td>0.015</td>
</tr>
<tr>
<td>CEP</td>
<td>2,0911,68</td>
<td>2,251,51</td>
<td>0.458</td>
</tr>
<tr>
<td>VDS</td>
<td>1,0401,59</td>
<td>1,4801,58</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion. A high presence of PTS and impaired venous disease specific QoL, symptom severity and venous disability scores was observed in VBD in our study. Venous disease specific 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 venous disease specific 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 papill Millennium. 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 papill Millennium (n=5), bilateral optic disc pallor (n=4) and fibrotic scars around optic disc (n=5). Sensorynal type hearing loss was detected in 4 patients. Neurological examination was found to be normal among 43 patients with isolated CVST, 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 unequivocal: visual acuity or field may be impaired totally or partially because of optic disc atrophy; in addition hearing deficits may occur.
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 TF/TFPI 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 starting infliximab (IFX) for uveitis before and after 2013.

Methods. The charts of 17 patients (15 men, 2 women; age at the initiation 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 initiation of IFX in the right eye (Median LogMAR=0.29 for new group: 0.3, for old group: 0.7; p=0.58) but the baseline VA of the left eye of the new group (median LogMAR: 0.22; IQR: 0.05-0.45) 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) 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 (95%) 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.

References

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±11.1 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 (Mm) 9,10±0,95 (from 2 to 19). All the BD patients were treated by systemic anti-inflammatory/ immunosuppressive drugs such as systemic corticosteroid
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 cytokymes, 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 observed occasionally 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. PBMC 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-remittted 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-γ.

Conclusions. Th1-, Th2-, and Th17-related cytokines by PBMCs upon IRBP stimulation were suppressed after infliximab infusion preferentially in BD pa-tients without recurrent uveitis. Measurement of these cytokines by IRBP-stimu-lated PBMCs would be a clue to evaluate quantitatively the efficacy of infliximab treatment for uveitis in BD patients.

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 cytokymes, 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 recur-ent 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 observed occasionally 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. PBMC 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-remittted uveitis group but not in BD-recurrent uveitis group.

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-remittted uveitis group than in BD-recurrent uveitis group. Especially, IFN-γ.

Conclusions. Th1-, Th2-, and Th17-related cytokines by PBMCs upon IRBP stimulation were suppressed after infliximab infusion preferentially in BD pa-tients without recurrent uveitis. Measurement of these cytokines by IRBP-stimu-lated PBMCs would be a clue to evaluate quantitatively the efficacy of infliximab treatment for uveitis in BD patients.
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.

Table II. Prevalence of psychiatric disorders.

Conclusions. Our results show a high frequency of psychiatric disorders in BD patients. This elevated prevalence both in BD patients with or without neurological involvement, in presence or absence of disease activity and in a higher frequency than in disease controls, strongly suggest that BD 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 (BD) estimated 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 fulfilling 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 severe in 23.4% of cases. The majority had sensorineural hearing loss (94.1%), classified deafness endolymphatique in 13 cases (81.25%) and retrocochlear in 3 cases (18.75%). Patients with CI were significantly older (p=0.034) with a late onset of CI compared to control patients (p=0.015). However, the duration of CI 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 pseudolipoïdités necrotique 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 regularly 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 bone associated arthritis in BD, bone scintigraphy was performed in patients with BD to determine the level of 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
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: 37.3±6.7 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: 33.4±7.1 years) were not under regular oral hygiene education in each visit (Comparative (CP) group). The mean follow-up periods were 31.9±6.9 years in RF group and 37.3±6.7 years in CP group. The number of BD patients were similar between RF group and CP group (p>0.05).

Results. 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±1.0) and follow-up (1.9±0.8; 1.6±1.2, respectively) at the CP group (p<0.05). Moreover, 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 (41.2%) than the RF group (35.2%) (p=0.02). As expected, the frequency of tooth brushing was higher in RF group (1.3±0.8) than the CP group (0.4±0.5) (p<0.000) at follow-up.

Conclusion. A stability in oral health was accomplished in BD patients by oral hygiene education 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 during 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 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<9.58, 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.

<table>
<thead>
<tr>
<th>Measurage (SD)</th>
<th>Behçet’s syndrome</th>
<th>Rheumatoid arthritis</th>
<th>General population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>78/131</td>
<td>21/125</td>
<td>74/75</td>
</tr>
<tr>
<td>Mean of patients with steroid (n)</td>
<td>32 (15 M/17 F)</td>
<td>85 (13 M/72 F)</td>
<td>-</td>
</tr>
<tr>
<td>Mean n of patients with at least 1 papulopustular lesion</td>
<td>5.917±8</td>
<td>1.5±3.0</td>
<td>6.6±19.0</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the legs (SD)</td>
<td>2.3±3.4</td>
<td>0.8±1.9</td>
<td>3.2±4.6</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the face (SD)</td>
<td>3.8±5.5</td>
<td>0.7±1.5</td>
<td>3.1±4.9</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the back (SD)</td>
<td>7.8±9.2</td>
<td>2.8±5</td>
<td>6.3±9.7</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the legs (SD)</td>
<td>1.1±1.8</td>
<td>0.3±1.5</td>
<td>0.3±1.2</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the face (SD)</td>
<td>4.8±6.5</td>
<td>1.3±2.5</td>
<td>6.7±8.4</td>
</tr>
<tr>
<td>Mean n of papulopustular lesions on the back (SD)</td>
<td>1.2</td>
<td>0.01±0.9</td>
<td>0.2±0.9</td>
</tr>
</tbody>
</table>

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.
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 (149.95 [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 macro-cutaneous symptoms; 45.1% ocular involvement; 35.9% musculoskeletal symptoms; 34.8% gastrointestinal manifestations; 31.4% constitutional symptoms; 23.5% neurologic involvement. The most common musculoskeletal symptoms were recurrent oral aphthae (93%); genital ulcers (27%); pseudo-folliculitis (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 papillitis, 5 papillitis, 3 episcleritis, 1 band keratopathy and keratitis. The most common musculoskeletal symptom was arthralgia (n=50), 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). IHLA-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), metotrexate (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.
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 (40.8±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 MCS 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 (BDCF), 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 BDCF.

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-Whitney 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, 18.9–6.5, 9.4), IC 73 (20.5, 10.5–17.5, 15.4–14.5, 22.2), p was 0.02*, 0.009*, 0.001* Skin (Sk): AC 12 (30.7, 25.4–19.2, 25.1–17.4, 35.4), IC 23 (19, 16.5–9.9, 11.5–16.9, 13.9), p was 0.33, 0.46, 0.38. Pseudofolliculitis (PF): AC 15 (18.3, 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 0.13, 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 0.13, 0.12, 0.10*. Erythema nodosum (EN): AC 8 (37.0, 25.9–27.1, 27.8–3.4, 1.8), IC 27 (19.7, 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 0.13, 0.12, 0.10*. In genital aphthosis (GA): AC 14 (34.1, 21.6–19.2, 18.9–6.5, 9.4), IC 73 (20.5, 10.5–17.5, 15.4–14.5, 22.2), p was 0.02*, 0.009*, 0.001*.

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 (CNPBD) is characterized by progressive deterioration leading to disability and death. It has been appreciated that methotrexate is effective for CNPBD. In addition, recent studies have demonstrated that infliximab is effective for patients with recalcitrant CNPBD 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 CNPBD 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 CNPBD to the introduction of infliximab (r=0.677, 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 CNPBD. Thus, it is recommended that infliximab should be administered as soon as possible for the patients with CNPBD 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 MULTI-CENTER, 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 discontinued or experienced 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 (decolonoscopy, 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.

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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. 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 agents 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-1 drugs is efficacious and safe with an overall acceptable retention on treatment.