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The Mediterranean Journal of Rheumatology (Mediterr J Rheumatol, e-ISSN 2529-198X, supported and published by the Greek Society for Rheumatology and Professional Association of Rheumatologists) is an international peer-reviewed, platinum open-access journal covering issues of pathophysiology, diagnosis, treatment and prevention of musculoskeletal, autoimmune and autoinflammatory diseases, which are prevalent in countries of the Mediterranean basin and neighboring regions. Topics of rehabilitation, musculoskeletal care, patient education, and continuing professional development in rheumatology are prioritised to comprehensively cover the challenges encountered by patients, nurses, students, and specialists in rheumatology and allied specialties.

TYPES OF PUBLISHED ARTICLES AND THEIR PRIORITY FOR THE JOURNAL

This Journal publishes the following types of articles: Original Research articles, Narrative and Systematic Reviews, Expert Opinions, Case-based reviews, Images, Lectures, Reports on Clinical and Pathological conferences, Interviews with leading experts, Research Protocols-Proposals and Letters to the Editor. Items of exceptional interest to a broad professional audience are prioritised and considered for fast-track processing.

PREPARATION AND FORMATTING OF ALL SECTIONS OF MANUSCRIPTS, COVER LETTERS, AND SUPPLEMENTARY MATERIALS

The Journal only accepts manuscripts submitted online at <http://www.mjrhume.org/submit>.

The Journal follows the international format of medical papers (Vancouver system), and adheres to the updated guidelines of the International Committee of Medical Journal Editors (<http://www.icmje.org/icmje-recommendations.pdf>). The Journal editors also adhere to ethical norms and resources publicised by the Committee on Publication Ethics (COPE) (<http://publicationethics.org/resources>) and the World Association of Medical Editors (<http://www.wame.org/policies-and-resources>).

All articles should be written in a Word file (*.doc), be double-spaced, in standard A4 page size, with margins

of no less than 3.5 centimeters. All articles must be numbered at the top center, beginning with the title page. Upon acceptance, the authors are allowed to do only minor editing corrections which do not relate with the scientific or clinical component of their accepted manuscript. Articles should have the following format:

- Title
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- Acknowledgements
- Conflicts of interest disclosures
- Funding
- Ethics approval and written informed consents statements
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Figures are submitted in separate file(s).

1. Title page

This should include:

- The paper title (should not exceed 30 words; all main keywords should be reflected in the title).
- The name, middle name initial (optional), and last name of each author. The ORCID iD of each co-author with full information about correct names, biography, affiliations, publications, and other academic activities should be provided at the submission (<http://orcid.org/>).
- Affiliations of each author (department/unit, organisation/university, city, country).
- The full name, address, phone number, fax and e-mail address of the corresponding author.

2. Abstract and Keywords

The abstracts of original or review articles should be structured and limited to 250 words. For other types of articles, non-structured abstracts with up to 150 words are acceptable. Lectures, imaging quizzes and Letters to the Editor should not include abstracts.

In original articles, abstracts should be divided into the following sections: Objective/Aim, Methods, Results, and Conclusion. The same page should contain 4-6 keywords corresponding to the international terms. You can look up the NIH MeSH Browser for help.

3. Main Text

Research articles should have the following format:

Introduction, Materials and Methods, Results, and Discussion. In the Introduction, state the rationale and objective of the work. All relevant keywords of the study should be explored in this section.

Case studies should have the following format: Introduction, Case Description, and Discussion of similar published cases.

All other types of articles are formatted according to the demands and goals of the authors.

Original and review articles should not exceed 4,500 words from Introduction until Discussion and should have less than 15 Tables and/or Figures. Review articles should contain detailed search strategy describing systematic and comprehensive searches through multidisciplinary (Scopus, Web of Science) and specialist databases (MEDLINE/PubMed, CINAHL, PEDro, SPORTDiscus, Global Health/CABI). The adherence to the following recommendations is advisable: <https://www.ncbi.nlm.nih.gov/pubmed/21800117>

Imaging quizzes and Letters to the Editor should not exceed 3 double-spaced pages, and 4 Tables or Figures.

All other articles should not exceed 2,500 words from Introduction until Discussion and 10 Tables or Figures.

Any pharmaceutical substances should be written by their common (generic) names, except biologicals that are written by both their common and commercial names.

Abbreviations should be explained at their first appearance in the text. Subsequently, only the abbreviation should be given.

4. Acknowledgements

Acknowledgements should be addressed to individuals who provided help but do not meet the ICMJE authorship criteria, and institutions which supported the article. It is strongly recommended to acknowledge efforts of authors' editors and editing agencies in line with the Good Publication Practice (GPP3) guidelines.

Grant funding and any other financial support should be also stated.

5. References

References are numbered according to the order they appear in the text, as exponents after a full stop or comma. In review articles, references should not exceed 150. In Original research articles references are up to 50. In Imaging quizzes, case reports, and Letters, the references should be limited to 10, and in other types of articles, they should not exceed 30.

Cite primary sources rather than secondary and tertiary items (e.g., textbooks). Cite one reference to a scientific fact. Multiple citations to a single fact should be avoided (one fact – one reference).

Each reference includes author last names and initials (when more than six authors, only the first six are written followed by "et al."), the title, the journal name in short, the year of publication, the volume and page numbers, e.g.: Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum* 1990;33:1601-10.

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Articles appearing ahead of print should have after the journal name the Digital Object Identifier (DOI).

For further guidance on the style and integrity of referencing, please refer to the updated recommendations of the ICMJE. It is strongly recommended to follow the recommendations of the San Francisco Declaration on Research Assessment (DORA).

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Tables should be written in a file compatible with the Word file (*.doc), and numbered according to the order they appear in the text. Table numbers and titles must be placed above the table, with any explanatory notes below it. Tables should have a portrait orientation and contain up to 10 columns. The tables should stand alone (be self-explanatory), and their information should not be repeated in the text.

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Editors of this journal endorse the principles of the integrity, transparency and quality of pre- and post-publication communications set by the Sarajevo Declaration on Integrity and Visibility of Scholarly Publications.

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The Journal is permanently archived by the National Library of Greece (www.nlg.gr) and PubMed Central (from 2017 onward). Its contents are also digitally preserved by PORTICO (<https://www.portico.org/publishers/mjrheum/>).

EDITORIAL POLICIES

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The Journal editors adhere to the editorial policies, ethical guidance and other recommendations of the International Committee of Medical Journal Editors (ICMJE; www.icmje.org), the Committee on Publication Ethics (COPE; <http://publicationethics.org/resources/guidelines>), the World Association of Medical Editors (WAME; www.wame.org), the Council of Science Editors (CSE; www.councilscienceeditors.org) and the National Information Standards Organisation (NISO; <http://www.niso.org/workrooms/pie/>).

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Submission to the Journal implies that all authors have read and agreed to its content, and they meet all the four criteria of the International Committee of Medical Journal Editors (<http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>).

Authorship requires:

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- (b) Drafting the work or revising it critically for important intellectual content; AND
- (c) Final approval of the version to be published; AND
- (d) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURES**Conflict of interest**

All authors are requested to disclose any conflict of interest including any financial or personal relationship with other people or organizations within three years of beginning the submitted work that could inappropriately influence their study (<http://www.icmje.org/conflicts-of-interest/>). All authors are required to provide a Conflict of Interest Statement which is available at http://www.icmje.org/downloads/coi_disclosure.zip. This form should be uploaded with the revised manuscript upon submission. The forms should be uploaded as a single file.

The corresponding author must disclose any conflict of interest that any co-author may have. If there is no conflict of interest then the authors must state in the separate section: 'Conflict of Interest: The authors declare no conflict of interest'.

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Manuscripts of clinical trials must include a copy of the trial protocol along with the complete statistical analysis plan, a flow diagram and a completed trial checklist (the CONSORT checklist and template flow diagram can be found at <http://www.consort-statement.org/consort-statement/flow-diagram>). The trial registration number must be included on the title page of the manuscript of an enrolled and registered clinical trial.

Registration of clinical trials

Registration in a public trials registry is required for publication of a clinical trial in the Mediterranean Journal of Rheumatology in accordance with recommendations of the International Committee of Medical Journal Editors (ICMJE, <http://www.icmje.org>). Trials must register at or before the beginning of patient recruitment.

Trial registries are listed at

- <http://www.icmje.org>
- <http://www.anzctr.org.au>
- <http://www.clinicaltrials.gov>
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LANGUAGE

Papers should be written in standard British English. The Journal's Production Editor can help authors of accepted articles to polish language. However, submissions that require complete rewriting may be rejected.

STATISTICS

Statistical methods used in the study should be clearly stated. Unique or complex statistical methods should be referenced. Complex analyses must be performed with the help of a qualified analyst.

The actual p values should preferably be written, whether significant or not. Confidence intervals should be presented when possible. Complex analyses, such as Cox and logistic regression analysis, should be presented in detail, to ensure reproducibility of the results.

The Statistics Editor of this Journal may request access to the primary data in order to perform independent analysis and evaluation of the work.

UNITS

Use the international system of units (SI). If other units are used, please give their equivalent in SI.

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ORAL PRESENTATIONS (INVESTIGATOR AWARDS)

001

PROTEOMIC LANDSCAPE MAPPING OF ORGAN-RESOLVED BEHÇET'S DISEASE USING IN-DEPTH PLASMA PROTEOMICS FOR IDENTIFYING HABP2 EXPRESSION ASSOCIATED WITH VASCULAR DAMAGE

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Objectives: We aimed to elucidate the pathogenesis and heterogeneity associated with different organs and identify the biomarkers for clinical assessment and treatment of patients with Behçet's disease (BD).

Methods: The expression levels of proteins in plasma samples from 98 patients with BD and 31 healthy controls (HC) were measured using our in-depth proteomic platform with a data-independent acquisition mass spectrometer and antibody microarray. Bioinformatic analyses of the biological processes and signaling pathways that were changed in the BD group were performed. Furthermore, the proteomic landscape of the organ-resolved BD pathogenesis was constructed. Biomarkers that indicate the disease severity and the vascular subset were validated in an independent cohort of 108 patients with BD and 29 HCs by using enzyme-linked immunosorbent assay.

Results: The BD group had 220 differentially expressed proteins, which discriminate 88.6% of the patients and 95.5% of the HCs. The bioinformatic analyses revealed that these differentially expressed proteins participated in different biological processes associated with BD pathogenesis, including complement activation, wound healing, angiogenesis, leukocyte-mediated immunity, and so on. Furthermore, the first proteomic landscape of the organ-resolved BD was constructed, providing the proteomic features of BD associated with different organs and protein targets for the development of therapeutic treatment. HABP2, TNC, and SERPINA3 were validated as potential biomarkers for the clinical assessment of vascular BD and treatment targets.

Conclusion: Our results provide valuable insight into the pathogenesis of organ-resolved BD in terms of proteomic characteristics and potential biomarkers for vascular BD clinical assessment and treatment in the future.

002

SINGLE-CELL ANALYSES HIGHLIGHT THE PROINFLAMMATORY CONTRIBUTION OF C1Q-HIGH MONOCYTES TO BEHÇET'S DISEASE

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Background and Aims: Behçet's disease (BD) is a systemic vasculitis with unknown etiology, characterized by excessive activation of innate immunity. Monocytes are the key members of innate immunity, and our previous research has preliminarily found an aberrance of monocyte heterogeneity in BD [1]. For further investigation, this study aims to encode the landscape of BD monocytes comprehensively and find their pathogenetic contributions to BD.

Methods: Single-cell RNA sequencing (scRNA-seq) on magnetic-beads-sorted CD14⁺ monocytes (4 BD patients and 4 healthy controls) was performed. Correlation analysis between a novel monocyte subset and clinical indices of BD was conducted. Flowcytometry, phagocytosis, IFN- γ stimulation assays, and bioinformatic analysis were conducted to investigate the presence, function and differentiation of the novel monocyte subset.

Results: Single-cell deconvolution of monocyte populations revealed 8 heterogeneous subpopulations, including a novel cluster featured by C1q (C1q-high monocytes). Pseudotime inference indicated that BD monocytes markedly shifted differentiations toward C1q-high monocyte-ended and inflammation-accompanied trajectory. C1q-high monocytes were increased in active BD patients ($1.28 \pm 0.99\%$ vs $0.73 \pm 0.44\%$, $p=0.0024$), positively correlated with ESR ($r=0.46$, $p=0.004$), and decreased after treatment ($1.28 \pm 0.99\%$ vs. $0.73 \pm 0.44\%$, $p=0.0024$). Further assays showed that C1q-high monocytes enhanced phagocytosis and proinflammatory cytokine secretion. Differentiation of C1q-high monocytes was induced by IFN- γ -activated JAK/STAT1 signaling and could be inhibited by tofacitinib treatment.

Conclusions: Our study comprehensively illustrated the immune landscape of BD monocytes and revealed the unrecognized contribution of C1q-high monocytes to BD hyperinflammation, showing their potential as therapeutic targets and clinical assessment indexes.

Competing interests: None declared.

Reference

1. Li C, Liu J, Yu X, Li L, Wang Z, Shi J, Zeng X, Zhang F, Chen H, Zheng W. Aberrant monocyte subsets in patients with Behçet's disease. Clin Immunol. 2021 Apr;225:108683.

003

A GENETICALLY AND IMMUNOLOGICALLY DISCERNABLE BD ENDOTYPE ENTAILS HLA CLASS I-RESTRICTED OLIGOCLONAL CD8 EFFECTOR T CELL EXPANSIONS

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Strongly Behçet disease (BD)-associated variants in the MHC and ERAP regions suggest an HLA class I-restricted process resulting in CD8 T cell activation, but evidence for CD8 T cell involvement at effector sites in BD is scarce, their phenotypes and function remain poorly understood, and genotype immune-phenotype studies in carriers and non-carriers of HLA-B*51 have not yielded conclusive results. Here we aimed to determine whether HLA class I-restricted CD8 T cells in BD are present at an important effector site (the eye), define their clonality and activation-dependent phenotypes, and determine whether carrier status of ERAP1-Hap10/HLA-B*51 – the strongest currently known risk variant for BD – impacts CD8 T cell clonotypes, phenotypes, and function.

Methods: We obtained anterior chamber fluid cells from BD uveitis patients for scRNA sequencing with VDJ analysis, genotyped and immune-phenotyped a cohort of 26 untreated BD patients and 22 HD, generated CRISPR-Cas9 ERAP1 KO LCL resembling the hypo-trimming ERAP1-Hap10 allotype in an HLA-B51 restriction context, and assessed their effects on CD8 T cell function.

Results: Oligoclonal CD8 T cell expansions were found in the aqueous humor during BD uveitis and their clonotypes matched highly expanded clones in autologous, time-matched peripheral blood. CD8 T cell phenotypes in blood showed shifts between antigen-experienced and naive CD8 T cells, which depended on ERAP1-Hap10/HLA-B*51 carrier status and estimated peptide trimming activity. ERAP1 KO altered immunogenicity to CD8 T cells in assays assessing proliferation, cytokine secretion, and toxic degranulation.

Conclusion: Our results support the notion that HLA class I-restricted processes drive BD in a genetically identifiable, susceptible subset of patients which may represent a disease endotype. This endotype carries the strongest currently known genetic risk variant for BD, shows measurable immunologic features of HLA class I-restricted immunity, and may be targetable with compounds that modulate ERAP1 activity.

004

SEX-SPECIFIC ANALYSIS IN BEHÇET'S DISEASE REVEALS HIGHER GENETIC RISK IN MALE PATIENTS

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Objectives: Behçet's disease tends to be more severe in men than women. However, the reasons for this gender effect are unknown. This study was undertaken to investigate sex-specific genetic effects in Behçet's disease.

Methods: A total 1,762 male and 1,216 female patients with Behçet's disease from six diverse populations were studied. Genotyping was performed using an Infinium ImmunoArray-24 v.1.0 or v.2.0 BeadChip, or extracted from available genotyping data. Following imputation and extensive quality control measures, genetic association was performed comparing male to female patients. A weighted genetic risk score for Behçet's disease was calculated and compared between male and female patients.

Results: Genetic association analysis comparing male to female patients with Behçet's disease from Turkey revealed an association with male sex in MICA/HLA-B within the HLA region with a GWAS level of significance (rs2848712, OR= 1.46, P= 1.22x10⁻⁸). Meta-analysis of rs2848712 across six populations confirmed these results. Genetic risk score analysis showed significantly higher genetic risk for Behçet's disease in male compared to female patients, which was largely attributed to higher genetic risk within the HLA region in male patients. Higher genetic risk for Behçet's disease

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was observed in male patients in HLA-B/MICA (rs116799036, OR=1.45, $P=1.95 \times 10^{-8}$), HLA-C (rs12525170, OR = 1.46, $P=5.66 \times 10^{-7}$), and KLRC4 (rs2617170, OR=1.20, $P=0.019$). In contrast, IFNGR1 (rs4896243, OR= 0.86, $P=0.011$) was shown to attribute to higher genetic risk in female compared to male patients.

Conclusions: Male patients with Behçet's disease are characterized by higher genetic risk compared to female patients. This genetic difference is largely explained by risk within the HLA region. These data suggest that genetic factors might contribute to differences in disease presentation between men and women with Behçet's disease.

O05**A THERAPY STRATEGY TO COMBAT IMMUNOSENESCENCE OF BEHÇET'S DISEASE**

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Behçet's disease (BD) is a rare disease characterized by recurrent mucocutaneous ulceration and chronic multi-systemic inflammation; however, its pathogenic mechanisms have not been fully discovered. We previously showed that the frequency of senescent CD8 T cells (CD3+CD8+CD27-CD28-) are higher in the blood of BD patients compared to healthy controls. The difference was presumed to be associated with different cAMP levels in the T cells. Apremilast, a phosphodiesterase-4 inhibitor related with cAMP pathway, had showed significant efficacy in few clinical trials of BD patients. Therefore, we aimed to evaluate the effect of apremilast in CD8 T cells and investigate the possibility of apremilast as a therapeutic option for BD. Peripheral blood mononuclear cells (PBMCs) were sampled from healthy participants based on their age group (ranging from 30s to 60s). We treated the cells to mimic the condition of BD in vitro, and also treated various doses of apremilast. Afterwards, we evaluated the frequency of senescent CD8 T cells using flow cytometry. The proportion of senescent CD8+ T cells were decreased when treated with apremilast, with partial correlation to dosage increment. Our results suggest that the efficacy of apremilast in BD patients might be related to a resolution of immunosenescence from reduction of senescent CD8+ T cells, which might be mediated by a cAMP-dependent manner.

Disclosure of potential conflict of interests: None

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BIOBEHÇET'S: OPTIMAL UTILISATION OF BIOLOGIC DRUGS IN BEHÇET'S DISEASE: A RANDOMISED CONTROLLED TRIAL OF INFliximab VS ALpha INTERFERON, WITH GENOTYPING AND METABOLOMIC PROFILING, TOWARDS A STRATIFIED MEDICINES APPROACH TO TREATMENT

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Background/Objective. High-quality randomised trials and predictive biomarkers are required to optimally target biologic therapy in BS. Undertake a randomised controlled clinical trial of infliximab versus Roferon in BS, and identify potential predictive biomarkers

Design: Pragmatic, prospective, standard of care, single masked, randomised, two arm, parallel head-to-head UK trial, with exploratory study of IFNL3 and IFNL4 SNPs and urinary metabolomics as biomarkers.

Participants: Patients with active BS (ISG 1990 criteria), with inadequate response to/intolerance of first line treatment.

Intervention: Randomisation to infliximab (5mg/kg ivi) or Roferon (subcutaneous injection).

Outcomes: Primary: modified Behçet's disease activity index (mBDAI) at 12 weeks of therapy. Secondary: (a) mBDAI at 24 weeks, (b) significant improvement at 12 and 24 weeks in vitreous haze and best corrected visual acuity change; oral ulcer severity score; number of genital ulcers; arthritis pain; adverse events; reduction in dose of glucocorticoid; Quality of Life and Physician's Global Assessment (disease activity).

Sample Size: Bayesian analysis of covariance model (80% credible interval): initial sample size 45/arm (Bayesian power 90%). With anticipated 10% drop-out, recruitment of 100 patients planned. Following recommendations to reduce the overall length of the trial, this was revised down to 80 patients (36/arm allowing for 10% drop out): 80% equi-tailed credibility interval, Bayesian power 88%.

Methods: Stratified block randomisation, based on randomly permuted blocks with random block sizes of 2 and 4. Follow up at weeks 12 and 24 following standard of care.

Results: Both infliximab and Roferon equally effective (with trend for minor benefit favouring infliximab for tolerability and treatment persistence). Genetic data suggested potential association between patient outcome and carriage of either rs4803221 or rs7248668 variants in IFNL3 (IL-28B) gene locus in Roferon-treated arm. However, statistical significance was lost when correcting for multiple testing. Metabolomic analysis identified potential markers for response to treatment with infliximab.



POSTERS

P001**TRANSCRIPTOMIC ANALYSIS HIGHLIGHTS IMPORTANCE OF MACROPHAGES IN ERYTHEMA NODOSUM-LIKE LESIONS OF BEHÇET'S DISEASE**

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Behçet's disease (BD) is an autoinflammatory vasculitis disorder with predominant pathogenic role of the innate immune system.

The role of innate immune system in the development of erythema nodosum like lesions (ENL), a representative clinical skin manifestation of BD, remains elusive. In this study, we aimed to understand global transcriptomic changes and to dissect differentially expressed genes related to immune cells infiltrated in ENL of BD. We extracted total RNA from 4 to 5 mm punch biopsies from ENL of BD patients and analyzed transcriptome using bulk tissue RNA sequencing.

A total of 7 ENL and 3 nonlesional samples was sequenced. Principal component analysis have shown different transcriptomic expression patterns in ENL compared to nonlesional skin. Upregulated genes in ENL includes important genes related to the activated innate immune system and polarization of macrophages. Pathway analysis of upregulated genes in the ENL were related to both 'lymphocyte activation' and 'positive regulation of immune responses'. Deconvolution analysis of bulk RNA-seq have shown that significantly increased myeloid compartment, particularly M1 macrophages in ENL. Therefore, transcriptomic analysis reveals genes related to innate immune system, particularly inflammatory macrophages are highly upregulated in ENL suggesting a pivotal role of innate myeloid cells in the development of ENL in BD.

P002**A HUMAN PERIPHERAL NEUTROPHIL ATLAS REVEALS SEX-SPECIFIC HETEROGENEITY IN BEHÇET'S DISEASE PATHOGENESIS**Qingfeng Wang¹, Yuan Gao², Peizeng Yang¹

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Behçet's disease (BD) is a multi-systemic inflammatory vasculitis, with a high incidence and more serious course of intraocular inflammation (Behçet's uveitis) in males.^{1,2} Female gender has also been suggested as a good prognostic factor in IFN- α 2a therapy on Behçet's uveitis. However, the etiology of sex-biased Behçet's uveitis is largely unknown. Here, we provide clinical and laboratory data elucidating an important contribution of neutrophils in the sex-biased ocular involvement of BD. Focusing on neutrophils, we uncovered pronounced sexual dimorphism in human peripheral neutrophils at single-cell resolution. We observed expansion of chemotactic and inflammatory neutrophils subsets in male patients with BD. By contrast, female patients with BD showed higher proportions of type I interferon responding neutrophils, whose gene signatures were associated with response to IFN- α . More importantly, we linked these sex differences in neutrophil composition of BD with male-specific immune-microenvironment and genetic factors by Genome-wide association study (GWAS) analysis and circulating exosomal proteomics and miRNA analysis. In summary, our comprehensive neutrophil profiling in patients with BD provide a possible explanation for the observed sex bias in BD, and provide an important basis for the development of a sex-based approach to the treatment targeting neutrophils of female and male patients with BD.

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The authors declare that there is no conflict of interest.

P003

DEREGULATED DNA DAMAGE RESPONSE-REPAIR NETWORK IN BEHÇET'S DISEASE

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Objective: Behçet's disease (BD) is a chronic, relapsing systemic vasculitis of unclear pathogenesis. Since deregulated DNA damage response-repair (DDR/R) is involved in aberrant inflammatory responses, we examined the potential involvement of this network in BD.

Methods and Results: Twenty-six patients with BD of various disease activity (23 men, aged 40.7±9.9 years) and 26 age- and sex-matched healthy controls were studied in parallel. Using single-cell gel electrophoresis we found that patient-derived peripheral blood mononuclear cells (PBMCs) displayed higher levels of single-/double-strand DNA breaks (Olive Tail Moment, mean±SD: 8.7±4.5) than controls (5.3±1.8, p=0.001). Also, BD-derived PBMCs showed 2-fold increased oxidative stress levels and 3-fold increased abasic sites, resulting to excessive formation of DNA damage. On the other hand, functional analysis after ex vivo treatment of PBMCs with UVC-irradiation or melphalan revealed defects in 2 central DNA repair mechanisms, namely nucleotide excision repair and double-strand DNA break repair, in BD patients. In line with this, next generation RNA-sequencing of PBMCs derived from 14 patients (12/14 with active BD) and 11 healthy controls revealed that expression of DDB1 gene, the central nucleotide excision repair enzyme, was decreased in BD and its levels showed a strong negative correlation with UVC-induced damage accumulation (r=-0.738, p=0.001). Moreover, expression of central DNA repair enzymes, including ATM and NEIL1, was decreased in BD, whereas expression of the senescence gene p21/CDKN1A was increased. Of interest, individual DNA damage levels in PBMCs showed a negative correlation with expression of both ATM (r=-0.600, P=0.002) and NEIL1 genes (r=-0.503, P=0.010) and a positive correlation with CDKN1A gene expression (r=0.450, P=0.024).

Conclusion: Inflammation in BD is associated with excessive DNA damage formation and defective DNA repair in PBMCs, which may be partly mediated by transcriptional downregulation of central DNA repair enzymes. Whether the subsequent DNA damage accumulation further aggravates the inflammatory cascade warrants further study.

P004**SALIVA PROTEOMICS IN BEHÇET'S : A NEW POSSIBLE DIAGNOSTIC TOOL?**

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Introduction: Saliva is an important diagnostic fluid that contains numerous proteins that may be associated with disease phenotype. Given that Behçet's Disease (BD), Inflammatory Bowel Diseases (IBD) and Mucous Membrane Pemphigoid (MMP) are inflammatory mucosal diseases that manifest within oral ulceration, analysis of the saliva proteome offers the potential to develop early diagnostic and/or discriminatory biomarkers.

The aim of this study was to investigate the saliva proteome of patients with BD, MMP and IBD comparing it to healthy controls (HC) to determine specific proteins that are uniquely correlated as well as specific to each disease.

Methods: Saliva was collected from each cohort (10 on each) and assessed for proteomic differences. Briefly, samples were tryptically digested before isobaric labelling. The combined labelled digest were separated by high pH reverse phase high pressure liquid chromatography to improve resolution prior to mass analysis with the Q Exactive instrument in the Advanced Mass Spectrometry Facility at the University of Birmingham. Proteome discoverer was used for data processing. Each protein's function was reviewed using Uniprot programme and by DAVID to explore them collectively using gene ontology.

Results: Comparing diseased samples to HC, 16 proteins were increased and 27 were decreased. 6, 8 and 10 were uniquely increased and 12, 16 and 13 decreased in the BD, IBD and MMP cohorts respectively. Galectin 7 and Annexin A1 were over expressed in all 3 cohorts. In the BD group, over expression of the secretory leukocyte protease inhibitor SLPI was seen. Interleukin-1 and Immunoglobulins as well as Desmoyokin were increased in the MMP and IBD group respectively.

Conclusion: This novel study has identified over and under expressed proteins specific to BD as well as uniquely correlated to IBD and MMP patients. To verify this results, a secondary and complementary technique- enzyme linked immunosorbent assay (ELISA) will be used.

P005**A NOVEL POLYMORPHISM OF VITAMIN D RECEPTOR (VDR) GENE IN A GROUP OF ITALIAN PATIENTS WITH BEHÇET SYNDROME**

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Introduction and aim: Vitamin D was recently studied in several investigations to better understand the pathogenesis of various autoimmune diseases due to the pleiotropic and tolerogenic role of Vitamin D. this immunomodulatory role is mediated by vitamin D receptor (VDR). VDR (RefSeq: NG_008731.1) common single nucleotide polymorphisms (SNPs) were studied in various human diseases, including Behçet syndrome (BS), in order to understand if and how the variations could lead to the ineffectiveness of the hormone regulatory actions affecting the Vitamin D /VDR binding. Conflicting data are now available about VDR SNP in BS susceptibility and pathogenesis.

The aim of our study was to genotype the mutational hot spot (3' end) of VDR gene in a group of Italian patients with BS with an integrated approach of genomics and bioinformatics.

Patients and methods: We recruited consecutive BS patients fulfilling the ISG criteria. gDNA was extracted from whole blood and polymerase chain reaction (PCR) was performed for VDR 3'end coverage using home-made primer pairs. Direct sequencing and in silico analysed using specific bioinformatics tools were downstream performed.

Results: We studied 52 BS patients (28 male: 24 female; median age: 43.6 ± 12.3 years) for characterizing VDR 3' end. A novel VDR variation (NG_008731.1:g.65023A>G, HGVS nomenclature) was found in heterozygosity state in 3/52 BS patients (5.77 % of cases). It was recognized in association with rs731236 VDR known restriction fragment length polymorphism in heterozygosity state (TaqI).

Conclusions: This is the first cohort study genotyping VDR 3'untranslated region (UTR). A low frequency of rs731236 CC genotype and C allele was found in our cohort of BS patients. No association between disease clinical manifestations and genotypes were found. A novel VDR variation; analyses of larger cohort are required to better understand the haplotype role in BS pathogenesis.

No conflict of interest

P006

NEUTROPHIL EXTRACELLULAR TRAPS (NETS) IN PATIENTS WITH BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a systemic vasculitis characterized by neutrophil hyperactivation. Neutrophil extracellular traps (NETs) are thought to be increased in patients with BD. It is not clear whether NET levels correlate with disease activity or inflammatory markers in patients with Behçet's disease.

Objective: to determine the role of NETs observed in blood smears in Behçet's disease.

Methods: 22 patients with confirmed Behçet's disease (17 with active BD and 5 with inactive BD, 6 with vascular involvement and 16 without vascular manifestations) and 32 healthy donors (HD) without acute infections or autoimmune diseases were included. Active BD was defined as transformed index score ≥ 5 in Behçet's Disease Clinical Activity Form (BDCAF). NETs were investigated in standardized thin blood smears produced from citrated whole blood and stained by the Giemsa method.

NETs percentage to the number of neutrophils was calculated (%NETs). A complete blood count was performed with the XN-1000 automated hematology analyzer (Sysmex, Japan).

%NETs median levels between groups are compared using the Mann-Whitney Test. Spearman's correlation was utilized to find a possible correlation between %NETs and disease activity, leukocytes, C - reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophil-to-lymphocyte ratio (NLR).

Results: %NETs was higher in patients with Behçet's disease compared to healthy controls (7,95 [5,3-12], vs. 4,4 [3,5-8,8], respectively, $p=0,020$). NETs positively correlated with WBC ($r_s=0,24$, $p=0,01$). There was no correlation between %NETs and BDCAF ($p=0,98$), CRP ($p=0,85$), ESR ($p=0,60$), NLR ($p=0,66$) in patients with BD. %NETs did not differ between patients with active and inactive diseases. In addition, no difference in NET levels were observed between patients with and without vascular involvement.

Conclusions: neutrophil extracellular trap levels were significantly increased in patients with Behçet's disease. No significant difference was observed between NET levels and disease activity or vascular manifestations in patients with Behçet's disease.

P007

THE PRESENCE OF NEUTROPHIL EXTRACELLULAR TRAPS IN SUPERFICIAL VENOUS THROMBOSIS OF BEHÇET'S DISEASE

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Behçet's disease (BD) is an inflammatory multi-system disorder causing recurrent oral, genital ulcers, skin lesions including acne-like eruptions and erythema nodosum-like lesions, and uveitis in addition to neurological and gastrointestinal manifestations. BD has a heterogeneous spectrum of disease manifestations featuring different organ involvement and could be characterized by different aspects in the clinical department in charge. A hierarchical clustering analysis of the hospital-based, BD was identified as five clinical independent clusters, which consist of mucocutaneous, mucocutaneous with arthritis, gastrointestinal, neurological, and ocular without other involvement subtypes. We reviewed BD patients of our hospital retrospectively and investigated neutrophils producing neutrophil extracellular traps (NETs) presence in BD patients. Immunolabeling of myeloperoxidase and histone citrullination proteins was performed on the skin biopsies of three BD patients who had skin biopsy-proven superficial vein thrombophlebitis in their erythema nodosum-like lesions. We observed a higher proportion of female patients, and higher incidence of acne-like eruptions among the BD patients we saw at our dermatology department, while there was a higher incidence of ocular and gastrointestinal involvement among BD patients treated in other departments. We suggest that the gender statistical trends could lead to the co-development of different manifestations, and may help clinicians to choose the best therapeutic approaches, tailoring them to a patient's specific phenotype, rather than one based on single disease manifestations. NETs were found in neutrophils of panniculitis concurrent with superficial vein thrombophlebitis. We suggest that the pathogenesis of BD-related thrombosis could be associated to neutrophil activation and NETs are released in the panniculitis of the affected skin lesions, erythema nodosum-like lesions.

P008**THE COMBINATION OF HSV-1, STRESS AND ENVIRONMENTAL MICROBES ON THE INDUCTION OF BEHÇET'S DISEASE: USING A MOUSE MODEL**

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The purpose of this study is to elucidate the correlation between stress and environmental factors for Behçet's disease (BD) induction using a BD mouse model infected with herpes simplex virus type-1 (HSV-1). BD is a chronic multisystemic inflammatory disease of unknown etiology. Environmental factors, immune dysfunction, and HSV-1 infection might be triggers of BD. In order to investigate the influence of the environmental factors on BD induction, mice were inoculated with HSV-1. To compare the incidence of BD, mice were maintained in either a conventional facility or a specific pathogen free (SPF) facility. The incidence of BD was also tracked by adding stressors such as substance P (anxiety stress), 4 °C (cold stress), xanthine sodium salt (oxidative stress), and 77 dB noise (noise stress). To elucidate the immune mechanisms involved in differences in the incidence of BD due to various stresses, dendritic cell (DC) activation markers were analyzed using flow cytometry. The combination of conventional environment, noise stress, and HSV had the highest rates of BD (38.1%) among all groups. In contrast, the incidence of BD was lowest in the HSV-1 inoculated group maintained in the SPF environment (2.2%). Frequencies of DC activation markers such as CD40, CD83, CD80 and CD86 were expressed differently under various stresses. Noise stress increased the frequencies of CD83 positive cells. Noise stress upregulated the transcription factors T-bet and RORγt. Inhibition of CD83 by CD83 siRNA improved BD symptoms even after mice were exposed to noise stress. 16S rRNA sequencing analysis showed different gut microbial compositions between SPF and conventional environments. In this study, we showed that environment and stress influenced the incidence of HSV-1 induced BD. In particular, noise stress affects the HSV-1 induced BD induction rate, which is associated with the expression of CD83. Microbial diversity due to environmental differences might be one explanation for regional differences in incidence of BD.

Keywords: Behçet's disease, stress, environment, herpes simplex virus, gut microbiota, mouse model

P009

INCREASED FREQUENCY OF TFH-LIKE GAMMA DELTA T CELLS IN PATIENTS WITH BEHÇET'S DISEASE PRESENTING OCULAR MANIFESTATIONS

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Introduction: Behçet's disease (BD) is a rare condition with unclear pathogenesis. Altered immune responses and abnormalities in the frequency and function of immune cells such as gd T, B, and NK cells have been reported. In human blood, gd T cells are unconventional T cells that, under appropriate conditions, express surface markers, shared by the follicular helper T cells (Tfh), to support T cell-dependent B cell differentiation. Whether gd T cells are involved in autoantibody production in BD has not been investigated.

Materials and Methods: Peripheral blood mononuclear cells (PBMCs) from 26 BD patients with mucocutaneous (MBD; n=13) or ocular manifestations (OBD; n=13) and 12 age- and gender-matched HCs were analysed. FACS analysis with a 15-marker panel was performed to identify different Vd1+ and Vd2+ gd T cell subpopulations (based on the expression of CD27, CD28 and CD16), and to evaluate the expression of membrane markers (CD40L, ICOS, CXCR5, and PD-1) which have been associated with a Tfh phenotype. Using the same panel, the frequency of CD19+B cell subpopulations (as defined by expression of IgD and CD27) was determined. Statistical analysis of data was performed with Prism software (GraphPad) using t-tests and one-way ANOVA.

Results: The frequency of total gd T cells and B cells was significantly reduced in patients with BD compared with HCs. Significant differences were also detected in T and B cell subpopulations. Strikingly, Vd1+ gd T cells from OBD patients expressed statistically significant increased levels of CXCR5 and PD-1 compared to MBD patients and HC. In the B cell compartment, increased frequency of memory B cells in patients with BD was observed.

Conclusion: The increased levels of markers associated with Tfh expressed by OBD patients suggest an enhanced interaction between gd T cells and B cells, that might lead to increased production of autoantibodies in these patients.

P010**USEFULNESS OF MEASURING LYMPHOCYTE SUBSETS IN BEHÇET'S DISEASE**

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Introduction: Behçet's Disease (BD) is a rare systemic vasculitis of unknown aetiology characterised by recurrent orogenital ulcers and uveitis. There is little published work on routine lymphocyte subset results in BD. However, this is an under-utilised resource, providing highly accurate, precise and reliable results. In this study we aim to determine the relevance of measuring lymphocyte subsets and the correlation of lymphocyte subsets with clinical features.

Lymphocyte subsets assays are validated to UKAS ISO 15189 standards in NHS pathology laboratories. The use of internal QC ensure results are precise. Submission of results to external quality assurance schemes ensure results are accurate. Assays are performed and results are authorised by competency assessed Health and Care Professions Council registered Biomedical and Clinical Scientists.

Materials and Method: Lymphocyte subsets; absolute counts and percentages of CD3+ T cells, CD3+ CD4+ T cells, CD3+ CD8+ T cells, CD19+ B cells and CD16+ CD56+ NK cells, were requested on patients attending the London Behçet's Centre of Excellence over a period of 3 years. Testing and analysis was performed by flow cytometry in the Department of Immunology, Bart's Health NHS Trust. 909 samples were taken from 635 patients, 65% were female and 35% were male. 49.8% were longitudinal samples.

Results: Preliminary analysis compared results of first samples for all patients to published reference ranges. At least one of the measured parameters were outside of references ranges in 79% of first samples. Initial analysis of longitudinal samples demonstrated a significant difference in CD3% and NK% between first and second samples. There was also differences between male and female. Other clinical outcomes were also analysed

Conclusion: The high number of samples with results outside published reference ranges suggests that routine enumeration of lymphocyte subsets is relevant to BD. Further analysis correlates lymphocyte subsets with symptom severity scores and investigate the impact of clinical outcomes on lymphocyte subsets by regression analysis.

P011**THE EULAR STUDY GROUP ON MHC-I-OPATHY**

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On behalf of the participants of the EULAR study group on MHC-I-opathy

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Aims: To develop a unified concept and understanding of the MHC-I-opathies. Elucidate the distinct basis from the classical autoimmune diseases.

Background: MHC class I proteins present peptide products of intracellular protein turnover on their antigen binding groove and are capable of triggering an immune response. Axial SpA, Behçet's syndrome, Psoriasis and Birdshot retinitis are well-known examples of diseases which are highly associated with MCH-I (i.e. HLA-B*27, -B*51, -C*06 and -A*29, respectively). Although recognizable as separate entities, they share clinical and pathophysiological pathways, including ERAP-1 and IL-23R.

We want to facilitate collaboration, sharing of research and clinical expertise, across the borders of the different diseases. Included in the study group are researchers and clinicians from relevant basic, translational and clinical aspects of MHC class I diseases, including rheumatology, ophthalmology and dermatology, as well as patient partners.

We performed a literature review with arguments supporting our hypothesis. We already started some projects.

This Study group is part of the EULAR Research Committee. More participants are welcome.

Chairs: Franktien Turkstra and Ahmet Gül

Patient partners: Kees Bosman, Peter Böhm

Other members: Akiko Arakawa, Ayşe Boyvat, Charlotte Krieckaert, Danijela Mrazovac, Dennis McGonagle, Dillon Mintoff, Dirk Elewaut, Efstratios Stratikos, Elsa Sousa, Fabian Lötscher, Félicie Costantino, Floor Kerstens, George Bertsias, Gertjan Wolbink, Hanane El Khaldi, Ilknur Tugal, Ines Leal, Ina Kötter, Ivan Padjen, John Bowes, Joke de Boer, Jonas Kuiper, Jörg Prinz, Marija Bakula, Marleen van de Sande, Maxime Breban, Natasa Vidovic, Niek de Vries, Piotr Kusnierczyk, Rik Lories, Russka Shumnalieva, Sebastian Springer, Seçil Vural, Simon Glatigny, Simon Powis, Tony Kenna

P012

GENITAL AND ORAL MICROBIOME AND BEHÇET'S DISEASE ACTIVITY

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Introduction: Oro-genital ulceration presents in over 90% all Behçet's patients and appears to influence disease outcome. We hypothesised the dysregulation of genital and oral microbiome coupled with dysfunctional immune response might play a role in the aetiopathogenesis of Behçet's Disease (BD) during active or inactive phases.

Materials and Methods: 153 BD patients' samples; 70 matched oral and genital samples (Female: Male, 58:12; mean age, 42±13.9: 39.3±10.3), plus 12 samples were not matched; 16s rRNA sequencing were applied for all the samples. V1/V2 and V3/V4 regions used for analysis and investigate the hypothesis.

Results: The alpha and beta diversity were significantly different between genital and oral samples; p values<0.05. However, in case of considering the groups: ulcer and no ulcer they were not significant (p-value>0.05). V1/V2 and V3/V4 showed 4 and 19 unique bacterial genera shared between oral and genital samples respectively. V3/V4 analysis of genital samples demonstrated that *Gardnerella* and *Lactobacillus* were significantly 20x more in females than males (p-adj <0.05). In comparing genital ulcer groups indicated the *Gardnerella*, *Lactobacillus*, and *Atopobium* were significantly increased in females than males, while *Peptoniphilus* and *Corynebacterium* were significantly increased in males than females. When oral ulcers present; *Streptococcus* is significantly increased while *Veillonella* significantly decreased. V1/V2 demonstrates that oral ulcer and genital ulcer samples are assigned to genus *Escherichia-Shigella*. However, V3/V4 are assigned to genus; *Lachnospiraceae*, *Saccharimonadales*, *Coriobacteriales*. In addition, the presence of *Staphylococcus* is associated with BD disease activity.

Conclusion: *Streptococcus*, *Veillonella*, *Gardnerella*, *Lactobacillus*, *Atopobium*, *Peptoniphilus*, *Corynebacterium* and *Staphylococcus* might be microbial markers of BD activity.

P013**DISSECTION OF OCULAR AND PERIPHERAL BLOOD IMMUNE PHENOTYPES SUGGESTS PREFERENTIAL TRANSMIGRATION OF CD16+ MONOCYTES TO EFFECTOR SITES IN BEHÇET'S DISEASE**

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Background: Cellular immunity of Behçet's Disease (BD) remains poorly understood. Previous work has provided clues pointing to most innate and adaptive immune cell types in BD, but strong signals from non-immunogenetic studies are rare and often inconclusive. Here we aimed to identify highly BD/HD discriminant immune cells in semi-biased and targeted approaches and determine their significance at a BD-relevant effector site.

Methods: We utilized multi-parametric flow cytometry to dissect cellular phenotypes in PBMC of untreated BD patients (n=27) and HD (n=22) consisting predominantly of active ocular and major vascular BD subjects. Data were subjected to supervised machine learning (CITRUS) and results verified with targeted gating. We also analyzed anterior chamber (AC) fluid cells and autologous PBMC from BD uveitis subjects with scRNA seq.

Results: CITRUS identified CD16+, CD14low, CD4low, CD3-, CD19- cells as the only BD/HD discriminant cellular expression pattern at an FDR of <0.05. Targeted gating confirmed highly significant differences with large effect sizes in PBMC of BD vs HD for "non-classical" (CD14lowCD16hi) and "intermediate" (CD14+CD16+) monocytes at decreased frequencies for BD in peripheral blood. CD16+ dendritic cells (DC) were also significantly decreased in BD PBMC. "Classical" (CD14++CD16-) monocytes were significantly more abundant in BD PBMC than in HD, but with smaller effect sizes. CD14+ cells showed high abundance in the AC during BD uveitis and co-expressed CD16 far more frequently than CD14+ cells in autologous peripheral blood.

Conclusions: Significantly lower frequencies of CD16+ monocyte and DC subsets in PBMC of untreated active BD vs HD strongly point to their importance in BD. The high abundance of CD14+ cells with CD16 co-expression in the eye during uveitis relative to their frequency in autologous peripheral blood, suggests their transmigration into or, less likely, interconversion within the eye during BD uveitis rather than a stochastic process.

P014**RISK OF BLINDNESS AND OCULAR COMORBIDITIES AMONG PATIENTS WITH BEHÇET'S DISEASE. A POPULATION-BASED COHORT STUDY**

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Background/Aims: To compare the risk of blindness and vision-threatening ocular comorbidities in patients with Behçet's disease (BD) versus the general population.

Methods: We conducted a population-based cohort study using the 2002-2017 Korea National Health Insurance Service database. Newly diagnosed BD patients and age- and sex-matched non-BD controls were included at a 1:5 ratio. The primary outcome was blindness defined as a best-corrected visual acuity of $\leq 20/500$ in the better-seeing eye. Secondary outcomes were visual impairment, vision-threatening ocular comorbidities (cataract, glaucoma, and retinal disorders) requiring surgical interventions, and incident uveitis. We used Cox proportional hazard models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the outcomes.

Results: We included 31,228 newly diagnosed BD patients and 156,140 age- and sex-matched controls. During a mean follow-up of 9.39 years, the incidence rate of blindness per 1,000 person-years was 0.24 and 0.02 in BD and controls, with the HR [95% CI] of 10.73 [7.10-16.22] comparing BD to controls. The risk of secondary outcomes was also higher among BD patients, with a HR [95% CI] of 4.94 [4.26-5.73] for visual impairment, 2.06 [1.98-2.15] for cataract surgery, 5.43 [4.57-6.45] for glaucoma surgery, and 2.71 [2.39-3.07] for retinal surgery. Among participants free of uveitis at baseline, the HR [95% CI] of incident uveitis was 6.20 [5.83-6.58].

Conclusion: In this nationally representative population-based cohort study, BD patients compared with the general population, have a 10.7-fold greater risk of blindness and also a substantially higher risk of diverse ocular comorbidities that pose potential threats to blindness.

P015**THE PREVALENCE AND INCIDENCE OF BEHÇETS DISEASE IN THE HOSPITAL EPISODE STATISTICS IN ENGLAND BETWEEN 2011 AND 2020; A RETROSPECTIVE VALIDATION STUDY NESTED WITHIN THE BIRMINGHAM CENTRE OF EXCELLENCE FOR BEHÇETS DISEASE**

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Sandwell and West Birmingham NHS Trust

Introduction: Behçet's disease (BD) is a rare immune mediated multisystem auto-inflammatory disorder. For a rare disease such as Behçet's, case ascertainment needs to be from a wide range of sources, the Centres of Excellences may miss those at the milder end of the disease spectrum. In this validation study, we will establish the validity of the England wide Hospital Episode Statistics (HES) against the Birmingham CoE. In addition, the differences between the populations/outcomes at the CoE compared to non-specialist centres will allow service evaluation.

Methods: A retrospective cross-sectional analysis of medical records of patients ≥ 18 years with a specialist MDT confirmed ICD-10 diagnosis of BD between 2012 and 2019 at the BD CoE in Birmingham, UK. We extracted all patients with a BD code in HES between 1/4/2011 to 31/3/2020. Proportions pertinent to demographics, prevalence of BD and outcomes were compared between the Centre attenders and non-attenders.

Results: The numbers of prevalent cases of BD nationwide were 4891, of which 545 were identified in the Birmingham CoE, closely aligned to the MDT confirmed prevalence (559) at the CoE. Only 935 cases had attended any of the three CoE. The most prevalent BD symptoms were genital ulceration (11.1%), thrombophlebitis (6.7%) and PE (4%) in the HES cohort. Comparatively, 80.4% and 63.9% of patients in the CoE reported oral and genital ulcerations respectively. HES coded Ocular signs in 4.7% compared to 30% in the CoE cohort.

Conclusions: To our knowledge this is the largest population based study to systematically identify patients with a diagnosis of BD disease in England, validated against MDT confirmed cases at the Birmingham CoE. The disease phenotypes differ in the national and CoE cohorts, likely due to differences in coding practices. It is also plausible that the more severe phenotypes attend the CoE.

P016**SKIN MANIFESTATION AS AN EXPLAINING FACTOR OF HETEROGENEITY IN BEHÇET'S DISEASE**

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Behçet's disease (BD), a chronic multi-systemic disorder, presents diverse clinical manifestations depending on patient ethnicity and geographic region. Use of varying diagnostic criteria augments clinical heterogeneity. We aimed to characterize heterogeneous manifestations in patients with full-blown BD fulfilling major diagnostic criteria in use. We retrospectively analysed 338 patients diagnosed with complete BD based on Japanese diagnostic criteria, which fulfil both International Study Group (ISG) criteria and the International Criteria for BD (ICBD) from 2005 to 2020 at a tertiary referral Hospital. Unbiased clustering analysis was performed to elucidate the heterogeneous spectrum, followed by subgroup analysis of identified clusters. Complete BD patients included more females (65.1%), with dominant skin lesions of erythema nodosum like lesions.

Oral ulcer showed the earliest onset among diverse manifestations and all major diagnostic criteria had earlier onset in men. Results of unbiased clustering analysis identify dominant skin lesion type as an important factor that determines clustering. Among 3 clusters, patients with dominant papulopustular lesions had less vascular involvement compared to ENL and both dominant skin types. Therefore, dermatologic manifestation is an important factor in understanding the heterogeneity of BD. Analysis highlights a link between dermatologic manifestation and clinical outcomes, suggesting a more specific diagnostic approach on skin type dominance may help clinicians better predict disease course.

P017

THE DIFFERENCE OF JAPANESE BEHÇET'S DISEASE (BD) PATIENTS' CLINICAL FEATURES BETWEEN IN THE SAITAMA MEDICAL CENTER, JICHI MEDICAL UNIVERSITY (TOKYO SUBURBS ON THE NORTH SIDE) AND THE INSTITUTE OF RHEUMATOLOGY, TOKYO WOMEN'S MEDICAL UNIVERSITY (METROPOLITAN TOKYO)

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Objective: To investigate the clinical features of our Japanese Behçet's Disease (BD) between Saitama (Tokyo suburbs on the north side) and the center of Tokyo.

Methods: We enrolled 154 Japanese BD patient in this study: 24 BD patients (12 males) in our current hospital (Saitama Medical Center, Jichi Medical University) who continued arriving at April 1st, 2018, and 130 BD patients (33 males) in our previous hospital (Institute of Rheumatology, Tokyo Women's Medical University) who continued arriving at April 1st, 2015, respectively, and those populations were not overlap. The both were all fulfilled the Japanese BD criteria. We analyzed their age, gender, each symptom of BD, the diagnose criteria of International Study Group (ISG) or International Criteria of BD (ICBD), treatment, etc, statistically in both groups.

Results: The median ages (Saitama/Tokyo) were 48/42 year-old (y/o): the lower interquartile range (IQR), 33/32 y/o and the upper IQR, 56/49 y/o, respectively. The comparison of each symptom of BD was as blow (Saitama/Tokyo): oral aphthous ulcers (OU), 24 (100.0%)/146 (100.0%); genital ulcers, 16 (66.6%)/102 (78.5%); skin lesions, 20 (83.3%)/123 (94.6%); uveitis, 18 (75.0%)/40 (30.8%); arthritis, 23 (95.8%)/77 (59.2%), intestinal lesions, 9 (37.5%)/23 (17.7%); neural lesions, 1 (4.2%)/8 (5.5%); vascular lesions, 5 (20.8%)/9 (6.9%); positive pathergy test, 2 (8.3%)/6 (4.6%); epididymitis, 0 (0%)/2 (1.5%). The treatments were performed with interveinal methylprednisolone to 6 (22.2%)/9 (6.9%) cases; mean dose of oral steroid, 3.2/0.5 mg/day, 14/62 cases (60.9%/47.7%) were exactly taken; CyA, 2/5 cases; MTX, 3/3; TAC 0/2; AZT, 3/2; MZR 0/1; 5-ASA, 2/2; SSZ, 2/7; colchicine, 15/73; IVCY, 2/0; warfarin, 3/0; biologics, 0/4.

Conclusions: There were differences: The BD patients in Saitama were elder, lower frequency of positive HLA-B51 and the ocular lesion, and higher arthritis, than Tokyo's; then there is no biologics user and more high dose GC users.

Table. The clinical features of Japanese BD patients in the present study.

Hospital	SaitamaMC, JMU	IOR, TokyoWMU	Fisher's test	Fisher's test (Bonferroni correction)
Duration	2,008-2,018	2,006-2,015	p-value (<0.05)	p-value/17 (<0.0029)
Number (male)	23 (12)	130 (33)	1.00	
Oral aphthous (%)	23 (100.0)	130 (100.0)	0.29	
Genital ulcer (%)	16 (69.6)	102 (78.5)	0.16	
Ocular lesion (%)*	18 (78.3)	40 (30.8)	6.6 x10 ⁻⁵	6.6 x10 ⁻⁵
Skin lesion (%)	20 (87.0)	123 (94.6)	0.07	
Arthritis (%)	21 (91.3)	77 (59.2)	0.0003	0.0003
Positive Pathergy (%)	2 (8.7)	6 (4.6)	0.61	
Intestinal lesion (%)	9 (39.1)	23 (17.7)	0.051	
Neural lesion (%)	1 (4.3)	5 (3.9)	1.00	
Vascular lesion (%)	5 (21.7)	9 (6.9)	0.045	
Epididymitis (%)	0 (0.0)	2 (1.5)	1	
HLA-B5 (%)	3 (42.9) (n=7)	105 (80.8) (N=123)	9.0 x10 ⁻⁹	9.0 x10 ⁻⁹
HLA-B51 (%)	2 (28.6) (n=7)	88 (67.7) (N=123)	3.0 x10 ⁻⁶	3.0 x10 ⁻⁶
HLA-A26 (%)	4 (57.2) (n=7)	30 (4.2) (N=116)	0.78	
unfulfilled-Japan (%)	0 (0.0)**	0 (0.0)	1	
unfulfilled-ISG (%)	3 (13.0)**	2 (1.5)	0.027	
unfulfilled-ICBD (%)	1 (4.3)*†	8 (5.5)	1	

P018**THE JAPAN MULTICENTER REGISTRY IDENTIFIES FIVE CLINICAL SUBSETS BASED ON RESIDUAL SYMPTOMS IN BD PATIENTS**

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Objective: To determine the clinical subtypes based on currently existing symptoms in Japanese patients with Behçet's disease(BD).

Methods: From February 2019, we have opened a BD disease registry consisting of multiple research institutes in Japan centered on Yokohama City University. Patients who were 18 years of age or older, had a disease duration of 6 months or longer, and met the ISG criteria were selected, regardless of whether they are on oral therapy or not.

Patient backgrounds, treatment, disease activity by Behçet's disease current activity form (BDCAF), and patient/physician disease assessments using face scales were prospectively monitored annually.

We employed unsupervised machine learning cluster analysis, and examined the interval changes in individual patients for a year.

Results: A total of 215 consecutive patients were extracted. The average age was 49.5 years, 44.2% were male, and the average duration of illness was 14.1 years. The median BDCAF score was 2 (IQR 1-3) both at registration and one year later, indicating that two symptoms remain. The percentages of patients receiving colchicine, TNF inhibitors and glucocorticoids, and patients not receiving systemic therapy at the time of the registration survey were 65.1%, 34.4%, 23.7% and 11.6% respectively.

The most common residual symptom was oral ulcer followed by arthralgia, irrespective of the observation points. The machine learning cluster analysis classified patients into five groups by patterns of residual mucocutaneous symptoms: asymptomatic (complete remission, 38.9%), oral ulcer (22.3%), arthralgia (12.6%), oral ulcer and arthralgia (12.0%), oral ulcer, arthralgia and cutaneous symptoms (14.3%). The patients' disease assessment was the worst in the group of oral ulcers, arthralgia, and cutaneous symptoms.

Conclusion: This study showed that oral ulcer was the most common as a residual symptom and that patterns of residual symptoms determined five distinct clinical subsets in Japanese BD patients.

P019

PHENOTYPE CLUSTERS IN BEHÇET'S SYNDROME, MYTH OR REALITY: A SYSTEMATIC REVIEW

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Background: The presence of distinct clinical phenotypes with clustering of certain organ manifestations were suggested in Behçet's syndrome. However, studies from different cohorts have shown variability in the phenotypes that were defined. This finding challenges the concept of phenotype clusters since organ manifestations that cluster together would be expected to be uniform across cohorts.

Methods: An electronic search was carried out in PubMed, EMBASE, and Cochrane Library to find articles published until February 2022, using the key words of Behçet, cluster and factor analysis. Two reviewers independently performed a screening of titles, abstracts, and the full-texts using Covidence.

Results: Amongst 7685 studies searched, 32 full-texts were assessed, and 11 studies were identified as relevant for data extraction. Eleven articles studied 13 different cohorts, 3 from China, 4 from Turkey, 3 from Japan, 1 from South Korea, 1 from Israel, and 1 from Greece. 10/11 studies demonstrated clustering of organ manifestations (12 cohorts); whereas no clusters were identified in one study. We identified the following items as possible predictors of the differences in clusters reported in these studies: a. study design (database vs multicenter vs single center cohort), b. statistical analysis method (hierarchical cluster analysis vs factor analysis) c. patient population (pediatric vs adult), d. setting (dermatology vs rheumatology), e. diagnostic criteria (ISG vs ICBID), f. disease duration g. definition of organ involvement (such as papulopustular vs folliculitis, or parenchymal nervous system involvement vs dural sinus thrombosis, h. ascertainment of manifestations (confirmed gastrointestinal involvement vs any diarrhea), i. time interval (manifestations throughout the disease course vs manifestations that were active during the last 3 months, and j. change in natural history of BS over decades.

Conclusion: Differences between studies in clinical phenotype clusters may result from differences in study characteristics rather than real geographic or ethnic differences.

P020**BEHÇET'S DISEASE IN DIFFERENT ETHNIC GROUPS**

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Introduction: Early diagnosis and identification of predominant organ system involvement in Behçet's disease (BD) is crucial for identifying most optimal treatment. The study evaluates 6 described phenotypes of BD - cutaneous-mucous, articular, ophthalmic, vascular, neurological and intestinal in different ethnic groups.

Objective: To assess the occurrence of Behçet's disease (BD) phenotypes in different ethnic groups.

Materials and methods: The study included 202 patients with BD from the 5 most common ethnic groups. The male-female ratio was 2.4:1. Patients' mean age was 31 years [24;37], mean age at the disease onset was 21 years [15;28]; and mean disease duration was 7 years [3;14]. The severity of BD (mild, moderate and severe) was assessed based on the I. Krause's Clinical Severity Scoring for BD.

Results: Severe BD was more often diagnosed in Azerbaijanis and indigenous residents of Dagestan compared to Russians (75 and 70.4% vs. 36.2%), in Armenians - 50% and Chechens - 54.5% out of all BD cases.

Russians were significantly more likely to have a neurological phenotype (15.5% vs. 0-9.4% in all other ethnic groups) and intestinal phenotype (36.2% vs. 13.8-22.7 in all other ethnic groups). Azerbaijanis demonstrated higher prevalence of ocular involvement (68.7% versus 36.2% in Russians, 50% - in Chechens and Armenians, and 57% - in Dagestanis). Dagestanis were more likely to have a vascular phenotype (40.7% versus 15.6% in Azerbaijanis and 18.9% in Russians). The male/female ratio among Russian patients was 1:1, among Dagestanis 4.4:1, Azerbaijanis 3.5:1, Chechens and Armenians 2.6:1.

Conclusion: BD phenotypes vary and demonstrate significant association with the patient's ethnic affiliation therefore, ethnicity should be viewed as the prognostic marker of specific organ-system involvement in case of a disease.

P021

2022 REPORT OF THE GERMAN REGISTRY OF ADAMANTIADES-BEHÇET DISEASE

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The German Registry of Adamantiades-Behçet Disease (ABD) provides data of 900 ABD-patients, which are permanent residents of Germany.

32 clinics and practices transferred patients' data to the registry via standardized registration forms. Demographic data, frequencies of manifestations, familial occurrence and HLA-B5 have been evaluated.

355 (40.1%) patients were of German and 390 (44.1%) of Turkish descent, along with 31 other countries of origin. First manifestation was predominantly in the third decade of life (median age: 26 years).

Full disease developed in 2.4 years on average (median: 3 months). The median age of full clinical picture was 28.5 years. Most frequent features included oral aphthae (98.1%), genital ulcers (64.8%), cutaneous lesions (64.4%), ocular manifestations (46.0%), arthritis (56.1%), vascular complications (20.9%), CNS-involvement (11.9%) as category of neurologic manifestation (20.8%), prostatitis-epididymitis (11.3%), gastrointestinal (10.0%), pulmonary (2.9%), cardiac (2.3%), kidney involvement (1.7%), and positive pathergy test (27.2%). Among skin manifestations, folliculitis (52.6%), erythema nodosum (38.4%), pyoderma (12.3%), skin ulcers (11.0%) and superficial thrombophlebitis (12.0%) were noted. As the most severe complications total blindness (5.8%), meningoencephalitis (2.9%), disabling arthritis (2.2%), fatal outcome (1.0%), hemoptysis (0.9%) and gastrointestinal perforation (0.6%) were registered. Most frequently reported onset symptoms

included: oral aphthae (83.1%), uveitis (2.6%), joint manifestation (2.9%), genital ulcers (2.9%) and erythema nodosum (1.6%). There was a positive family history in 12.1% among the entire collective of the German Registry. In case of German origin, family history was lower than in case of Turkish origin (3.7% versus 14.6%; $p < 0.001$). Patients of Turkish descent showed androtopism in contrast to those of German descent (male:female 1.8:1, $p < 0.001$). Turkish patients suffered more often from uveitis compared to Germans (58.1 vs. 39.1%, $p = 0.03$). The HLA-B5 showed an association with uveitis ($p < 0.001$), gastrointestinal manifestations ($p < 0.001$), erythema nodosum ($p < 0.001$) and superficial thrombophlebitis ($p = 0.23$).

P022

AN UPDATE ON THE EPIDEMIOLOGY OF BEHÇET'S DISEASE IN SOUTHERN SWEDEN

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Background/Objectives: Behçet's disease (BD) is a variable-vessel vasculitis with a distinct geographical distribution of high prevalence along the ancient Silk Route, extending from eastern Asia to the Mediterranean. The prevalence and incidence rate in southern Sweden have previously been estimated to 4.9 per 100 000 adults and 0.2 per 100 000 person-years, respectively.[1] Since then, the proportion of the population of non-Swedish ancestry has increased in southern Sweden. Furthermore, immigration patterns might have an increasing influence on epidemiology of BD. This study is aimed to update the epidemiology of Behçet's disease in southern Sweden.

Methods: The study area was the county of Skåne with an adult (≥ 18 years) population of 1 080 664 on 31st of December 2019. Patients assigned to the ICD-10 code M35.2 between 1998 and 2019 were retrospectively identified by search in population-based data base. Patients fulfilling the International Study Group diagnostic criteria for Behçet's disease were included. The point prevalence per 100 000 adults was estimated on the 31st of December 2019. Incidence rate of Behçet's disease was estimated per 100 000 adult person-years. Non-Swedish ancestry was defined as a person being born outside of Sweden or with two parents born outside of Sweden. A case was considered incident when the diagnosis was made within Skåne with a minimum of 3 years of residence in Sweden prior to diagnosis.

Results: One hundred and one patients fulfilling the diagnostic criteria for Behçet's disease were identified (61 men and 40 women). The point prevalence was 9.1/100 000 adults (95% CI 7.3, 10.9) and higher among the population of non-Swedish ancestry (19.3 vs. 4.8/100 000, $p = 0.001$) and higher among men (11.2 vs 7.0/100 000, $p = 0.027$). There were 58 adult incident cases diagnosed between 1998 and 2019. The incidence rate was 0.3/100 000 person-years (95% CI 0.2,0.3) and was higher among the population of non-Swedish ancestry 0.7 vs. 0.2/100 000, $p = 0.001$). There was no significant increase in incidence rate of Behçet's disease over time (Table 1). All patients presented with oral ulcerations, 90% with genital ulcerations, 84% with skin lesions and 53% with eye disease. Eighteen percent experienced thromboembolic events over the course of the disease, 14 men and 4 women.

Conclusions: The prevalence of Behçet's disease in southern Sweden has increased since last estimated. The incidence rate of Behçet's disease has not increased significantly during the study period, despite an increased proportion of the population being of non-Swedish ancestry. Although the study was in a population-based setting the low sample size is a limitation.

Disclosures: The authors declare no conflict of interest.

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Table 1. Incidence-rate of Behçet's disease in adults in southern Sweden 1998-2019.

Period	Cases	Person-years	Incidence rate (95% CI)	Rate ratio (95% CI)
1998-2005	16	7178222	0.2 (0.1;0.3)	
2006-2012	19	6826433	0.3 (0.2;0.4)	1.3 (0.6;2.5)
2013-2019	23	7325315	0.3 (0.2;0.4)	1.4 (0.8;2.7)

P023**QUANTITATIVE AND QUALITATIVE BIBLIOMETRIC ANALYSIS OF ORIGINAL RESEARCH IN BEHÇET'S DISEASE PUBLISHED BETWEEN 2000 AND 2019**

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Objectives: To perform a bibliometric analysis of published original articles on Behçet's disease (BD) and to systematically describe their quantitative and qualitative features, in order to assess the publication trends and shed light on possible further research.

Methods: A relevant search in PubMed database was performed for original research articles published between 2000 and 2019 on BD, excluding meta-analyses. We calculated the number of articles by country of origin and categorized them by type of study (basic, clinical, translational research). We also assessed their impact by using the individual citation numbers from Google Scholar search engine and by calculating median annual citation rates, both per country of origin and type of study.

Results: A total of 2381 original research articles were captured. With regard to the type of research, the majority was clinical (52.6%, excluding case reports), followed by translational (46%) and only a minority reported basic research findings (1.4%). Of the 51 publishing countries, Turkey was the most productive (39% of articles), whereas 31% came from four other countries (Korea, China, Japan and Italy) where BD is relatively prevalent. Regarding median annual citation rates, France was first (4), followed by UK (3), Germany (2.8) and Israel (2.6). The number of articles has almost doubled between 2010- 2019 versus 2000-2009. However, the median annual citation rates across either clinical or translational research had a slightly downwards trend, suggesting that research quality may be mildly decreased over time.

Conclusions: During the last two decades, countries where BD is more prevalent were the most productive in terms of original research, as expected, albeit with lower impact comparing to countries with higher research budgets, in general. A considerable growth of BD literature is observed over time, but further funding may be warranted for a parallel increase in the respective scientific impact.

P024**A CASE OF CARRY-OVER JUVENILE IDIOPATHIC ARTHRITIS: UVEITIS, POLYARTHRITIS IN LARGE JOINTS, RECURRENT ORAL APHTHOUS ULCERS, AORTITIS, RELAPSING POLYCHONDritis, SACROILIAC ARTHRITIS (BILATERAL GRADE 2), AND POSITIVE HLA-B27**

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Objective: To present a case with developing multiple-diseases.

Methods: We presented as a case report.

Results: A 33 year-old male was admitted our hospital with inflammation. His left uveitis was occurred controlling with glucocorticoid eye-drops and his left knee arthritis was occurred when he was 10; then, he was diagnosed JIA and performed synovial-removal of his left knee. His expressive aphasia and his right hemiplegia were occurred when he was 16; thereafter, discovering his bilateral regions of origin of carotid arteries stenosis with his ascending aortic aneurysm and mild aortic regurgitation, he was diagnosed Takayasu's-arteritis. Moreover, he was diagnosed Behçet's-disease because he has already had recurrent oral aphthous ulcers since his childhood; then, taking daily PSL 30 mg was started, and after a while, tapering of it was started. Another, his right auricular-chondritis, his left labyrinthitis and episcleritis were occurred and recurred from the age 17 to 20. He was fulfilled McAdam's criteria and diagnosed as having relapsing-polychondritis when he was 21. Then, adding azathioprine, MTX and CyA on PSL therapy; however, his inflammation was uncontrolled, and he complained his anteflexion-disorder. His sacroiliac-arthritis was detected as bilateral grade 2 and he had positive HLA-B27; thus, he was diagnosed as having ankylosing-spondylitis and his treatment with PSL 40 mg/day and CyA 75 mg/day was resumed. More CyA and another MTX were added, whenever tapering his PSL, his arthritis was recurred. Using PSL 20 mg/day, TAC 3 mg/day made his CRP controlled as 1 mg/dL. When he was 26, his CRP was controlled as a normal, he was performed Bentall's-valve-replacement and partial-arch-aortic-replacement for his dyspnea on exertion, palpitations, worsent AR, and expand ascending aneurism. Post-operation, he kept good condition with mPSL from 14 to 16 mg/day and TAC 3 mg/day.

Conclusion: We experienced a case with carry-over JIA presenting multiple disease.

P025**ANTI-GANGLIOSIDE ANTIBODIES IN A BEHÇET'S SYNDROME PATIENT WITH HASHIMOTO'S THYROIDITIS UNDERGOING THERAPEUTIC PLASMA EXCHANGE**

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Background: Behçet's Syndrome (BS) is a rare, autoinflammatory, multisystemic syndrome which can cause orogenital ulceration, skin lesions, arthropathy, ocular disease, neurological, gastrointestinal, and vascular symptoms. Treatment is individualised for each patient. Therapeutic plasma exchange (TPE) can be used as treatment for autoimmune conditions, however in BS it is a last resort treatment and can be particularly beneficial for those with neurological complications. In addition, several neurological conditions are associated with anti-ganglioside antibodies (AGAs), and there are case reports demonstrating a further association with thyroid disease.

Case presentation: A 38-year-old female initially presented with ocular BS and a co-morbidity of Hashimoto's Thyroiditis. Her main problem was neurological disease which was non-responsive to treatment after exhausting the treatment pathway, from colchicine to the use of biologics. Her disease remained active with orogenital ulcers, erythema nodosum, folliculitis, gastrointestinal symptoms, and neurological manifestations. She was treated with TPE for her multisystem BS which led to a marked improvement in her symptoms. When TPE was paused due to the pandemic, her symptoms returned. In addition, she had elevated AGA levels which were monitored due to her neurological disease. AGA levels decreased with TPE and increased again when treatment was stopped. Prior to an increase in AGAs, Thyroid stimulating hormone (TSH) levels were also noted to increase.

Conclusion: This case demonstrates TPE may be advantageous in managing BS when the treatment pathway has been exhausted. TPE led to a decrease in AGAs and therefore may have a role in managing patients with neurological BS. Furthermore, peaks in AGA levels were shown to correspond with TSH levels, showing a possible link between AGAs and thyroid disease.

P026**NEURO-BEHÇET'S SYNDROME PRESENTING TO THE EMERGENCY DEPARTMENT**

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Background: Behçets Syndrome (BS) is a multisystemic autoinflammatory condition affecting which can present with oral ulcers, genital ulcers, uveitis, cutaneous lesions, arthralgia, gastrointestinal and vascular effects. Furthermore, there can be neurological involvement. Neurological BS causes parenchymal inflammation in the central nervous system or venous sinus thrombosis. Rarely, there is involvement of the peripheral nervous system.

Case presentation: Case 1 is a 39-year-old HLA-B51 positive Kurdish female with a background of orogenital ulcers and acneiform lesions. She discontinued systemic therapy and presented with a left sided facial droop, abducens nerve palsy, ptosis and exotropia. She displayed dysarthria and limb weakness. CT head showed an area of hyperdensity around the left thalamus and was initially thought to be a space-occupying lesion and treated with dexamethasone. A subsequent MRI scan showed a tumefactive inflammatory lesion. On review she was found to have active disease with mucocutaneous manifestations. Treatment was promptly started with infliximab and prednisolone. Two weeks later, her neurological symptoms had significantly reduced and after five months, a repeat MRI showed a considerable improvement.

Case 2 is a 52-year-old Turkish female diagnosed with ocular BS. She presented with a third cranial nerve palsy. Her symptoms were blurred vision, diplopia and headache. A CTA showed no aneurysmal change but infection or vasculitis was suspected. CT head was normal, however neurological symptoms persisted and she developed pustular lesions. An urgent MRI was consistent with Neuro-Behçet's and she was commenced on infliximab and prednisolone. Following a few weeks of treatment her neurological symptoms had improved and repeat MRI showed regression of the inflammatory lesion.

Conclusion: BS is a rare condition and approximately 9% of patients have neurological involvement. In these cases, prompt treatment with anti-TNF agents and corticosteroids resulted in excellent outcomes and improvement in neurological symptoms.

P027

A CONTROVERSIAL MIMICKER OF PANUVEITIS IN BEHÇET'S DISEASE

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Introduction: Panuveitis can be caused by multiple infectious agents, sarcoidosis or idiopathic. Its prevalence in Behçet's disease (BD) is estimated at 50-90%, with a quarter of patients risking blindness.¹ Syphilis can also be responsible for eye manifestations like papillitis and uveitis and should be considered since the misdiagnosis leads to erroneous treatment strategy.²

Materials and methods: Case presentation.

Results: A 64-year-old Caucasian female, diabetic, presents an episode of sudden loss of vision in both eyes. Emergency evaluation diagnoses bilateral panuveitis with retinal detachment and prompt methylprednisolone pulse therapy was initiated with incomplete visual acuity recovery. Medical history was insignificant apart from a mild episode of genital lesions that the patient did not investigate. A cerebral computed tomography scan was performed with no noticeable feature. Further investigations revealed negative hepatitis B, C and HIV infections, negative Quantiferon test and Toxoplasma gondii antibodies. However, positive VDRL and TPHA tests were identified, suggesting secondary syphilis infection, thus guideline-based antibiotics were administered. Patient denied sexual intercourse in the last two years. Considering that the uveitis repeatedly relapsed when systemic corticosteroid dose was lowered, HLA B51 was determined and found positive. Pathergy, neurological and vascular manifestations were absent. Incomplete BD was discussed, and immunosuppression was started with no further ocular relapses.

Discussions: Panuveitis can be the initial manifestation in multiple conditions. False positive serology for syphilis can occur in patients with BD[3]. However, positive HLA B51 is highly suggestive of BD in the absence of all clinical criteria. Antibacterial monotherapy had no benefit in the patient, thus systemic corticosteroids and immunosuppression were added.

Conclusion: The case highlights clinical and biological similarities to secondary syphilis, with false positive VDRL test in a patient with incomplete Behçet's disease.

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P028**IRREVERSIBLE DAMAGE DUE TO NON-COMPLIANCE IN BEHÇET'S DISEASE**

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Introduction: Eye involvement in Bechet's disease is the most common targeted organ, affecting all eye chambers and being responsible for blindness if not promptly treated in more than 25% of patients.¹ Poor sight prognosis is due if relapses of posterior eye segment occur.

Materials and methods: Case presentation.

Results: An 18-year-old male patient of gipsy origin presents with sudden onset of intense pain and lowered vision in the right eye. He is diagnosed with panuveitis, mild retinal detachment and macular edema, thus both topical and systemic corticosteroid treatment are initiated. Medical history included an episode of knee arthritis and multiple oral lesions that were interpreted as fungal infection. Patient associates multiple genital ulcers and pseudofolliculitis-like lesions of the posterior thorax. Suspicion of Behçet's disease (BD) is raised despite unavailability of HLA B51. Patient's visual acuity improved considerably, and he is discharged and recommended azathioprine, colchicine, and medium-dose corticosteroids. However, four months later, the patient presents with complete blindness of the right eye confirming not taken medication as prescribed.

Discussions: Since EULAR has released recommendations for management in BD, clinicians have a more targeted therapeutic approach for this patient population.² Patients should be aware of visual-threatening potential in BD and that lack of treatment might lead to irreversible damage.

Conclusion: The case highlights the importance of treatment adherence and patient follow-up because of high risk of recurrence of intraocular inflammation causing cecity and disability.

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P029

A RARE SITE OF ULCERATION IN BEHÇET'S DISEASE

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Objective: Behçet's disease (BD) is a systemic vasculitis with multiple organ involvement. Among them, urinary tract involvement is rarely cited, most data mentioning bladder dysfunction that can occur in neuro-BD1.

Material and method: Case presentation.

Result: A 34-year-old female patient diagnosed with BD presents with dysuria and right low back pain. Abdominal ultrasound shows grade 2 hydronephrosis for which repeated ureteroscopies are performed with the installation of a ureteral stent, without detectable lesion. Persistent pain, hematuria, and aggravation of hydronephrosis on removal of the stent led to an MRI that excludes the presence of a possible compressive tumor. The worsening of the patient's condition requires ureteroscopic reassessment with the highlighting of an ulcerative lesion on the right ureter, either secondary to multiple local interventions or active vasculitis. The biopsy performed confirmed fragments of urothelium with inflammatory lymphocytic infiltrate, polymorphonuclears in the interstitial perivascular areas, compatible with BD. Due to the unusual and severe localization of the disease activity and the lack of response to methotrexate and azathioprine, the patient received cyclosporine together with colchicine and low-dose corticosteroids. Periodic urological reassessment showed a slow healing of ureteral ulceration, with restoration of mucosal integrity and removal of the stent with normalization of renal function and ultrasound appearance.

Discussion: BD is a variable-size vessel vasculitis, with urogenital damage such as genital ulcers or epididymitis and rarely bladder manifestations². Ureteral ulcers are mentioned in case reports and do not benefit from targeted recommendations but require immunosuppressive or immunomodulatory treatment.

Conclusions: BD with ureteral ulcerative lesion is a rare occurrence, especially in women. A multidisciplinary approach with disease control and local interventions is needed for optimal results.

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P030**PSEUDO INFLAMMATORY TUMORS AND BEHÇET'S DISEASE**

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Introduction: Behçet's disease (BD) is a multisystemic, inflammatory vasculitis. The combination of inflammatory pseudotumors and Behçet's disease is only exceptionally reported and poses a real diagnostic and therapeutic challenge. We report three specific cases of pseudo inflammatory tumors revealing BD.

Case 1: Patient, 32 years of age, consults for left hemiparesis, associated with headaches which have revealed a BD. The MRI notes the presence of right pseudo inflammatory tumor capsulo thalamic and mesencephalic. Therapeutically, the patient had received 2 boluses of methylprednisolone relayed by oral corticosteroid therapy and 6 boluses of cyclophosphamide then Azathioprine with very good clinical and imaging progress.

Case 2: Right mediastino-hilar process with pulmonary embolism revealing Behçet disease in a 31-year-old patient. Bronchoscopy objectified a simple inflammatory condition. Biopsy after mediastinoscopy objectified a reactive chronic lymphadenitis aspect without malignant tumor or granuloma. The patient had received corticosteroid and subsequently 3 monthly boluses of Cyclophosphamide with Azathioprine relay. A very good clinical and imaging progress was noted.

Case 3: Patient aged 33, consults for paraparesis with pseudo inflammatory tumor of the spinal cord revealing BD. Therapeutically, the patient was put on high-dose corticosteroid therapy and anti-TNF with marked clinical improvement and MRI.

Discussion/ Conclusion: Pseudo Inflammatory Tumors represent a group of heterogeneous conditions, with unknown etiologies and localization, most often neurological. Their main differential diagnosis is a malignant tumor process. Knowledge of the possibility of the occurrence of pseudotumor forms during Behçet's disease is essential in order to propose without delay an adequate treatment to improve the prognosis.

None conflict of interests.

P031**OUR MONOZYGOT TWINS DIAGNOSED WITH BEHÇET'S SYNDROME AND THEIR CLINICAL FEATURES**

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Behçet syndrome (BS) was first described by Hulusi Behçet in 1937.¹ In this case report, we will share the clinical features of our monozygotic twins, who had a different disease course and severity, lived in the same house, and were diagnosed with BS when one was 28 years old and the other was 32 years old.

Case 1: A 33-year-old male patient with no known systemic disease has been followed up with the diagnosis of BS for about 5 years. While being examined for deep vein thrombosis (DVT), it was learned from his history that he had oral aphthae and occasional erythema nodosum for many years, and he was diagnosed with BS. Upon the development of aneurysmatic dilatation in the left lower lobar branch of the pulmonary artery 2 years later, the maintenance treatment was switched to infliximab treatment. The patient is currently being followed in remission.

Case 2: A 33-year-old male patient with no known systemic disease was invited to our Rheumatology Polyclinic to be examined because his twin brother had BS. In his history, it was learned that he had oral aphthae for many years. On physical examination, sequelae of papulopustular lesions and erythema nodosum at the right foot were detected. His treatment with colchicine, azathioprine and low-dose corticosteroids was arranged.

Discussion: Although BS is a multisystemic disease of unknown cause, it has been suggested that genetic and environmental factors have an effect (1). The most obvious clue to genetic susceptibility in BS was the association of HLA-B5 observed in the Mediterranean Basin and Japan populations where the disease is common (2). Familial predisposition has been reported in Turkish and Japanese populations (3). Although studies on twins are important to reveal the interaction between genetic and environmental factors, our data on this subject is limited (1).

Conflict of interest statement: The authors declare no conflicts of interest.

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P032**NEOPLASIA AND BEHÇET'S DISEASE: RARE CASE OF ASSOCIATION OF BEHÇET'S DISEASE AND MULTIPLE MYELOMA**

Introduction: Behçet's disease is a multisystemic inflammatory disorder characterized by recurrent acute attacks with a clinical and evolutionary polymorphism and whose pathogenesis remains obscure. Ocular involvement in Behçet's disease is classically manifested by non-granulomatous anterior uveitis, and posteriorly by hyalitis and vasculitis. We describe the case of a young patient with an atypical association of Behçet's disease and multiple myeloma.

Observation: A 34-year-old female patient, followed for Behçet's disease revealed by a bipolar aphthosis evolving for 4 years, admitted for a decrease of visual acuity and ocular redness of sudden onset. The ophthalmological examination showed bilateral episcleritis and Roth's spots on the fundus, suggesting retinal vasculitis. The extraocular signs were characterized by an episode of oral aphthosis, arthromyalgia, and altered general condition. The biological workup revealed an inflammatory syndrome, malignant hypercalcemia, renal failure with a GFR of 24ml/min, and a profound regenerative anemia of 4g/dl. An emergency myelogram showed 85% plasma cells, confirming the diagnosis of multiple myeloma. Plasma protein electrophoresis showed a monoclonal peak in gamma globulin at 30 g/l. Serum immunofixation identified a monoclonal IgG Kappa immunoglobulin. Serum free light chain assay showed an elevation of the Kappa chain level to 569.5mg/L and a Lambda chain level to 1.98mg/L with a pathological ratio of 287.63. The bone workup showed cookie cutter lesions on the skull X-ray and at the spinal level. The MRI showed a cervical-dorsal-lumbar myeloma with no signs of compression. The patient was put on polychemotherapy (bortezomib, dexamethasone and thalidomide) with bone marrow autotransplantation scheduled.

Discussion/Conclusion: Ocular involvement in Behçet's disease is very frequent, including retinal involvement, whereas ophthalmologic involvement in multiple myeloma is very rare but can affect all structures of the eye: orbital involvement (affecting the orbital muscles and the adnexa of the eye), intraocular involvement (retinal vasculitis, uveitis, chorioretinitis) and neuro-ophthalmologic involvement. The mechanisms that explain ophthalmologic involvement in myeloma are: either extra-medullary infiltration of tissues by monoclonal plasma cells; or a hyperviscosity syndrome secondary to monoclonal gammopathy. When retinal vasculitis revealed by Roth's spots is diagnosed, the etiological work-up should include a systematic search for monoclonal gammopathy that may reveal the existence of multiple myeloma.

P033**CORONARY ANEURYSMS REVEALING BEHÇET'S DISEASE**

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Introduction: Behçet's disease is a vasculitis that is characterized by a triad associating oral aphthosis, genital aphthosis as well as uveitis. The disease must also be suspected in the presence of vascular and neurological manifestations, which may be potentially life-threatening for the patient. Coronary artery disease is extremely rare. We report a case of acute coronary syndrome revealing Behçet's disease.

Observation: A 57-year-old woman with demyelinating disease of the central nervous system of undetermined origin, revealed ten years earlier by imaging performed at the time of the onset of headaches and memory disorders, stable in the absence of treatment, was referred to internal medicine for a suspicion of vasculitis in the setting of an acute coronary syndrome with no cardiac risk factor. The patient had presented with stage 2 angina, accompanied by palpitations on effort. The ECG showed negative T waves in the inferior territory associated with an incomplete right branch block. His troponin T level was negative and there was no inflammatory syndrome. Trans-thoracic echocardiography showed inferoseptal hypokinesia and a decrease in LVEF estimated at 47%. A coronary angiography was performed and revealed significant aneurysms and ectasias of the anterior interventricular and right coronary arteries. Cardiac MRI showed a minimal circumferential pericardial effusion of 5 mm. The diagnosis of Behçet's disease was retained according to the International Team for the Revision of the International Criteria of Behçet's Disease, in view of the notion of recurrent oral aphthosis, a history of genital aphthae and erythema nodosum, but also in view of the neurological involvement and the recently discovered coronary aneurysms. Due to the severity of the patient's vascular involvement, following the European League Against Rheumatism (EULAR) 2018 recommendations, treatment with cyclophosphamide 1000 mg was initiated, in combination with corticosteroid therapy 1mg/kg/d with gradual decrease, colchicine 1 mg/d and effective antiaggregation. Because of the patient's neurological condition, treatment with anti-TNF-alpha drugs, particularly Infliximab, is not an option. Following six cycles of cyclophosphamide, a relay with Azathioprine was planned. The evolution was marked by the persistence of the thoracic pain, which led to a new hospitalization twenty days after the beginning of the treatment, during which the occurrence of a new ACS was excluded, and the pain was related to pericarditis.

Discussion: Vascular involvement is more common in young men and may be indicative of the disease. It most often concerns the venous system. Arterial impairment is less frequent. It is characterized by the presence of aneurysms, occlusions or stenoses, essentially of the aorta, femoral, pulmonary or iliac arteries. Coronary involvement is extremely rare and severe. Cardiac complications are also possible, in particular pericardial involvement which may clinically mimic a coronary syndrome and which tends to recur. Patients with angio-Behçet require control of the inflammation before any vascular procedure is performed in order not to aggravate the disease, which is difficult when the disease is revealing, as in our patient.

Conclusion: Coronary involvement in Behçet's disease is rare and potentially fatal, requiring the use of corticosteroids and immunosuppressors. As it may reveal the disease, it should be considered in any young patient with a coronary syndrome without cardiovascular risk factors, in order to avoid delaying the diagnosis and to adapt the therapeutic management.

P034**ADAMANTIADES-BEHÇET'S DISEASE IS NOT ASSOCIATED WITH A SEVERE COVID-19 COURSE**

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Background: The pathophysiology of COVID-19, which causes hyperstimulation of the immune system, is leading to well-described sequelae with high morbidity and mortality. On the other hand, the interplay between COVID-19 and hyperergic inflammatory conditions, such as Adamantiades-Behçet's disease (ABD), is still unclear.

Case presentations: Among the over 900 patients of the German Registry of Adamantiades-Behçet's disease only two patients, a 52 year-old man, and a 45 year-old woman were reported infected with SARS-CoV-2. The first patient presented with severe COVID-19 symptoms as well as an intensification of oral aphthosis and arthritis. Azathioprine which was previously managing the ABD was discontinued, and the patient was hospitalized for 19 days, including 12 days in intensive care. He recovered with ongoing fatiguability. The patient was treated with apremilast and responded well.

The second patient presented with moderate COVID-19 symptoms without a ABD flareup. ABD was being managed with topical analgesia and triamcinolone paste. She recovered under an outpatient oral doxycycline treatment and recovered without long-term sequelae.

Conclusion: In contrast to other immunological diseases with severe COVID-19 course¹, COVID-19- infected ABD patients seems to exhibit a less severe course than the general population^{1,2}. This fact may be associated with the young average age of ABD patients in comparison to patients with other immunological diseases and/or a specific immunological background of ABD contradicting COVID-19.

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P035

COVID-19 INFECTION AND BEHÇET'S DISEASE: TWO YEAR EXPERIENCE IN IRANIAN PATIENTS

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Objectives: To present the clinical characteristics, disease course, management and outcomes of COVID-19 in Iranian patients with Behçet's disease (BD) in the last 2 years.

Methods: We retrieved BD patients with diagnosis of COVID-19 infection from our cohort of 7798 patients. Data regarding BD characteristics and features related to COVID-19 infection, pharmacological treatments and clinical outcomes were collected. Comparisons between patients diagnosed during 2020 and 2021 were performed. Appropriate statistical comparisons were done, and $p < 0.05$ considered significant.

Results: We identified 107 BD patients with COVID-19 infection (59 in 2020, and 48 in 2021). Fifty-four percent were female. The median age was 49 years (IQR:15), and the median disease duration was 245 months (IQR:195). Sixty-two BD patients (60%) had non-active disease, 41% had a comorbid disease apart from BD. COVID manifestations were the same as seen in the general population. Flu-like symptoms (fatigue and myalgia) were the most common (84%), followed by headache (65%), fever (57%), ageusia/anosmia (55%), and pulmonary involvement (50.5%). There was no change in BD symptoms in 86%. Twenty-three patients (21.5%) were hospitalized, 4 (3.7%) had recurrent infection and one patient (0.9%) died due to severe respiratory failure. Patients infected in 2021 were younger (44 vs. 51, $p < 0.0003$) with a higher male/female ratio (1.53 vs. 0.51, $p < 0.007$). COVID presentation were similar except for higher rate of cough (71% vs. 47%, $p < 0.02$) and common cold symptoms (sore throat, rhinorrhea) in them (40% vs. 22%, $p < 0.05$). Corticosteroids (36% vs. 12%, $p < 0.003$) and antiviral drugs (32% vs. 10%, $p < 0.006$) were more prescribed for treating COVID infection in 2021.

Conclusion: The clinical feature of COVID-19 infection in Iranian BD patients was not significantly changed in the second year of pandemic.

They showed higher rate of cough and cold symptoms, and were treated more with corticosteroids and antiviral drugs.

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P036

THE IMPACT OF THE COVID-19 PANDEMIC ON PATIENTS WITH BEHÇET'S SYNDROME WITHIN THE FRAMEWORK OF MASLOW'S HIERARCHY OF NEEDS VS. PATIENT EMPOWERMENT STRATEGIES IN THE DISEASE MANAGEMENT

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Introduction: The aim of this online survey was to assess the impacts of the COVID-19 pandemic on patients with Behçet's syndrome (BS) using the Maslow hierarchy of needs and patient empowerment strategies in the disease management.

Materials and Methods: 68 BS patients from the UK filled an online questionnaire that covered three components of Maslow's hierarchy of needs regarding Physiological needs (sleep, food, mobility), Safety needs (employment, health), Social needs (relationships), personal precautions, main concern regarding COVID-19 as well as patient empowerment strategies in the study.

Results: The majority of them were female (80,9%), British/English/Scottish (77,9%) and ≥40 years old (75,9%). During lockdown, decreases in weekly working hours (20.79±17.94 vs 26.65±13.86), frequency of exercise (4.39±1.94 vs 3.71±2.26) and healthy food consumption (56,9 % vs 38,4 %) per week were found in comparison to those in prior to lockdown in patients with BS (p=0.017; p=0.007; p=0.001). Furthermore, employment rate was decrease (32.6% vs 26.7%), patients experienced sleeping less (54.4%) and feeling lonely (66.1%) as outcomes of the lockdown.

Empowerment strategies for patients were performed by the collaborations of NHS, the Behçet's Centres of Excellence (BCE) and the Behçet's Patients Support. The NHS sent a letter advising shielding (66.2%). BS specialists were accessed by Tele-medicine services by using telephone consultations (44.1%) and e-mails (27.9%) at lockdown. Moreover, patients received mental health support in the BCE. When considered self-empowerment of patients, both official government and Behçet's corporate health web pages served as information sources for patients with BS.

Conclusion: A holistic approach based on Maslow hierarchy of needs addressed significant points for the improvements of patients' life during the lockdown. Patient empowerment as an important component of chronic disease management was essential point to overcome the negative impact of lockdown on patients' life and disease management in the framework of patient-centred care.

P037

COMPARISON OF HUMORAL RESPONSE AFTER TWO DOSES OF INACTIVATED OR MRNA VACCINES AGAINST SARS-COV-2 IN PATIENTS WITH BEHÇET'S SYNDROME

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Objectives: To compare SARS-CoV-2 antibody response after two doses of inactivated (Sinovac /CoronaVac) or mRNA (Pfizer/BioNTech) vaccines in patients with Behçet's syndrome (BS) and healthy controls (HCs).

Methods: We studied 166 (92M/74F) patients with BS (mean age: 42.9±9.6 years) and 165 (75M/90F) healthy controls (mean age: 42.4±10.4 years), in a single-center cross-sectional design between April 2021 and October 2021. A total of 80 patients with BS and 89 HCs received two doses of CoronaVac, while 86 patients with BS and 76 HCs were vaccinated with BioNTech. All study subjects had a negative history for COVID-19. Serum samples were collected at least 21 days after the second dose of the vaccine. Anti-spike IgG antibody titers were measured quantitatively using a commercially available immunoassay method.

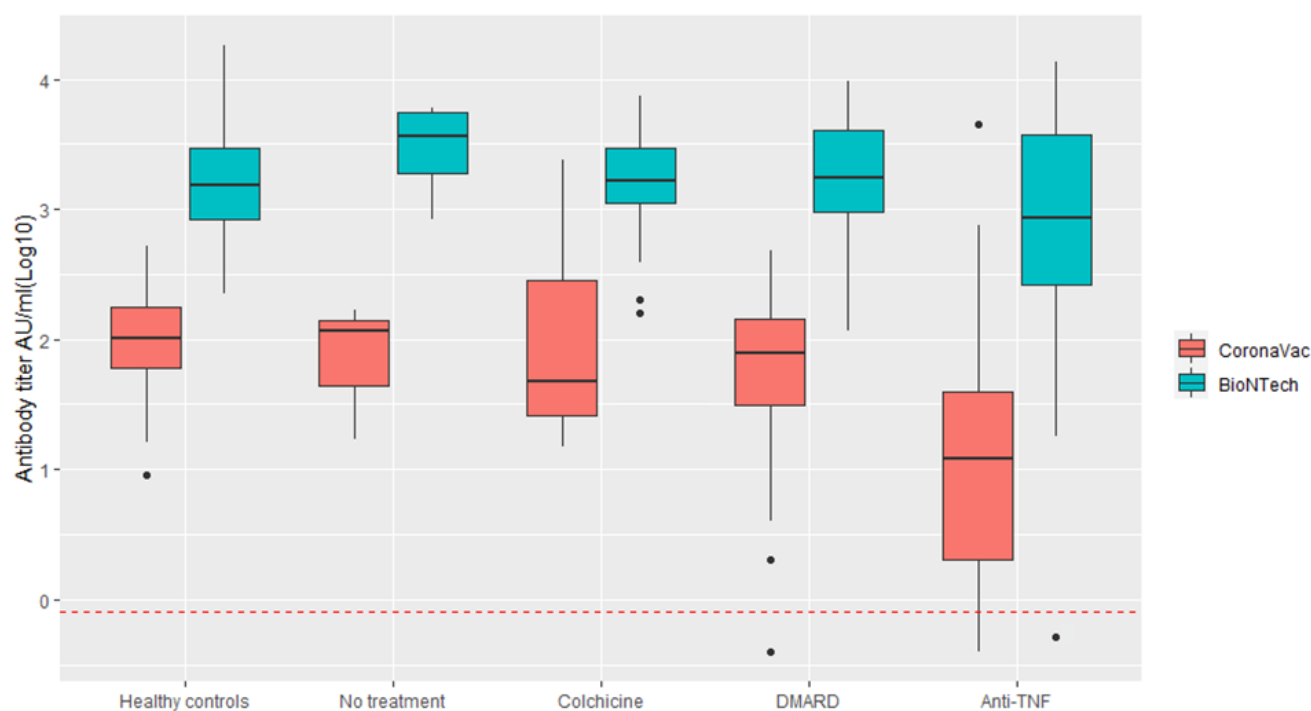
Results: The great majority among both patients and HCs had detectable antibodies after either CoronaVac (96.3% vs 100%) or BioNTech (98.8% vs 100%). Among those vaccinated with CoronaVac, BS patients had significantly lower median (IQR) titers compared to HCs [36.5 (12.5-128.5) vs 102 (59-180), $P<0.001$]. On the other hand, antibody titers did not differ among patients with BS and HCs who were vaccinated with BioNTech [1648.5 (527.0-3693.8) vs 1516.0 (836.3-2599.5), $p=0.512$]. Among different treatment regimen subgroups in both vaccine groups, those who were using anti-TNF based treatment had the lowest antibody titers. However, the difference was statistically significant only among those vaccinated with CoronaVac. Among patients vaccinated with BioNTech there was no statistically significant difference between different treatment regimen groups.

Conclusions: Compared to inactivated COVID-19 vaccine, mRNA-based vaccine elicited higher antibody titers among BS patients. Only in the CoronaVac group, patients especially those using anti-TNF agents were found to have low titers compared to healthy subjects. BS patients vaccinated with BioNTech were found to have similar seroconversion rates and antibody levels compared to healthy controls. Further studies should assess whether the low antibody titers are associated with diminished protection against COVID-19 in both vaccine groups.

Key Words: antibody response, humoral response, COVID-19, vaccination, Behçet's syndrome, BioNTech, CoronaVac

P037

Figure. Box plots showing log transformed antibody levels regarding vaccine type across different treatment regimens groups and healthy controls.



Dotted line shows cut off line for seropositivity.

DMARD: disease modifying anti-rheumatic drug; TNF: tumor necrosis factor.

P038**IMPROVED SENSITIVITY OF SKIN PATHERGY TEST WITH POLYSACCHARIDE PNEUMOCOCCAL VACCINE ANTIGENS IN THE DIAGNOSIS OF BEHÇET DISEASE**

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Objective: The skin pathergy test (SPT) is an important tool in the diagnosis of Behçet Disease (BD), but its decreasing sensitivity over years has limited its use. This study aimed to improve the sensitivity of SPT without compromising its specificity.

Methods: BD patients, patients with other inflammatory diseases, recurrent aphtous stomatitis, and healthy controls were comprised the study group. SPT was induced by 20G needle and 21G lancet pricks, or with additional application of 23-valent polysaccharide pneumococcal vaccine (PS-23), Alum, or ATP to prick site. Development of erythema and induration at 24h/48h were evaluated by the same observer. Induration (≥ 2 mm) with erythema at 48h was accepted as positive. Proinflammatory cytokine production following stimulation with LPS or PS-23 was investigated by whole blood assay (WBA) in a subgroup.

Results: Stimulation of forearm skin by PS-23 and 20G needle prick showed the highest sensitivity and specificity in all BD patients (64.3% and 100%, respectively), especially in patients with active disease (80.3% and 100%, respectively) compared to the sensitivity of 4.8% in all and 6.1% in active patients using a single 20G prick. Positive result was associated with the disease activity and not using immunosuppressives. In WBA analyses, significantly increased IL-1 β and IL-1Ra production in response to PS-23 was observed only in active BD group, while cytokine responses to LPS were similar in all groups.

Conclusion: SPT induced by 20G needle-prick and PS-23 antigens was shown to be a promising tool for the diagnosis of BD owing to its significantly improved sensitivity compared to the standard applications. Replication of these findings are being awaited in other ethnic groups.

Keywords: Behçet disease, skin pathergy reaction, polysaccharide pneumococcal vaccine, whole blood assay, IL-1 beta

P039

WHICH SYSTEM TO CHOOSE? FIRST RESULTS SHOW LARGE DIFFERENCES IN SENSITIVITY IN DIFFERENT CLASSIFICATION SYSTEMS OF ADAMANTIADES-BEHÇET DISEASE

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Adamantiades-Behçet disease is a multi-system disease that is diagnosed based on clinical symptoms and classification systems. A variety of classification systems are available for this purpose.¹ Thirteen of the 17 known classification systems were evaluated using the original literature: Curth (1946), Hewitt (1969), Mason and Barnes (1969), Japan (1972), Hubault and Hamza (1974), O'Duffy (1974), Cheng and Chang (1980), Dilsen (1986), Japan revised criteria (1987), revised International Study Group on Behçet's disease I and II (ISG criteria, 1992), Iran Classification Tree (1993), revised international Criteria for Behçet's Disease (2013).¹

Subsequently, the criteria were examined regarding their sensitivity in 900 German patients of the German Registry of Adamantiades-Behçet's disease.²

A first evaluation showed large differences in the sensitivity of the individual classification systems for the German patients with Adamantiades-Behçet's disease.

This could indicate that certain classifications might be more suitable for detecting Adamantiades-Behçet disease in patients of different national origin.

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P040**HOW MEANINGFUL IS THE MANSON AND BARNES CLASSIFICATION SYSTEM IN TERMS OF SENSITIVITY FOR GERMAN PATIENTS WITH ADAMANTIADES-BEHÇET'S DISEASE?**

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Over the last 76 years, 17 systems for the classification of Adamantiades-Behçet's disease have been developed by different authors and working groups.¹ In 2013, the International Team for the Revision of the International Criteria for Behçet's disease reported criteria with regard to their sensitivity and specificity on the basis of 2556 patients with Adamantiades-Behçet's disease and 1163 patients in the control group.¹ Representative for Germany, 43 patients with Adamantiades-Behçet's disease and 19 patients in the control group were included.¹ Patients with Adamantiades-Behçet's disease in Germany have been included in the German Registry for Adamantiades-Behçet's disease since 1990.² The registry currently comprises over 900 patients. Patients included in the register provide a standardised questionnaire with 216 items.²

To calculate the sensitivity of the classification systems for the patients of the German registry, all classification systems were evaluated using the original literature. In a second step, the individual symptoms of the classification systems were assigned to the items of the German registry. The example of the classification according to Manson and Barnes shows that the sensitivity of the German patients recorded in the registry could possibly differ significantly from the sensitivity previously assumed for the German cohort.³

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P041

HOW MEANINGFUL IS THE HEWITT CLASSIFICATION SYSTEM IN TERMS OF SENSITIVITY FOR GERMAN PATIENTS WITH ADAMANTIADES-BEHÇET'S DISEASE?

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Over the last 76 years, 17 systems for the classification of Adamantiades-Behçet's disease have been developed by different authors and working groups.¹ In 2013, the International Team for the Revision of the International Criteria for Behçet's disease reported criteria with regard to their sensitivity and specificity on the basis of 2556 patients with Adamantiades-Behçet's disease and 1163 patients in the control group.¹ Representative for Germany, 43 patients with Adamantiades-Behçet's disease and 19 patients in the control group were included.¹ Patients with Adamantiades-Behçet's disease in Germany have been included in the German Registry for Adamantiades-Behçet's disease since 1990.² The registry currently comprises over 900 patients. Patients included in the register provide a standardised questionnaire with 216 items.²

To calculate the sensitivity of the classification systems for the patients of the German registry, all classification systems were evaluated using the original literature. In a second step, the individual symptoms of the classification systems were assigned to the items of the German registry. The example of the classification according to Hewitt shows that the sensitivity of the German patients recorded in the registry could possibly differ significantly from the sensitivity previously assumed for the German cohort.³

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P042**DEVELOPMENT OF POSTERIOR UVEITIS IN BEHÇET'S SYNDROME PATIENTS WITH VITREOUS CELLS WITHOUT ANY OTHER POSTERIOR INVOLVEMENT**

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Background: A considerable number of patients with Behçet's syndrome (BS) have vitreous cells on slit lamp examination at the time of diagnosis. However, the prognostic importance of vitreous cells (VC) and their association with the development of posterior uveitis (PU) requiring immunosuppressive treatment is unknown.

Methods: The charts of 144 consecutive BS patients fulfilling ISG criteria who were registered between 2010 and 2011 were reviewed. At baseline visit 59/144 patients had VC in one eye or both eyes. Among the remaining patients, 66 patients had bilateral pan or posterior uveitis, 3 had no eye involvement, and 9 had insufficient data in their medical records. Among the 59 patients with VC, 42 patients with a follow-up of ≥ 2 years were included in this study.

Results: At baseline, among the 42 included patients (23 men, mean \pm SD age: 30.3 \pm 8.7 years), 22 had VC in both eyes, 10 had VC in only one eye, and 10 had VC in one eye and PU in the other eye. There was anterior uveitis (AU) in addition to VC in the same eye in 7 patients at baseline.

New PU developed in 13 patients during a mean follow-up of 1.8 \pm 1.2 years.

4 patients that developed PU in the eye with VC had had PU in the contralateral eye at baseline. This means 4 of 10 patients with VC in one eye and PU in the contralateral eye developed bilateral PU despite treatment. Additionally, 4 patients that developed PU in the eye with VC had anterior uveitis in the same eye at baseline.

Conclusion: Careful follow-up is required for patients with VC since almost one third developed PU within 2 years. The presence of PU in the contralateral eye and AU in the same eye may be risk factors for the development of PU in patients with VC.

P043**IS THIS BEHÇET'S SYNDROME?**

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Background: Mucocutaneous lesions are the most common manifestation of Behçet's Syndrome (BS). Other manifestations of the disease include arthralgia, uveitis, neurological, gastrointestinal, and vascular disease. There is currently no diagnostic test for BS, therefore careful examination and investigation is required by an experienced team of clinicians. Patients should also fulfil the International Criteria for Behçet's Disease (ICBD).

Case presentation: We present 9 patients referred with a suspected diagnosis of Behçet's disease to the London Behçet's Centre of Excellence. Their age range was from 8 years old to 76 years old and they were predominantly female. The patients had a range of presentations of mucocutaneous lesions alongside other systemic symptoms.

All patients presented with oral ulcers as one of their symptoms. Six of the patients also had concurrent genital ulceration or soreness. Other symptoms included ocular erythema, periorbital swelling, nasal ulceration, epistaxis, mucosal and cutaneous bullae, rash, abdominal pain, nausea, arthralgia, recurrent fevers, and fatigue. All these symptoms were attributable to Behçet's disease.

Previous treatment including antivirals, antifungals, and antibiotics were ineffective.

All were thoroughly assessed, examined, and appropriately investigated. One patient had a biopsy with results consistent with a diagnosis of bullous pemphigoid. A further patient was diagnosed with bullous pemphigoid following immunofluorescence studies. Gene analysis performed revealed a patient to have LPIN2 gene mutation leading to a diagnosis of Majeed Syndrome.

Careful history and examination elicited diagnoses of erythema multiforme, chronic iron deficiency anaemia, illness triggered by Epstein Barr virus, morsicatio buccarum and self-harm, erosive lichen planus and recurrent oro-genital ulceration. With the correct diagnoses all patients were managed appropriately.

Conclusion: Many conditions can cause mucocutaneous lesions. Particularly oral ulceration or oral and genital lesions. These patients evidence the need for careful assessment by an experienced multidisciplinary team to achieve the correct diagnosis and effective management with good outcomes.

P044

UNUSUAL SITE OF VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE

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Introduction: Behçet's disease (BD) is a chronic inflammatory systemic disease, affecting mainly young men, and characterized by various manifestations like vascular involvement.

Patients and Methods: This is a monocentric retrospective descriptive, analytical and observational study, conducted in the department of internal medicine in Rabat (2012-2022). We collected 531 records of patients followed for Behçet's disease. Statistical results were analyzed by the software JAMOV version 1.6.

Results: 59/531 patients presented unusual location for vascular manifestation. The mean age was estimated at 39 years (23-69), Sex ratio H/F= 2,6.

Among the sites found: 2 patients presented an aneurysm of the carotid artery (0.37%), an aneurysm of the mesenteric artery occurred in three patients (5%), a single aneurysm of the hepatic artery was found, aneurysm of the pulmonary artery was found in 39 patients (66%), and an aneurysm of the aorta in 10 patients (16%). There were 5 thrombosis of the brachiocephalic trunk, 5 thrombosis of the jugular vein (8%), 3 thrombosis of the supra-hepatic veins, and 2 thrombosis of the dorsal vein of the penis. Symptomatology was dominated by pain. Diagnosis was based on echo Doppler and angio-CT.

All patients are treated by corticosteroids and colchicine, cyclophosphamide in 33% of cases, and Azathioprine in 30 patients, one patient was treated by infliximab. Anticoagulant treatment was instituted in 12 patients (20%). 6 of the aneurysms were treated surgically.

The evolution was favorable in 70% of the cases, 30% of the patients presented vascular relapse. One aneurysm rupture was noted causing the death of the patient.

Unusual vascular localization was statistically related to: age (35-65 years) ($p=0.03$) joint involvement ($p<0.001$), ophthalmological involvement ($p=0.001$), and genital aphthae ($p<0.001$), cardiac involvement ($p=0.02$) and death ($p=0.03$).

Conclusion: Our study suggests that patients over 35 years of age with genital aphthae, ophthalmic and cardiac involvement should be screened for unusual vascular involvement to improve their management.

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P045

DIGESTIVE INVOLVEMENT IN BEHÇET DISEASE

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Introduction: Behçet's disease (BD) is a systemic vasculitis with a wide range of clinical manifestations, including gastric involvement, which are rare but can have a significant impact on patients' quality of life and vital prognosis.

Patients and Methods: This is a monocentric retrospective descriptive and observational study, conducted in the Department of Internal Medicine at the University Hospital of Rabat over 10 years, between January 2012 and January 2022. We collected 531 records of patients followed for Behçet's disease.

Statistical results were analyzed by JAMOVI 1.6 software and statistical tests: chi 2.

Results: Among the 531 patients managed for Behçet's disease, 21 presented with digestive involvement. The average age was 38 years, the sex ratio was 9.5 (19 M / 2 F).

Digestive involvement was manifested by: abdominal pain 18 (85%), transit disorder in 10 patients (47%), rectorrhagia 4 (19%), rectitis 14.28%, intestinal aphthae 28%, peritonitis 4.76%, intestinal perforation 4.76%, hepatosplenomegaly occurred in 5 patients (23%), vascular involvement namely aneurysms of the mesenteric artery occurred in 3 patients or 14,2 %.

The diagnosis was based on fibro-coloscopy with biopsies, 50% of patients had a favorable evolution, 38% patients relapsed, and 4.67% died. All patients were put on colchicine and corticotherapy, cyclophosphamide was used in 3 patients (14%), and anti-TNF in 4.7% of patients.

Digestive tract involvement was statistically related to skin

involvement: genital aphthae ($p = 0.005$). Cardiac involvement and carotid artery aneurysms are also significantly related to digestive involvement ($p = 0.002$). The high number of relapses was also related to digestive involvement ($p < 0.001$).

Conclusion: Digestive involvement in Behçet's disease is rare, but it poses diagnostic problems because of the similarity of symptoms with other diseases, particularly chronic inflammatory bowel disease (Crohn's and UC), hence the interest in using histological examination and the diagnostic score.

P046**OPHTHALMOLOGIC INVOLVEMENT IN BEHÇET'S DISEASE**

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Introduction: Ophthalmic involvement is part of the diagnostic criteria of Behçet's disease, and constitutes one of its severe manifestations.

Patients and Methods: This is a monocentric retrospective descriptive and observational study, conducted in the department of internal medicine in Rabat (2012 - 2022). We collected 531 records of patients followed for Behçet's disease. Statistical results were analyzed by JAMOV software version 1.6.

Results: 225/ 531 patients treated for Behçet's disease presented with ophthalmologic involvement. The average age was 34 years; the sex ratio M/F: 3.35 Ophthalmic involvement was manifested by: a decrease in visual acuity in 70.3% patients, retinal vasculitis was found in 59 patients (27.8%), papilledema in 30 patients (16.6%), maculopathy presented 12, 6% , retinal ischemia 8.6%, hyalitis affected 14 patients (5.3%), chorioretinitis 2.3%, optic nerve damage constituted 3.3% . Cataract 21 patients (8.2%), glaucoma 7.2%, anterior uveitis affected 3.3%, posterior uveitis 17%, and intermediate uveitis 4.4%, panuveitis 36%.

19 patients (7, 9%) had blindness. Biologically, CRP was elevated in 58%.

78% of the patients had a favorable evolution, 17% had a relapse on the ophthalmic level; 4% died. All patients are treated by colchicine and corticosteroid, cyclophosphamide was used in 62 patients (23%), anti TNF in 21 patients (8.2%).

Ophthalmologic involvement was statistically related to cerebral trunk involvement ($p = 0.04$). Retinal vasculitis is significantly related to DVT ($p = 0.002$). High number of relapses was associated with the occurrence of ocular involvement ($p < 0.001$). low visual acuity, presence of retinal vasculitis, ischemia, and high number of relapses were risk factors for the occurrence of blindness ($p = 0.009$).

Conclusion: The results of our study have shown that ophthalmic posterior pole involvement is closely related to the involvement of the cerebral trunk, and constitutes a risk factor for relapse that is responsible for serious complications, notably blindness.

P047

PLACE OF BIOTHERAPIES IN THE THERAPEUTIC MANAGEMENT OF BEHÇET'S DISEASE: ABOUT A SERIES OF CASES

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Introduction: The manifestations of Behçet's disease can be life threatening and functionally challenging. The aim of our study was to describe the clinical and paraclinical characteristics and the evolution of patients with Behçet's disease treated with a biotherapy, and to compare them with the literature.

Methods: This is a retrospective cross-sectional study of 23 patients with Behçet's disease treated with biotherapies between January 2017 and August 2021. The cases were collected from the Medicine A department of Ibn Sina Hospital and the Medicine A and B departments of the Mohamed V Military Training Hospital. All of our patients met the international criteria of the ICBID 2013

Results: All patients were male with a mean age of 35.27 years.

Mucocutaneous involvement was present in all patients, ocular in 21 (91.3%) patients, vascular in 7 (30.4%) patients and neurological in 4 (17.39%) patients.

The indications of the biotherapies were: Ocular involvement n=20 (86, 95%), vascular involvement n=3 (13,04%), neurological involvement n=2 (8,69%). The biotherapies used in these patients were: Adalimumab n=15 (65.21%), Tocilizumab n=2 (8.69%) and Infliximab n=8 (34.78%). They were indicated as first-line therapy in 4 (17.39%) patients. The evolution was marked by remission in 18 (78.26%) patients, therapeutic failure in 1 (4.34%) patient, and death in 4 (17.39%) patients.

The main complication was tuberculosis observed in 4 (17,39%) patients.

Conclusion: Biotherapies have shown their efficacy in severe and/or treatment refractory forms of Behçet's Disease. Prospective studies are needed to define their indications and to evaluate their adverse effects.

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P048**NEUROBEHÇET**

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Introduction: Ophthalmic involvement is part of the diagnostic criteria of Behçet's disease, and constitutes one of its severe manifestations.

Patients and Methods: This is a monocentric retrospective descriptive and observational study, conducted in the department of internal medicine in Rabat (2012 - 2022). We collected 531 records of patients followed for Behçet's disease. Statistical results were analyzed by JAMOV software version 1.6.

Results: 225/ 531 patients treated for Behçet's disease presented with ophthalmologic involvement. The average age was 34 years; the sex ratio M/F: 3.35 Ophthalmic involvement was manifested by: a decrease in visual acuity in 70.3% patients, retinal vasculitis was found in 59 patients (27.8%), papilledema in 30 patients (16.6%), maculopathy presented 12, 6% , retinal ischemia 8.6%, hyalitis affected 14 patients (5.3%), chorioretinitis 2.3%, optic nerve damage constituted 3.3% . Cataract 21 patients (8.2%), glaucoma 7.2%, anterior uveitis affected 3.3%, posterior uveitis 17% and intermediate uveitis 4.4%, panuveitis 36%.

19 patients (7, 9%) had blindness. Biologically, CRP was elevated in 58%.

78% of the patients had a favorable evolution, 17% had a relapse on the ophthalmic level; 4% died. All patients are treated by colchicine and corticosteroid , cyclophosphamide was used in 62 patients (23%), anti TNF in 21 patients (8.2%).

Ophthalmologic involvement was statistically related to cerebral trunk involvement ($p = 0.04$). Retinal vasculitis is significantly related to DVT ($p = 0.002$). High number of relapses was associated with the occurrence of ocular involvement ($p < 0.001$). low visual acuity, presence of retinal vasculitis, ischemia, and high number of relapses were risk factors for the occurrence of blindness ($p = 0.009$).

Conclusion: The results of our study have shown that ophthalmic posterior pole involvement is closely related to the involvement of the cerebral trunk, and constitutes a risk factor for relapse that is responsible for serious complications, notably blindness.

P049

INTRACARDIAC THROMBOSIS AND VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE: TWO SIDES OF THE SAME COIN?

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Background: Intracardiac thrombosis (ICT) is a serious complication of Behçet's disease (BD). Our work aims to describe the profile of these patients and study the link between ICT and vascular involvement in BD.

Methods: We retrospectively conducted a descriptive and monocentric study including 446 Behçet's patients admitted to our department between 2011 and 2022.

Results: Patients were mostly men (91.6%), aged 29 ± 6 years old (20-41). ICT was either the presenting form of BD (50%), or occurred after 4 years [1; 8] following the disease onset (50%). Patients mainly reported dyspnea (58%), chest pain (58%), and hemoptysis (41%). Signs of right (33%) and global (8%) heart failure were observed. ICT was located in the right heart (100%), with an extension to the inferior vena cava (50%) and the left cavities (17%). It was visualized as a fixed mass (83%), frequently accompanied by a floating one (60%). Associated cardiac lesions were often described (67%): pericardial effusion (41%), tricuspid (33%) or mitral insufficiency (16%), pericarditis (16%), endomyocardial fibrosis (8%), myocarditis (8%), and ischemic coronaropathy (8%). Pulmonary hypertension (75%) and dilated right cavities (58%) were frequent. Concomitant pulmonary artery involvement was predominant (83%), often bilateral and multiple, consisting of 75% thrombus and 41% aneurysms. Peripheral vascular thrombosis was common (33%), especially lower extremity vein thrombosis (25%). All patients were treated with immunosuppressants with a good response to therapy. One patient relapsed under poor compliance to treatment. No death was recorded.

Conclusion: ICT is a rare manifestation of BD, usually occurring in the first years of onset in young men with vascular manifestations. We believe that this strong association is highly suggestive that ICT in BD is a direct consequence of the underlying vasculitis.

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P050**BEHÇET'S DISEASE: ABOUT 531 CASES**

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Introduction: Behçet's disease is a vasculitis of unclear etiopathogenesis affecting vessels of different calibers and manifesting by different clinical signs. **Patients and Methods:** This is a retrospective monocentric descriptive analytical and observational study, conducted within the internal medicine department in Rabat spread over 10 years, between January 2012 and January 2022. The statistical results were analyzed by the JAMOV software version 1.6.

Results: 531 files of patients are collected. The mean age at diagnosis was 30.6 (16–56 years). Patients aged between 19 and 65 presented 96.6%. Sex ratio M/F was: 3.53. The average time to diagnosis is estimated at 4 years (0–26 years). Hypertension is found in 9.4% and tobacco in 18%. The patients had presented: mouth ulcers (100%) and genital ulcers (79.7%). 225 patients (42.4%) had ocular involvement: uveitis (57%), retinal vasculitis (27.8%), optic nerve damage 3.3%. Articular involvement was present in 161 patients (30.3%), digestive in 21 (4%), and central neurological in 65 (12.2%). AngioBehçet affected 254 patients (48%), that 58% suffered from thrombosis (148 cases) mainly deep veins thrombosis (55%) and 35% (89 cases) presented an arterial aneurysm. Heart damage is found in 6% of patients, intracardiac thrombosis 2.6%, coronary damage 0.9%, pericarditis 1.5%. The evolution was favorable in 460 patients (86.62%), 57 (10.7%) presented a relapse. We deplore 14 deaths (8.5%). All patients are treated by colchicine, 468 (88.1%) by corticosteroid therapy, 90 (19%) by azathioprine, 115 (21.66%) by cyclophosphamide, 21 by anti-TNF alpha, 227 (42.75%) by anticoagulation. Statistical analysis suggests significant links between vascular involvement and: inflammatory polyarthralgia ($p < 0.001$), cardiac involvement ($p = 0.005$), coronary involvement $p = 0.02$, neurological ($p = 0.002$). Femoral and iliac deep vein thrombosis are linked to: posterior uveitis ($p = 0.008$), retinal ischemia ($p = 0.01$). Femoral and iliac deep vein thrombosis are linked to: posterior uveitis ($p = 0.008$), retinal ischemia ($p = 0.01$). Involvement of the digestive tract is linked to: genital ulcers ($p = 0.005$), heart involvement ($p = 0.002$) and carotid artery aneurysms ($p = 0.002$). Joint damage ($p < 0.001$), pseudo-folliculitis and genital ulcers ($p = 0.039$) are common in women. Neurological ($p = 0.003$) and vascular ($p = 0.002$) damage is more common in men. Relapses are related to neurobehçet ($p = 0.03$) and digestive involvement ($p < 0.001$). Death is related to angiobehçet ($p = 0.03$) and neurobehçet ($p = 0.005$).

Conclusion: Our study suggests that the search for the different systemic manifestations is necessary in patients followed for BD in order to prevent relapses and improve the functional and vital prognosis.

P051

THROMBOSIS IN BEHÇET'S DISEASE

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Introduction: Thrombosis is a frequent clinical expression in Behçet's disease, without authenticated thrombophilic abnormalities of hemostasis.

Materials and methods: This is a retrospective descriptive analytical and observational monocentric study, conducted within the internal medicine department in Rabat, (2012-2022). We collected 531 patients followed for Behçet's disease. The statistical results were analyzed by the JAMOMI 1.6.

Results: Vascular involvement was observed in 254 patients (48%). Thrombosis constituted 58% (148 cases). The average age is estimated: 35 years

(16 - 65 years). The sex ratio M/F: 2.14 Diabetes is reported in 7 patients (1.3%), active smoking in 52 (18.2%). No arterial thrombosis was observed. All thromboses involved the veins essentially in the deep veins (55%): popliteal vein (11%), cerebral thrombophlebitis (9%), femoral vein (8%), inferior vena cava (7%), intracardiac thrombosis (4%) and pulmonary embolism (3%) and in both sexes without significant correlation.

They are statistically linked to digestive ($p=0.005$) and pulmonary ($p < 0.001$) involvement, mucocutaneous involvement ($p = 0.03$), erythema nodosum ($p = 0.01$). All the patients developed oral and/or genital ulcers and polyarthralgia ($p=0.007$). Neurological involvement is often preceded by TVMI ($p = 0.02$) especially femoral vein thrombosis ($p = 0.018$), cerebral thrombophlebitis, HTIC, parenchymal involvement and sphincter disorders ($p < 0.001$).

There are associations between ophthalmological manifestations and thrombosis of the femoral and iliac veins: posterior uveitis ($p= 0.008$), retinal ischemia ($p= 0.01$), retinal hemorrhage ($p= 0.005$), chorioretinitis ($p < 0.001$). Diabetes could present the 1st risk factor linked to the development of venous thrombosis ($p < 0.001$).

Relapses present in 16% of patients are probably related to thrombosis ($p = 0.06$). All patients are treated by colchicine and corticosteroid and anticoagulants, 10.6% are treated by antiplatelet agents, cyclophosphamide in 52 patients (20.4%) and Azathioprine in 54 (21.2%), Methotrexate in 4.7% patients.

Conclusion: Our study confirms the literature data concerning the frequency of this clinical manifestation in Behçet's disease. It suggests close links with the various extravascular ophthalmic, neurological, digestive, articular and mucocutaneous manifestations. Diabetic control could limit the occurrence of venous thrombosis in Behçet's disease.

P052**BEHÇET'S DISEASE IN WOMEN**

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Introduction: Behçet's disease is a systemic vasculitis that can affect arterial or venous vessels of different sizes with a male predominance.

Patients and Methods: This is a retrospective monocentric descriptive analytical and observational study, conducted within the internal medicine department in Rabat spread over 10 years, between January 2012 and January 2022. The statistical results were analyzed by the JAMOMI software version 1.6.

Results: Of the 531 records collected, 117 were female. Their average age is estimated at 34.6 years, the sex ratio: 4.5. Patients presented ophthalmic involvement in 56 cases (47%): retinal ischemia 14.6%, papilledema 15.6%, posterior uveitis 2.6%, anterior uveitis 3.5%, blindness 4.7%, vascular involvement in 42 patients (36.5%) including 16.4% deep vein thrombosis, skin involvement in 82 cases (71%): mouth ulcers 100%, genital ulcers 82%, pseudo folliculitis 17%, erythema nodosum 1%. Joint involvement was present in 38 patients (33%), cardiac involvement in 3 patients (2.6%), neurological involvement in 11 patients (9.6%): HTIC 6.2%, cerebral thrombophlebitis (8.8%), meningitis (3.5%). Digestive involvement is present in 2 patients (1.8%). CRP was elevated in all patients.

The evolution was favorable in 86% of the patients.

10.4% had relapses all types of damage. We deplore 4% of deaths.

Statistical analysis between the two sexes suggested the predominance of joint involvement ($p=0.001$), pseudo-folliculitis and genital ulcers ($p=0.039$) in women. Neurological ($p=0.003$) and vascular ($p=0.002$) damage was more frequent in men.

Conclusion: Our results agree with those of the literature, thus confirming that women are less exposed to severe forms of Behçet's disease.

P053

ANGIOBEHÇET: ABOUT 254 CASES

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Introduction: Vascular involvement is a severe and a frequent clinical manifestation of Behçet disease.

Patients and Methods: This is a retrospective descriptive analytical and observational monocentric study, conducted within the internal medicine department in Rabat, (2012-2022). We collected 531 patients followed for Behçet's disease. The statistical results were analyzed by the JAMOWI 1.6.

Results: Vascular involvement was observed in 254 (48%) cases. Arterial aneurysms constituted 35% (89 cases) and venous thrombosis 58% (148 cases). The Sex ratio M/F was:5. the average age was:34.84 years. 26 patients had hypertension (10.23%), 6 (2.3%) diabetes, 27 (10.6%) active smoking, Pain in the lower limb is found in 90% of patients, redness and warmth in 60%. 5% of the patients presented ulcerations, a vascular murmur in 80%, 2% beating mass of the aorta, claudication of the limbs in 60%. We observed no arterial thrombosis, stenosis or occlusion. The arterial aneurysms are located at the pulmonary artery and its lobar branches (66%), the femoral artery (7%), the aorta (6%), the axillary artery - subclavian artery- and false aneurysms 3 cases each, i.e. 5%. 92.5% of patients had anemia and elevated CRP, conduction and repolarization disorders. 90% had received corticosteroids and 118 patients cyclophosphamide. 15 patients are operated for flattening and bypass and vena cava filter. 78% of the patients had a favorable evolution, 16.5% of the patients had relapses all disorders combined. 4.7% patients died.

Statistical analysis suggests links between vascular involvement and inflammatory polyarthralgia ($p < 0.001$), cardiac involvement ($p=0.005$), Coronary damage ($p=0.02$), neurological ($p=0.002$), Spinal cord involvement is closely linked to aortic aneurysms and cerebral thrombophlebitis with ($p<0.01$), genital ulcers ($p=0.019$), erythema nodosum ($p=0.036$), intermediate uveitis ($p=0.02$), surgical approach of aneurysms ($p < 0.001$) and to death ($p = 0.03$)

Conclusion: The results of our study suggests close links between vascular damage and other serious damage (cardiac, neurological and ocular). Patients with joint and skin involvement are at risk of developing angiBehçet's.

P054**THE LONG-TERM CLINICAL COURSE OF ORAL ULCERS OF BEHÇET'S DISEASE**

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Objectives: To describe the long-term clinical course of each manifestation of Behçet's disease (BD), and to clarify the factors involved in the remission of oral ulcers (OU) using clinical information from patients with BD.

Methods: We retrospectively studied 155 patients with BD who visited our hospital between 1989 and 2020. We defined remission criteria for each manifestation and examined the changes in the long-term clinical course. Furthermore, classification and regression trees and multivariable analyses were performed to investigate the prognostic factors of OU; hazard ratios were used to assign scores to prognostic factors deemed significant (OU prognosis score: OuP score). Risk stratification was examined by dividing the OuP scores into four stages.

OUs appeared earliest, with the slowest decline in prevalence observed post-BD diagnosis. OU presence was the most common factor inhibiting complete remission. Young age at OU onset, never smoker, presence of genital ulcers, positive pathergy test, no usage of tumour necrosis factor inhibitors or of immunosuppressants, and long-term non-treatment or symptomatic treatment for OUs were poor OU prognostic factors. Based on multivariable analysis, the area under the curve of the OuP score to predict OU prognosis was 0.678.

Conclusions: Remission criteria for each symptom clarified that OU had the greatest impact on complete BD remission. Faster OU remission was associated with earlier OU therapeutic intervention other than symptomatic treatment.

P055**WHETHER BEHÇET'S PATIENTS WITH LARGE VESSEL INVOLVEMENT HAVE CONCURRENT SMALL VESSEL INVOLVEMENT? A CASE CONTROL STUDY**

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Aim: Behçet's disease (BD) is a chronic multisystem disorder. The principal pathological finding in BD is vasculitis, and vessels of all sizes may be involved. Concurrence of small and large vessel involvement in BD patients is undetermined. The aim of this study is to evaluate small vessel involvement in BD patients with large vessel involvement.

Methods: 35 BD patients with large vessel involvement (cases) and 35 BD patients without large vessel involvement (controls) were included. For evaluation of small vessel involvement, capillaroscopy was done for all patients. Capillaroscopic findings were compared between two groups.

Results: All of our BD patients had small vessel involvement according to the capillaroscopic findings. The most abnormality was tortuosity (87.1%) followed by avascular areas (51.4%) and decreased density of capillaries (44.2%). Capillaroscopy findings were not statistically different between the case and the control groups. In the case group, the number of avascular areas was associated with superficial phlebitis ($p=0.044$) and deep vein thrombosis ($p=0.022$). There was a significant association between micro bleeding and the history of erythema nodosum ($p=0.015$), tortuosity and the history of skin aphthosis ($p=0.015$), architectural derangement and the history of uveitis ($p=0.029$), the number of avascular areas and active oral aphthosis ($p=0.021$) and architectural derangement and increased ESR ($p=0.011$).

Conclusion: We found no difference in nailfold capillary involvement between BD patients with and without large vessel involvement. Among BD patients with large vessel involvement, the number of avascular areas was significantly associated with superficial phlebitis and deep vein thrombosis.

Keywords: Behçet's disease, vascular involvement, nail fold capillaroscopy

P056**WHICH FACTORS PREDICTS RECURRENT VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE?**

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Aim: Behçet disease (BD) is a multisystemic autoimmune disease which classified among vasculitis. Vascular involvement associated with morbidity and mortality and follow a relapsing pattern. We aimed to evaluate the clinical and laboratory features which can predict relapse of vascular involvement in BD.

Methods: In this retrospective study, medical records of 23 BD patients who have had recurrent vascular involvement (cases) were reviewed. All patients fulfilled the diagnostic criteria of ICBD. Data regarding 6 months and 3 month before vascular relapse and at the time of vascular relapse were recorded. 23 BD patients with vascular involvement and at least 5 years follow up but without relapse of vascular involvement was considered as control group. Data were compared between two groups to identify the contributing factors.

Results: Among BD patients with recurrent vascular involvement, mean age was 29.00±9.17 years, and 78% of them was male and most of them was Turk. Oral aphthosis was the most common first presentations. According to physician global assessment the disease activity at the disease onset was moderate in 43.5% and severe in 22% of them. The mean time between diagnosis and vascular involvement was 4.86±3.55 years, and mean time between first vascular involvement and recurrent vascular involvement was 4.18±2.48 years. Type of vascular involvement was venous thrombosis in 19 patients, arterial thrombosis in 1 case, and arterial aneurysm in 4 patients. In recurrent vascular involvement, venous thrombosis in 21 patients, arterial thrombosis in 1 case, and arterial aneurysm in 1 patients was seen. About the number of vascular relapse, 4 patients had 1 relapse, 12 patients had 2 relapse, 5 patients had 3 relapse and 2 patients had 4 relapse. Disease activity at 6 months, 3 months and at the time of relapse time was moderate to severe in 78% , 74 and 58% respectively. Disease manifestations at the relapse time was OA in 96%, GA in 56%, mucocutaneous in 56.5%, eye in 22% and joint in 13%. High ESR at 6 months, 3 months and at the time of vascular relapse was see in 52%, 52% and 67% respectively ($p < .0001$). High CRP at 6 months, 3 months and at the time of vascular relapse was see in 43%, 36% and 50% respectively ($p = 0.109$). 6 months before vascular relapse, discontinuation of steroid and cytotoxic was seen in 5 and 7 patients respectively. At the time of vascular relapse, 34% was on low dose steroid, 4% on Cyclophosphamide, 19% on Azathioprine, 9% on low dose MTX, 36% on colchicine and 82% was on warfarin. Comparison of cases and controls showed no significant differences in age, sex, ethnicity, type of vascular involvement, first presentation, clinical manifestations during course of disease, disease activity at the disease onset, and time between disease onset and vascular involvement.

Conclusion: Disease activity and high ESR are risk factors of vascular relapse in BD patients with history of vascular involvement, so proper treatment is necessary for prevention of vascular relapse.

Keywords: Behçet's disease, vascular involvement

P057

COMMON FEMORAL VEIN WALL THICKNESS MEASUREMENT AS A DIAGNOSTIC TEST IN INCOMPLETE BEHÇET'S DISEASE

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Background: Diagnosing Behçet's Disease (BD) can be a clinical challenge in patients presenting with limited organ manifestations, especially with single major organ involvement. We reported the first controlled doppler ultrasound study showing increased common femoral vein (CFV) thickness in BD (1). We recently also showed that increased CFV thickness is a distinctive feature of BD with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm (2).

Objectives: In this study, we aimed to assess the diagnostic performance of CFV thickness measurement in patients with 'Incomplete' BD diagnosed by expert opinion.

Methods: We included 48 patients with incomplete BD (26 male, 22 female) diagnosed with expert opinion and followed in the Marmara University Behçet's Clinic. Demographic, clinical characteristics and treatment data were recorded during routine visits. CFV wall thickness was measured by an experienced radiologist on the same day.

Results: The mean age of the patients was 39.1 (SD:11.1). The mean duration of BD was 53.7 (SD: 51.4) months. 40 (83.3%) of BD patients had major organ involvement. 6 (12.5%) patients had pathergy positivity and 15 (31.3%) had familial BD. 20, 8, and 6 of the patients had vascular, ocular, and neurological involvement, respectively. Right CFV thickness was 0.72 (SD: 0.15) mm and left CFV thickness 0.72 (SD: 0.15) mm. Only 2 (4.2%) patients had CFV thickness values below the cut-off value of ≥ 0.5 mm.

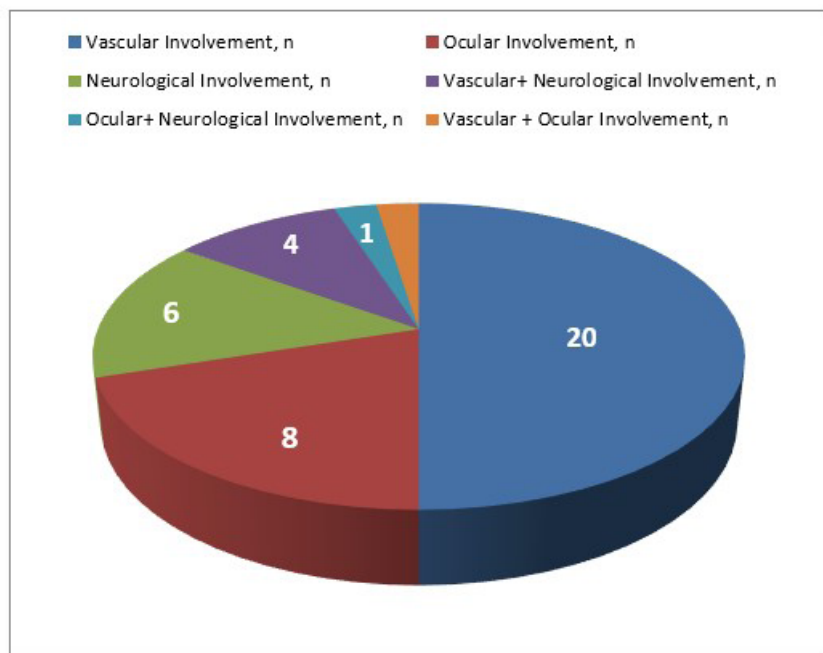
Conclusion: Diagnosing BD can be challenging in patients presenting with one major organ involvement, especially in countries with a low prevalence. These patients are generally diagnosed as 'incomplete' BD by 'expert opinion'. Early diagnosis is of utmost importance in some of these cases. Our results show that CFV thickness measurement with Doppler US, a non-invasive radiological modality, is a valuable diagnostic test in incomplete BD, especially with major organ involvement.

Disclosures: None

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Figure 1. Distribution of major organ involvements (n) in study group.**Table 1.** Subgroup analysis of incomplete BD patients.

	CFV (R), mean (SD), mm	CFV (L), mean (SD), mm
Incomplete BD, all group (n=48)	0.72 (0.15)	0.72 (0.15)
Incomplete BD with mucocutaneous involvement (n= 8)	0.68 (0.09)	0.70 (0.07)
Incomplete BD with major organ involvement (n= 40)	0.73 (0.16)	0.72 (0.16)
Incomplete BD only with vascular involvement (n=20)	0.73 (0.16)	0.73 (0.15)
Incomplete BD only with ocular involvement (n=8)	0.68 (0.12)	0.64 (0.14)
Incomplete BD only with neurological involvement (n=6)	0.83 (0.25)	0.81 (0.21)
Incomplete BD non-vascular major organ involvement	0.71 (0.19)	0.75 (0.19)

P058**MUCOCUTANEOUS INVOLVEMENT IS THE MORE FREQUENT REASON FOR IMMUNOSUPPRESSIVE NEED COMPARED TO MAJOR ORGAN INVOLVEMENT IN AN EARLY MALE BEHÇET'S DISEASE PROSPECTIVE COHORT**

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Objectives: Major organ involvement is one of the main causes of mortality and morbidity in Behçet's Disease (BD) (1). However, the prognosis and predictors of major organ involvement are insufficiently studied. We aimed to follow young, male BD patients with only mucocutaneous symptoms who have the highest risk for new major organ involvement prospectively.

Methods: Thirty-six male patients with BD were included in the study. Patients with BD were assessed prospectively at 3-6 months intervals and in any urgent visits. New major organ involvements and reasons for immunosuppressive (IS) need were assessed during prospective follow-up.

Results: At baseline, the mean disease duration was 3.3 years. All patients were under colchicine treatment. The mean follow-up duration was 90.7 months. Overall, 13 (36.1%) patients needed IS therapy during follow-up. The reason for IS need was major organ involvement in 5 (13.9%), refractory mucocutaneous involvement in 7 (19.4%), and articular involvement in 1 (2.8%) (Table 1, Figure 1). Major organ involvement was vascular in 3 patients, ocular in 1 patient, and ocular and vascular in 1 patient. In 8 of these 13 patients, step-up treatment was needed in ISs due to refractory disease or relapse.

Conclusion: Our study demonstrated a lower incidence of major vascular events in male BD patients during prospective follow-up compared to retrospective cohorts in the literature. Our results showed that refractory mucocutaneous involvement is a more frequent reason for IS need in BD than major organ involvement during prospective follow-up.

DISCLOSURES: None

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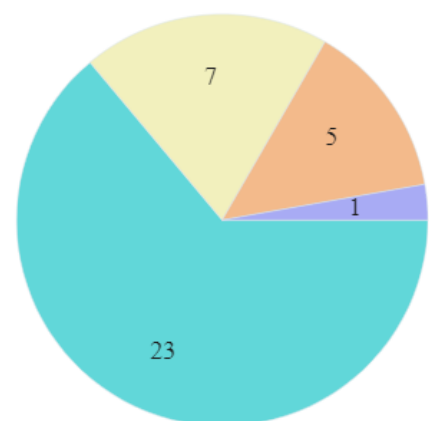
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Table 1: Clinical characteristics of patients with immunosuppressive treatment during follow-up

	Reason for IS use	Age at Diagnosis	Disease duration when IS started	IS agent
Patient 1	Pulmonary aneurysm	35	1 year	Azathioprine
Patient 2	Refractory OU	25	5 years	Cyclosporine
Patient 3	Deep venous thrombosis	38	10 years	Azathioprine
Patient 4	Uveitis	20	5 years	Azathioprine
Patient 5	Refractory OU	28	7 years	Azathioprine
Patient 6	Refractory OU	23	6 years	Cyclosporine
Patient 7	Refractory EN	35	1 years	Azathioprine
Patient 8	Deep venous thrombosis	23	1 years	Azathioprine
Patient 9	Arthritis	28	7 years	Methotrexate
Patient 10	Refractory OU	29	13 years	Azathioprine
Patient 11	Refractory EN + Articular Involvement	23	5 years	Azathioprine
Patient 12	Superficial Thrombophlebitis	29	2 years	Azathioprine
Patient 13	Refractory OU	28	3 years	Azathioprine

IS: Immunosuppressive, OU: Oral ulcer, EN: erythema nodosum

Figure 1: The reasons for immunosuppressive need in Behçet patients during follow-up (n)



No IS	23
Refractory Mucocutaneous Involvement	7
Major Organ Involvement	5
Refractory Articular Involvement	1

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A CROSS-SECTIONAL REVIEW OF THE PRESENTING OCULAR FEATURES OF BEHÇET'S DISEASE IN PATIENTS FROM A SINGLE CENTRE IN THE UK

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Background: Behçet's disease (BD) is a chronic multisystem inflammatory disorder with relapsing-remitting manifestations, including in the eyes.¹ Ocular involvement in Behçet's disease (BD) is common, being a component of the International Criteria of Behçet's Disease (ICBD).² Ocular manifestations vary with geographic location, however there is limited data from the UK population.³ It is important to understand how BD presents in the UK, to ensure rapid diagnosis and appropriate management.

Aims: To perform a cross-sectional analysis of all patients under the care of the Birmingham Behçet's Syndrome Centre of Excellence (BBSCE) since its inception, to determine the prevalence of ocular involvement in this population, and characterise the type and frequency of presenting ocular manifestations.

Methods: A retrospective review of electronic medical records for all 541 patients registered with the BBSCE was conducted. Data extracted included sample demographics, ocular manifestations (classified according to ICBD as 'uveitis': anterior, intermediate, posterior, pan or unspecified), or 'other' (episcleritis, scleritis, optic neuritis, neuroretinitis) and laterality of ocular features.

Results: 480 patients had ICBD-confirmed BD, with ocular involvement in 172 (312 eyes). Panuveitis was the most frequently presenting ocular manifestation overall (132 eyes; 42.3%). Anterior uveitis was the second most common feature (104 eyes; 33.3%). All ocular manifestations were more frequently bilateral than unilateral. Ocular manifestations other than uveitis presented the least frequently. Gender differences were observed in presenting manifestations, with panuveitis being the most common in males and anterior uveitis in females (53.4% and 39.4% respectively, $p < 0.05$). This was closely followed by panuveitis in females (36.2%).

Conclusions: This is the largest cross-sectional review of presenting ocular features of BD from a single clinic in the UK performed to date. It is hoped that this will be useful in helping clinicians in the UK recognise ocular BD, in order to initiate appropriate management early, ultimately improving patient outcomes.

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P060**LONG-TERM FEVER IN BEHÇET'S DISEASE: A CASE REPORT OF 12 PATIENTS**

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Introduction: Behçet's disease is situated at the crossroads of autoimmune and autoinflammatory diseases, with a complex etiopathogeny. Fever during the course of this disease is a rare situation that can reveal the disease and accompany systemic manifestations, particularly vascular ones.

Materials and Methods: This is a retrospective study of 522 cases of Behçet's disease over a 17-year period (2005-2021). Our patients met the international criteria for the diagnosis of Behçet's disease and all had a fever.

Results: Long-term fever in Behçet's disease was noted in 12 patients (2.29%), the average age was 32.72 years with extremes of 18 to 55 years. All our patients were male. Fever was inaugural in 10 patients (83.3%) and revealing in 16.6% of cases. It was associated with mucocutaneous involvement, dominated by bipolar aphthosis in 83.3% followed by erythema nodosum, vascular involvement in 7 patients (58.3%) (thrombosis and aneurysms), joint manifestations (arthritis and inflammatory arthralgia), neurological manifestations in 33.3% of cases, and digestive involvement in 2 patients (ulcerative colitis and erythematous pangastritis). Biologically, an inflammatory syndrome was present in 7 patients.

Discussion/ Conclusion: Contrary to monogenic auto inflammatory diseases, fever is rarely found in Behçet's disease, and may reveal the disease or complicate its course.

Although certain manifestations, particularly mucocutaneous ones, are frequent in Behçet's disease, associated or not to a fever, vascular involvement is closely related to the febrile nature of the disease.

The search for Behçet's disease must be part of the etiological assessment of unexplained long-term fever in young people, particularly in geographical areas where the disease is highly prevalent.

No conflict of interests.

P061**GASTROINTESTINAL INVOLVEMENT IN BEHÇET'S DISEASE**

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Introduction: Behçet's disease is a chronic inflammatory systemic disorder of undetermined etiology. Involvement of the digestive tract predominates in the ileocolonic region. Its frequency is variously assessed, ranging from 30% in Japanese series to less than 5% in European series.

Patients and Methods: Descriptive retrospective study over 41 years, involving 1532 records of patients with BD. Were selected patients meeting the diagnostic criteria of the ISGBD 1990 and having digestive involvement correlated to the disease, after exclusion of the differential diagnoses.

Results: Digestive involvement occurred in 141 patients (9.20%), 43 women and 98 men, the mean age at the time of diagnosis was 32.9 years. Minor manifestations occurred in 133 cases including transit disorders in 85 patients (60.28%), nausea and vomiting in 33 (23.40%), abdominal pain in 47 (33.33%), while colitis ulceration which constitutes a major manifestation was observed in 8 cases. A case of perforation complicating digging ulcerations and requiring urgent recourse to surgery was noted.

Discussion/Conclusion: A digestive presentation in the foreground should lead to a differential diagnosis (IBD). The functional symptomatology is aspecific without characteristic endoscopic or histological aspect. The presence of granuloma on the biopsies is the only sharp element against Gastrointestinal Involvement in Behçet Disease.

No conflict of interests

P062**LATE ONSET BEHÇET'S DISEASE: ABOUT 134 CASES**

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Introduction: Behçet's disease (BD) is a systemic vasculitis, characterized by a broad clinical spectrum. It is a condition of young adults, which rarely occurs after 40 years.

The aim of our study was to analyze the clinical manifestations of late-onset BD and to identify the specificities in relation to the clinical manifestations of young adults.

Patients and Methods: Descriptive retrospective study of 1532 patients with BD, selected according to 1990 ISGBD during 41 years (1981-2021), after exclusion of differential diagnoses, and having started their symptoms after the age of 40.

Results: 134 late-onset BD cases were collected /1532 cases (8.75%), with a male/female sex ratio of 1.5 vs 2.38 in young adults.

The mean age at onset of symptoms was 44.7 years and the mean age at diagnosis was 48.63 years (extremes between 40 and 70 years). 30% of the patients were between 50-70 years old.

Oral aphthosis was the predominant initial manifestation.

Ocular manifestations were present in 51.5% of cases vs 60.7% in young adults.

Joint manifestations were found in 50% of cases vs 43.08% in young adults.

Vascular involvement was noted in 19.4% of cases Vs 23.1% in young adults.

Neurological involvement was found in 19.4% of cases (parenchymal 69.2%, mixed 15.4% and extra parenchymal 15.4%) vs 18.21% in young adults.

We had 14.92% digestive involvement (major in 33.3%) vs 9.2% in young adults.

Pathological associations were noted: 3 cases of tuberculosis and 1 case of lung cancer.

Conclusion: Late onset Behçet's disease is rare, women are much more affected compared to young adults. Ocular involvement is much less common than in young adults.

Digestive involvement is more common with a tendency to have more major involvement compared to young adults.

Some associated pathologies were noted unlike in young adults.

Behçet's disease affects the young adult but has to be evoked even at an advanced age, in order to treat adequately and prevent complications.

No conflict of interests

P063**PARTICULARITIES OF MUCOSAL-CUTANEOUS MANIFESTATIONS DURING BEHÇET'S DISEASE IN A NORTH AFRICAN POPULATION**

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Introduction: Behçet's disease (MB) is a ubiquitous vasculitis of vessels of all calibers, more common in patients from the Mediterranean, the Middle East and Asia. The diagnosis is essentially clinical, due to the absence of specific biological criteria. This study describes the main mucosal skin manifestations in a North African population.

Results: Our study included 1532 patients with Behçet's disease, including 1080 men and 452 women (sex ratio H/F: 2.38). The clinical manifestations were dominated by mucosal skin disease with oral aphtosis in 99.54% and genital aphtosis in 83.74% of cases. Giant aphthae were present in 61 patients. Pseudofolliculitis was observed in 60.11% of cases, erythema nodosum in 15.40%, and pathergia test was positive in 41.05% of cases. Other skin manifestations were observed in our patients, with skin aphthas in 73 patients, a corneal aphthae in 4 cases, a laryngeal aphthae in 6 cases, an aphthae in the throat in 2 cases, and in the glottis in 1 case. Superficial thrombophlebitis was observed in 63 patients and postphlebotic syndrome in 32 patients. Most of our patients 87% responded well to colchicine and short-term oral corticosteroids. Immunosuppressive therapy was required in 5% of cases.

Discussion-Conclusion: The mucosal skin manifestations are fundamental to objectify. Their presence is a crucial aid for a diagnosis of certainty of Behçet's disease. Some skin manifestations may pose a differential diagnosis problem with other lesions, such as superficial thrombophlebitis, which is often confused with a knotty erythema. Although the positive pathermic test is a key criterion in the diagnosis of Behçet's disease, its sensitivity varies greatly according to geographical origin. Our study confirms the frequency and diversity of dermatological manifestations during BMD, and shows the high frequency of pathermic test positivity in our population.

NB: No conflict of interest.

P064**HUGUES-STOVIN SYNDROME IN BEHÇET'S DISEASE -15 CASES**

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Introduction: Hughes-Stovin syndrome (HSS) is a rare entity, defined by the association of pulmonary arterial aneurysms (PAA) with deep vein thrombosis. The condition mainly affects young males and is accompanied by a high morbidity and mortality rate, due to the risk of overwhelming hemoptysis by rupture of arterial aneurysms. It is a rare but serious vascular variant of Behçet's disease. We describe the clinical, therapeutic and evolutionary particularities of this syndrome during Behçet's disease.

Patients and Methods: Descriptive study of 15 patients with Hugues-Stovin syndrome in a series of 1532 cases of Behçet's disease hospitalized in the internal medicine department of CHU Ibn Rochd over a period of 40 years (1981-2021). All patients met the criteria of the international research group on Behçet's disease.

Results: They are 10 men and 5 women with an average age of 33.6 years. Vascular involvement was deep vein thrombosis in 7 cases, aneurysms in 7 cases and both in 1 case. The thrombosis involved the inferior vena cava in 5 cases, the superior vena cava in 1 case, the ilio-femoro-popliteal axis in 2 cases, the supra-hepatic veins in 2 cases, the cerebral sinuses in 4 cases and it was intracardiac in 1 case. Pulmonary arterial aneurysms were multiple in 9 cases and bilateral in 8 cases. The treatment was based on the combination of corticosteroids and immunosuppressants in all cases, anticoagulation (isocoagulant dose) was prescribed in 2 cases and antiplatelet agents in 6 cases. The evolution was fatal in 3 cases. 8 cases of relapse were observed.. Anti-TNF was recommended in 1 case and surgery in 7 cases.

Discussion-Conclusion: Hughes-Stovin syndrome represents a rare but severe vascular form of Behçet's disease. The early diagnosis and management is a necessity, due to the high mortality. The main treatment for both HSS and BD patients includes corticosteroid, immunosuppressants, surgical resection, or embolization. However, the prognosis remains severe.

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JOINT DAMAGE DURING BEHÇET'S DISEASE: ABOUT 660 CASES

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Introduction: Behçet's disease is systemic vasculitis, described in 1937. Predominates in young male subjects. It associates recurrent bipolar aphthosis with ocular damage and may be accompanied by other manifestations including joint damage, which may initiate, reveal or appear during the course of the disease.

Our work details the main characteristics of joint damage during Behçet's disease.

Materials and Methods: We conducted a retrospective study of 1532 cases of Behçet's disease, 660 of which had joint damage, over a period of 41 years (1981-2021) in an internal medicine department. All our patients meet the international diagnostic criteria for Behçet's disease.

Results: The prevalence of joint manifestations in our study was 43.08%. The mean age of diagnosis was 33.5 years (9-70 years) with a diagnosis timeframe of 4 years. Sex ratio H/F was 2.38. Inflammatory arthralgia was the most common manifestations (67.27%) followed by polyarthritis (16,21 %), oligoarthritis (14,84 %) and monoarthritis(14.09 %). The preferred site of joint injury according to our results was the lower limb and more specifically the knees and ankles (61%). Evolutionary mode was intermittent in 71% of cases, acute in 17% and chronic in 12%. We noted the following special forms: 9 cases of deformative arthritis, 6 of which had progressed towards joint destruction, 5 cases of pseudo-gout, 3 cases of popliteal cyst, 15 cases of spondyloarthropathy, 5 cases of isolated sacroileitis and 1 case of arthritis simulating phlebitis. Treatment was based on colchicine, NSAIDs, low-dose corticosteroids and azathioprine in some forms resistant to the usual treatment.

The evolution were favorable in the majority of cases.

Discussion/ Conclusion: Joint damage during Behçet's disease is common, ranging from 48 to 70% of cases according to the series described in the literature. It is not uncommon that it can initiate the disease and precede aphthosis by several years.

Peripheral joint damage is most common, ranging from simple inflammatory arthralgia to true arthritis, including oligoarthritis, with predominance in the knees and ankles followed by the wrists, elbows and shoulders; however, hands and feet are much less common. All of this data partly reflects our results.

The development under symptomatic treatment is generally favorable, deformations and joint destruction remain very rare.

P066**SLEEPLAB_BEHÇET: A PROSPECTIVE LONGITUDINAL STUDY AIMED AT CHARACTERIZING CHRONOTYPES AND SLEEP PARAMETERS IN PATIENTS WITH BEHÇET'S DISEASE AND EXPLORING POSSIBLE CORRELATIONS WITH DISEASE SUBSETS**

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Background: Behçet's disease (BD) is a chronic systemic vasculitis mainly characterised by mucocutaneous, articular and neurological involvement. Sleep impairment is a common complaint in BD but a comprehensive overview regarding this issue and the assessment of relationship between chronotype and subsets of disease have never been performed. **Objectives:** to report the main findings of two-steps study consisting in: (i) a systematic literature review (SLR) aimed at exploring the existing evidence on the relationship between BD and sleep disturbances and (ii) a prospective longitudinal study examining chronotype, features and prevalence of sleep disturbances in a cohort of BD patients with regards to disease activity.

Methods: (i) a SLR conducted using "Behçet's disease" and "sleep" as search terms in PubMed database followed by screening for title, abstract and full text. Data extraction and reporting were performed according to the PRISMA guidelines. (ii) A cross-sectional evaluation comparing sleep quantitative parameters in 60 BD patients and 60 healthy controls (HCs), adopting an actigraph employing Artificial Neural Net technology, including evaluation of bipolar disorders and disease activity; a prospective evaluation on 100 consecutive BD patients regarding sleep parameters at 3 and 6-months follow-up with correlation to disease activity and therapy.

Results: (i) 15 out of 51 papers were retained with all of them being cross-sectional studies. BD patients showed lower quality of sleep as compared with HCs and potential development of specific sleep disturbances like restless leg syndrome and obstructive sleep apnea syndrome. (ii) Results will be compared with the evidence coming from the SLR.

Conclusions: existing evidence demonstrates sleep quality impairment in BD patients with higher rates of specific sleep disorders. Future results from our prospective study in real life are expected to be consistent with such observations and close the gaps regarding quantitative parameters of sleep and their correlation with disease activity, which are still lacking in literature.

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FERTILITY, PREGNANCY AND BEHÇET'S: WHAT RELATIONSHIP?

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Aim: To analyse the relationship between Behçet syndrome (BS) and pregnancy, investigating: 1) the prevalence and clinical characteristics of disease flares during pregnancy and 2) the pregnancy outcomes in a large cohort of Italian patients with BS.

Patients and methods: This retrospective study was conducted recruiting a cohort of BS patients according to the criteria of the International Study Group for Behçet (ISG), following at Rheumatology Institute of Lucania from January 2000 to March 2019. We reviewed medical records and collected demographic and clinical data besides pregnancy-related data, in particular: maternal age, infertility, disease flares during and after pregnancy, post-partum maternal and neonatal complications (up to 6 months after pregnancy).

Results: The results of this study are summarized in Table 1. We retrieved the medical records of 117 female BS patients and we studied 153 pregnancies in 96/117 subjects. 5 patients were diagnosed with infertility. 3 patients showed active disease (oral ulcers) at the time of conception. Disease flares were observed during gestation for 25/153 (16.3%) pregnancies, mainly mucocutaneous (oral and genital ulcers, erythema nodosum) and joint (arthralgia and arthritis) manifestations. 27/153 (17.6%) cases of disease flares were observed after pregnancy, with mucocutaneous (oral and genital ulcers, erythema nodosum) and joint (arthralgia and arthritis) involvement, as well as anterior uveitis. Miscarriages, preterm delivery, pre-eclampsia and eclampsia were observed in 27/153 (17.6%), 19/153 (12.4%), 6/153 (3.9%) and 2/153 (1.3%) pregnancies, respectively. No cases of neonatal complications or death were observed.

Conclusions: The results of the present study underlined that: a) BS disease clinical symptoms do not appear to aggravate during pregnancy and b) the pregnancy does not appear to be associated with an increase of gestational complications and adverse maternal-fetal outcomes in case of BS. However, due to the potential adverse events, especially of the vascular involvement, a strong pregnancy follow-up is recommended.

No conflict of interest

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Table 1. Demographic and clinical features of Behçet syndrome patients.

	BS patients (117) n (%)
Age at disease onset (years; average \pm SD)	23.7 \pm 13.1
Age at disease diagnosis (years; average \pm SD)	33.6 \pm 12.5
Disease Duration (years; average \pm SD)	23.1 \pm 11.6
Diagnostic Delay (years; average \pm SD)	10.8 \pm 9.9
Clinical manifestations	
Mucocutaneous involvement	
Oral aphthosis	117 (100.0)
Genital Ulcers	76 (65.0)
Erythema Nodosum	69 (59.0)
Folliculitis	18 (15.4)
Papulopustular lesions	54 (46.2)
Pathergy test	8 (6.8)
Ocular involvement	
Posterior uveitis	22 (18.8)
Anterior uveitis	22 (18.8)
Panuveitis	7 (6.0)
Articular involvement	
Arthralgia	61 (52.1)
Arthritis	30 (25.6)
Vascular involvement	
Deep venous thrombosis	1 (0.9)
Superficial venous thrombosis	15 (12.8)
Neurological involvement	29 (24.8)
Systemic involvement	
Fatigue	35 (29.9)
Fever	43 (36.8)
Gastrointestinal involvement	4 (3.4)
HLA-B51 positivity	69 (59.0)
Pregnancy (n=153)	
Age at conception (years; average \pm SD)	33.8 \pm 3.1
Disease flares during pregnancy, n (%)	25 (16.3)
Disease flares after pregnancy, n (%)	27 (17.6)
Miscarriages, n (%)	27 (17.6)
Premature labours, n (%)	19 (12.4)
Pre-eclampsia, n (%)	6 (3.9)
Eclampsia, n (%)	2 (1.3)

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WHEN IT LOOKS LIKE BEHÇET'S SYNDROME BUT IS SOMETHING ELSE: DIFFERENTIAL DIAGNOSIS OF BEHÇET'S SYNDROME: A TWO-CENTER RETROSPECTIVE ANALYSIS

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Objective: In low prevalence regions for Behçet's syndrome (BS), physicians are unfamiliar with the disease and its differentials, leading to a diagnostic latency and misdiagnosis. Furthermore, many clinicians rely on classification criteria (eg. ICBD criteria) when making the diagnosis. This study aimed to evaluate the differential diagnostic spectrum in patients with suspected BS in low prevalence regions. In addition, we determined the number of patients fulfilling ICBD criteria despite not having BS.

Methods: The retrospective study was performed in two referral centers in Hamburg and Amsterdam. Patients with confirmed BS (clinical diagnosis with fulfilment of ISG criteria or a score of > 5 points in the ICBD criteria) were excluded from the analysis. The patients were divided into ten differential diagnosis categories. If no definitive alternative diagnosis could be established, patients were termed 'probable BS' in case of (1) relapsing orogenital aphthosis without a clear differential explanation and either HLA-B51 positivity, origin from an endemic area or presence of an additional typical BS symptom that is not part of the classification criteria or (2) with 3-4 points scored in the ICBD criteria.

Results: In total 202 patients were included and categorized as follows: 58 (28.7%) 'probable BS', 57 (28.2%) skin disease, 26 (12.9%) chronic pain syndrome, 14 (6.9%) eye disease, 11 (5.4%) spondyloarthropathy, 9 (4.5%) gastrointestinal disease, 4 (2%) arthritis, 3 (1.5%) auto-inflammation, 3 (1.5%) connective tissue disease, 17 (8.4%) miscellaneous disease. HLA-B51 was positive in 41.6% (55/132); 37.1% (75/202) of the patients fulfilled the ICBD criteria.

Conclusion: In a low disease prevalence setting the straightforward application of the ICBD criteria may lead to overdiagnosis of BS. The spectrum of differential diagnoses is enormously broad. Clinicians should be aware, that HLA-B51 positivity is still not considered as a diagnostic feature in BS.

Table 1: Overview of differential categories and corresponding diagnoses with indication of ICBD-Criteria positivity

Abbreviations: BS, Behçet Syndrome; CNS, Central Nervous System; MAGIC, mouth and genital ulcers with inflamed cartilage syndrome; PAPA, Pyogenic Arthritis, Pyoderma gangrenosum, Acne; PFAPA, Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis; SpA, spondyloarthropathy.

Notes (number of patients):

† Including concomitant genital furunculosis (1)

‡ Including recurrent orogenital aphthosis in Steven Johnson Syndrome due to mycoplasma infection (1)

Including: gingivitis of unknown aetiology (1), atypical 'cut like' abnormality in the cheek mucosa (1), recurrent furunculosis / panniculitis on arms, with severe scarring (1), oral ulceration of unknown aetiology (1)

§ w/o other symptoms (1), pathergy test and DVT (1), polyarthritits (1), proctitis (1), acneiform skin lesions (1), thrombophlebitis (1)

± Including undifferentiated connective tissue disease (2) and limited cutaneous systemic sclerosis (1)

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Differential Categories	Total (%)	ICBD + (%)
Probable BS	58 (28.7)	40 (69.0)
Skin Disease	57 (28.2)	16 (28.1)
Habitual oral aphthosis †	17	0
Recurrent orogenital aphthosis ‡	11	11
Erythema exsudative multiforme	5	1
Herpes virus infection	4	0
Blistering disease (bullous pemphigoid, pemphigus)	4	2
Lichen sclerosus / lichen planus	4	1
Erythema nodosum	3	0
Ulcerative vulvitis	1	0
Acne inversa	1	0
Ulcer of the tongue	1	0
Psoriasis (of the nails)	1	0
Lymphomatoid papulosis	1	1
Unclassifiable skin disease #	4	0
Chronic pain (in combination with)	26 (12.9)	8 (30.8)
Habitual oral aphthosis	11	1
Oral aphthosis with or w/o other symptoms §	6	1
Herpes virus infection	2	1
Recurrent orogenital aphthosis	5	5
Recurrent folliculitis	1	0
Fibroma w. paraceratosis	1	0
Eye disease	14 (6.9)	1 (7.1)
Idiopathic anterior uveitis	3	3
Idiopathic posterior uveitis (including retinal vasculitis and retinitis)	3	3
Ocular sarcoidosis	2	2
Episcleritis	2	2
Optic disc vasculitis	1	1
Idiopathic intermediate uveitis	1	1
Skleritis	1	1
Vitreous bleeding	1	1
Spondyloarthropathy	11 (5.4)	3 (27.3)
Psoriatic arthritis	5	0
Axial SpA	3	1
SpA w. enteropathy	2	2
Reactive arthritis	1	0
Gastrointestinal Disease	9 (4.5)	2 (22.2)
Ulcerative colitis	4	0
Crohn's disease	3	1
Unclassified	2	1
Arthritis	4 (2.0)	1
Undifferentiated arthritis	3	0
Rheumatoid arthritis (with orogenital aphthosis)	1	1
Autoinflammatory Disease	3 (1.5)	1 (33.3)
Familial mediterranean fever	1	0
Unclassified (PFAPA syndrome possible)	1	0
PAPA syndrome	1	1
Connective Tissue Disease ±	3 (1.5)	1 (33.3)
Miscellaneous	17 (8.4)	2 (11.8)
<i>Neurological</i>		
Myopathy/Myositis	2	0
Multiple sclerosis	2	0
Moyamoya disease (with recurrent orogenital aphthosis)	1	1
CNS vasculitis	1	0
CNS disease of unknown aetiology	1	0
<i>Sarcoidosis</i>	2	0
<i>Infection</i>		
Urinary tract infection	1	0
Rectal ulceration in Hepatitis B	1	0
<i>Other</i>		
Tolosa-Hunt-Syndrome (possible)	1	0
C1 esterase inhibitor deficiency (possible)	1	0
Osteoarthritis	2	0
Osteoarthritis with open angle glaucoma, GN with nephrotic syndrome and non-healing wounds	1	0
MAGIC	1	1
All	202	75 (37.1)

P069

PREGNANCY OUTCOMES IN BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is multisystemic disease of unknown cause. The relationship between BD and pregnancy is reported in limited number of studies.

Objectives: To evaluate outcomes of pregnancies in BD patients (pts).

Methods: We retrospectively collected data of 45 women with BD diagnosis (according to ISGBD 1990 and ICBD 2014) and their 118 pregnancies. Pts' mean age was 31,3 [27;35] years., disease duration 6,0 [3;8] years. 11,1% pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), 31,1% pts had a moderate disease, 57,8% pts had a mild disease with mainly dermal-mucous manifestations.

Results: 118 pregnancies in 35 pts resulted in 75 live birth (6 cesarean section in 3 pts). Thirty-nine incomplete pregnancies were observed in 26 patients. Ten patients had 20 medical abortions on request before 12 weeks of gestation, one patient had an abortion due to medical reasons (rubella on the 7 th week of gestation), two patients had premature birth at 28 and 32 weeks with subsequent perinatal death of the baby. Fifteen out of 35 pts had 20 adverse pregnancy outcomes: 8 spontaneous abortion, 12 missed miscarriage. Nine patients had 12 Missed miscarriage at 6-11 weeks of gestation, one patient had 3 missed miscarriage, two had 2, and the others had 1 missed miscarriage. Six patients had 8 spontaneous abortions (early miscarriage). In the control group of 15 women, 7 had 15 pregnancies, 13 live birth of healthy children on time. Table 1 presents a comparison of pregnancy outcomes in patients with BD and healthy control.

Table 1. Pregnancy outcomes.

Pregnancy, n	BD, n=118 (%)	Control, n=15 (%)	p
Birth	77 (65)	13 (87)	0,01
Abortion	21 (18)	0	0,00
Unfavorable pregnancy outcome	20 (17)	2 (13)	ns
Missed miscarriage	12 (10)	0	ns
Spontaneous abortion	8 (7)	2 (13)	ns

Patients with BD were more likely to terminate pregnancy of their own volition compared to control group. All women with unfavorable pregnancy outcomes are re-pregnant, have healthy children born on time, all had a second or subsequent pregnancy with an unfavorable outcome. Immunosuppressive therapy of BD was not received by any of the pregnant women, which makes it possible to exclude the connection of the outcome of pregnancy with BD therapy.

The manifestation of BD with skin-mucous lesion of the patient in the first and third trimester of pregnancy was noted by 3 patients. In one patient, the appearance of a recurrent ulcer on the vulva was an indication for cesarean section. Only three women had one favorably completed pregnancy, all the others had from 2 to 7 pregnancies. Out of 45 patients, 10 patients did not have pregnancies, 9 of them are not married, 1 patient is planning a pregnancy. Table 2 shows the frequency of pregnancy pathology with varying degrees of severity of BD.

P069

Table 2. BD Severity and pathology of pregnancy.

BD Severity	N = 45 (%)	Intrauterine deaths/Miscarriage
Mild	25 (57,8)	5/6
Moderate	6 (31,1)	1/1
Severe	14 (11,1)	2/5

Adverse pregnancy outcomes were observed with varying severity of BD.

Out of 77 babies children born by BD patients only two had relapsing aphthous stomatitis and one – congenital glaucoma (“NeuroBehçet” inherited from the mother).

Conclusion: Patients with BD were more to terminate pregnancy compared to control group. Unfavorable outcomes of pregnancy were documented in pts regardless (with all grades of) BD severity.

Reference:

1. Zouboulis C., Vaiopoulos G., Macromichelakis N. et al. Onset signs, clinical course, prognosis, treatment and outcome of adult patients with Adamantiades – Behçet’s disease in Greece. Clin.Exp.Rheum.2003, 21, (suppl.30) S19-S26.

P070**INTESTINAL INVOLVEMENT OF BEHÇET'S DISEASE**

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Objectives: To analyze the severity and clinical features of intestinal manifestations of BD (IBD).

Methods: The study included 250 patients (male 177, female 73) with BD. The male-to-female ratio was 2,4:1, the mean age was $31,5 \pm 9,3$ yrs, the age of disease onset $21,8 \pm 9,62$ yrs, the median of disease duration was $10,25 \pm 8,32$ yrs. All those patients with gastrointestinal symptoms were subject to a gastroscopy and/or colonoscopy through which Crohn's disease and ulcerative colitis were excluded by the proctologists.

Results: Gastrointestinal symptoms were observed in 63 patients of 250 (25.2% pts), male pts 40, female pts 23. Symptoms of IBD include the abdominal pain in 62% pts, distension had 55%, diarrhea had 14%, nausea had 13%, blood in the bowel movement had 4,7%. The examination revealed: esophageal ulcers (1.6%, four cases), gastric ulcers (3.2%, eight cases), and duodenal ulcers (1.2%, three cases) were found using endoscopy. Also, 6.8% (17 patients) had gastro duodenal ulcers and 14.3% (nine patients) combined gastrointestinal involvement including esophageal and had gastro duodenal ulcers. Colonic ulcers were detected in 9.2% (23 cases) by colonoscopy, two patients had multisegmental diffuse ulceration, three patients had in the sigmoid colon and of everyone else in the ileum. Colitis without ulcers found in 5,6% (14 cases). Two patients had a clinic of appendicitis, the operation found that the appendix is not inflamed. Two patients were 0.8% (were on treatment) urgently operated due to perforation of ulcers of the ileum, the woman held suturing of perforated ulcer, and a man hemicolectomy. The last patient has a relaparotomy after 1 month and removal of the entire colon.

Conclusion: The IBD in Russia is affected in 1/4 of patients, but difficult refractory cases are not often.

P071

INTIMA-MEDIA THICKNESS OF CAROTID ARTERY IN PATIENTS WITH BEHÇET'S DISEASE

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Objectives: To evaluate the IMT of carotid artery in pts with BD.

Material: Forty two male patients with BD according ISBD (mean age - $31,5 \pm 7,9$, disease duration - $9,0 \pm 7,7$ yrs), 20 healthy controls matched for age and gender. IMT were assessed by using high-resolution B-mode ultrasonography. High-sensitivity C-reactive protein (Hs CRP) concentration in the serum samples were measured by immunonephelometric assay (BN-100 Analyzer; Dade Behring).

Results: Patients with BD and healthy controls on the basis results of IMT were divided into groups.

Groups	BD (I), n-42	SLE (II), n-42	P (I vs II)	Healthy (III), n-20	P (I vs III)
Mean IMT carotid artery	$0,60 \pm 0,11$	$0,74 \pm 0,14$	0,003	$0,70 \pm 0,12$	0,38
IMT = 0,3 – 0,59 mm	26,19%	11,9%	0,08	5%	0,04
IMT = 0,6-0,89 mm	66,66%	76,19%	0,2	95%	0,01
IMT = 0,9 – 1,1 mm	7,14%	11,9%	0,3	0	0,1
Atherosclerotic plaques	2,2%	16,6%	0,002	0	0,6
hs CRP	$5,1 \pm 23,3$	$2,44 \pm 18,84$	0,13	$0,57 \pm 0,80$	0,025

The mean carotid IMT in BD was significantly lower than in SLE. Relationship between IMT thinning and thrombosis was noted in 4 BD pts, one of them had multiple arterial aneurysms.

Carotid atherosclerotic plaques were found in 7 pts with SLE and only in one pt with BD, who had traditional cardiovascular risk factors (high body masse index, hypertension) and received a long time therapy with glucocorticoids.

Conclusion: We found no evidence of subclinical atherosclerosis in the patients with BD. The thinning IMT may be one of the risk factors for aneurysm formation in pts with BD. Hs CRP was higher in pts with BD then II and III groups.

P072

MYOCARDIAL INVOLVEMENT IN PATIENTS WITH BEHÇET'S DISEASE

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Objectives: To evaluate myocardial involvement noninvasively in patients with Behçet's disease by measuring QT dispersion and HRV.

Methods: The study included 74 BD pts and 47 healthy matched for age and gender. The following HRV parameters from 24h ECG ambulatory recording were assessed: MeanNN and time-domain variables, adjusted by MeanNN (SDNNn%, SDNNi n%, rMSSDn%). Additionally, all traditional cardiovascular risk factors.

Results: In BD patients HRV values (rMSSDn%) were significantly lower compared to healthy controls. HRV parameters in BD patients and control group

Parameters	Males		Females	
	BD (n=53)	Control (n=32)	BD (n=21)	Control (n=15)
Age, years	30 (24; 36)	30 (26; 35)	32 (26; 37)	28 (24; 31)
MeanNN, ms	810 (732; 849)	782 (732; 835)	776 (708; 830)	764 (694; 832)
SDNN n (%)	16,9 (13,6; 19,4)	17,2 (16,3; 21,1)	13,1 (11,3; 5,3)	12,2 (10,7; 14,6)
SDNNi n (%)	6,8 (5,1; 8,1)	6,8 (5,0; 8,3)	7,1 (6,1; 7,7)	5,2 (4,9; 5,7)
RMSSD n (%)	2,1 (1,5; 2,3)**	4,1 (2,7; 5,2)**	1,7 (1,4; 3,7)*	2,8 (2,2; 3,9)*

Data are presented in median values and interquartile range, *p<0,05, **p<0,005 vs controls.

There was a significant negative correlation in BD patients between HRV (SDNNi n%) and age (r= -0,4; p=0,00), disease duration (r= -0,3; p=0,00), BMI (r= -0,2; p<0,01), cholesterol levels (r= -0,3; p=0,00), LDLP (r= -0,3; p=0,00) and increased IMT (r= -0,2; p=0,04), and also between HRV (RMSSD%) and age (r= -0,2; p=0,04), disease duration (r= -0,2; p=0,01), cholesterol levels (r= -0,3; p=0,00), HDLP (r= -0,2; p=0,04); a positive correlation was established between HRV (SNNN%) and smoking (r= -0,2; p=0,04). The control group showed positive correlation between HRV (SNNN%) and increased IMT (r= 0,4; p=0,01).

Conclusion: HRV reduction reflects impaired sympathetic -parasympathetic regulation in BD pts, associated with pts' age, disease duration and presence of traditional cardiovascular risk factors: BMI, increased cholesterol levels, LDLP.

P073**MANIFESTATIONS OF BEHÇET'S DISEASE**

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Objective: To study on the severity of BD the influence of such factors as patient's gender, age disease onset and initials symptom of the disease . **Materials and methods:** 95 patients with confirmed BD were examined. The majority of patients were males (70 men, 25 women)The mean age was 29 years [22; 34], mean disease duration was 8 years [4; 15].

Results: The following clinical manifestations of BD were documented at disease onset (%): recurrent aphthous stomatitis in 63.1; skin lesions in 12.6; genital ulcers in 4.2; ocular lesions in 6.3; joint syndrome in 7.4; CNS lesions in 2.1; gastrointestinal tract involvement in 2.1; thrombosis in 1; epididymitis in 1. Recurrent aphthous stomatitis was more common in female patients at BD onset– 76% vs. 58.6%, $p=0.01$, while organ system involvement was more common in males-14% vs. 4% in females, $p=0.02$. BD onset in men and women was documented at approximately the same time. There were no signs or correlations indicating that patient's age at disease onset could be associated with specific clinical symptoms in males or females. First BD symptoms manifested in the majority of patients before the age of 30 years, with only 10% of patients with BD onset at the age of > 30 years. BD onset in men and women was documented at approximately the same time. There were no signs or correlations indicating that patient's age at disease onset could be associated with specific clinical symptoms in males or females.

Conclusion: Prognostically unfavorable BD signs were found in 11.6% of patients already at the initial stages of the disease in men. No correlation was found between the age at BD onset and clinical symptoms of the disease in both males and females.

P074**INTESTINAL ULTRASOUND: A NEW DIAGNOSTIC METHOD FOR BEHÇET'S DISEASE**

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Objective: To evaluate the possibilities of ultrasound examination of the intestine in patients with Behçet's disease (BD), to compare with the clinical picture of the disease.

Materials and methods: 29 patients (14 men, 15 women) with reliable BD were examined. All patients underwent percutaneous ultrasound of the small and colon with linear and convex sensors with a frequency of 7.5 and 3.5 MHz using Dopplerography in the energy mode.

Results: The average age of patients was 33 years; the average duration of the disease was 7.5 years.

Complaints from the gastrointestinal tract were presented in 18 patients: episodes of abdominal pain in 15, episodes of diarrhea in 12, often mushy stools in 7, flatulence in 15, constipation in 7, pain in the rectum in 3.

Intestinal ultrasound revealed changes in 17 patients. Ultrasound-signs of inflammation in the ileum in 15 patients (signs of a transferred process in 6, current inflammation of moderate activity in 9), localization in the terminal department in 9 patients. Signs of inflammation were in the cecum in 1 case, in the sigmoid colon in 2. Inflammation of the appendix was detected in 3 patients. Signs of hemorrhoids were in 2, proctitis in 1. Ultrasound signs of sigmoid colon diverticulosis were found in 4 patients. Colonoscopy was performed in 10 patients, early detected violations were confirmed by ultrasound in 9 patients.

Conclusion: Intestinal ultrasound is an effective method for detecting early signs of intestinal damage in BD, which contributes to timely diagnosis and therapy, and prevention of surgical treatment and disability development of patients.

P075

REPRODUCTIVE FUNCTION IN BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a multisystemic disease of unknown cause. Anti-Müllerian hormone (AMH) is one of the key parameters for assessing reproductive function and ovarian reserve. The levels of AMH correlates with the residual follicular pool in women of reproductive age.

Objectives: To assess AMH levels in BD female patients of child-bearing potential, and analyze the relationship between AMH levels and disease severity, as well as relationship between serum AMH levels and different therapeutic regimens.

Methods: The study group included 45 women with BD (according to ISGBD 1990 and ICBD 2014) aged 20-40 years, and the control group included 15 age-matching healthy women. Pts' mean age was 31,3 [27;35] yrs, disease duration 6 [3;8] yrs. 17,8% pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), 37,8% pts had a moderate disease, 44,4% pts had a mild disease with mainly dermal-mucous manifestations. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng / ml. Values <1.0 were interpreted as a decreased ovarian reserve.

Results: The mean levels AMH was 2.5 ng/ml in BD pts, and 3.1 ng/ml in control group, showing no statistical difference. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) was observed with the same frequency 18% in patient's vs. in control group 13%.

In the analysis of AMH, depending on the severity of BD, a decrease in ovarian reserve was more often observed in patients with moderate and severe forms of BD.

Table 1 - AMH and severe BD

severe	mild, n=20	moderate disease, n=17	severe, n= 8	p
AMH	2,7 [1,6-3,5]	2,5 [1,0-3,7]	1,9 [0,8;6,7]	ns
AMH >1 ng/ml, %	10	23	25	0,02

There are no correlations of levels AMH with treatment of BD.

A decrease in ovarian reserve was noted in two patients under 30 years old, one was 29 years old woman with "NeuroBehçet" with two children, and the patient with BB+AS was not married, had no pregnancies, and received colchicine therapy for a long time. Two BD patients with low AMH had no pregnancies - unmarried, all other patients with reduced ovarian reserve had from 1 to 6 children.

When analyzing the levels of AMH with the clinical picture and BD therapy, no correlations were found.

Conclusion: The average levels of AMH in women with BD and in the control group did not differ. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) occurred with the same frequency in patients with BD and controls. A decrease in ovarian reserve was more often observed in patients with moderate and severe BD.

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1. Zouboulis C., Vaiopoulos G., Macromichelakis N. et al. Onset signs, clinical course, prognosis, treatment and outcome of adult patients with Adamantiades – Behçet's disease in Greece. Clin.Exp.Rheum.2003, 21, (suppl.30) S19-S26.

P076**EVALUATION OF FACTORS EFFECTING ON INCIDENCE OF OCULAR INVOLVEMENT IN PATIENTS WITH BEHÇET'S DISEASE: A RETROSPECTIVE COHORT STUDY**

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Introduction: Eye involvement is one of the main manifestations of Behçet's disease. It usually manifests as recurrent panuveitis with retinal vasculitis and can cause severe loss of vision. Treatment of Behçet's disease uveitis relies on corticosteroid therapy, other immunomodulatory drugs, and biologic agents. This study was performed to identify the factors affecting the incidence of eye involvement, especially the role of early systemic treatment with immunomodulatory drugs on the incidence of ocular involvement.

Methods: This is a retrospective cohort study performed on 1166 Behçet's patients who referred to Behçet Clinic of Rheumatology Research Center. All patients were followed up for at least 10 years and maximum 15 years. Data analysis was performed using survival analysis models including Kaplan-Meier Survival Estimates, log rank test, and Cox's proportional hazards regression model.

Results: 727 out of 1166 patients (62.3%) had ocular involvement. 80 patients (6.8%) had ocular involvement as the first sign of their disease and 647 patients (55.4%) developed ocular involvement 7.8 ± 6.7 years after the first symptom. Immunomodulatory treatment before ocular involvement reduces the risk by 2.8 times (P-value <0.001). Also lower onset age and female sex had a significant effect on survival without ocular involvement (P-value <0.001 and 0.007 respectively).

Conclusion: This study showed that the most important factor in determining the prognosis of patients with Behçet's disease is the initiation of immunomodulatory treatment prior to eye involvement. Therefore, reducing the time from onset of disease symptoms to diagnosis and providing appropriate treatment can reduce eye complications of Behçet's disease.

P077

DOES PATIENT POSITION AFFECT COMMON FEMORAL VEIN WALL THICKNESS MEASUREMENT BY DOPPLER ULTRASONOGRAPHY AS A DIAGNOSTIC TEST?

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Background/Objectives: We reported the first controlled Doppler ultrasound (US) study demonstrating increased common femoral vein (CFV) thickness in Behçet's Disease (BD)¹. We also recently showed that this is a distinctive feature of BD, rarely present in other inflammatory diseases with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm (2). Standard lower extremity venous Doppler US is performed in erect position for venous thrombosis or insufficiency (3). However, we measured CFV thickness in supine position in our previous studies. In this study, we aimed to assess CFV wall thickness measurement by Doppler US both in supine and erect positions to validate the accuracy and practicability of this diagnostic method in BD.

Method: We included 42 patients (Male/Female:27/15, mean age:39.8 (10.04) years) with a diagnosis of BD and sex and age-matched 41 healthy controls (Male/Female:21/18, mean age: 36.5 (8.4) years). The clinical data were recorded during routine visits. Bilateral CFV thickness was measured with Doppler US both in erect and supine positions by an experienced radiologist on the same day.

Results: Clinical characteristics of BD patients were given in Table 1. Bilateral CFV wall thickness was significantly higher in BD than in healthy controls (0.74 vs 0.18 mm, $p<0.001$ for right, 0.74 vs 0.19 mm, $p<0.001$ for left). There was no statistically significant difference between erect and supine positioned measurements of CFV wall thickness both in BD and healthy control groups (Figure 1).

Conclusion: CFV measurement by Doppler US is a new, accurate and non-invasive diagnostic tool for the diagnosis of BD. Although lower extremity venous Doppler US is performed in erect position for the assessment of venous thrombosis or insufficiency, our study confirmed that patient position does not affect CFV wall thickness measurement. Both erect and supine positioned CFV wall thickness measurements can be done accurately for the diagnosis of BD.

Disclosures: None

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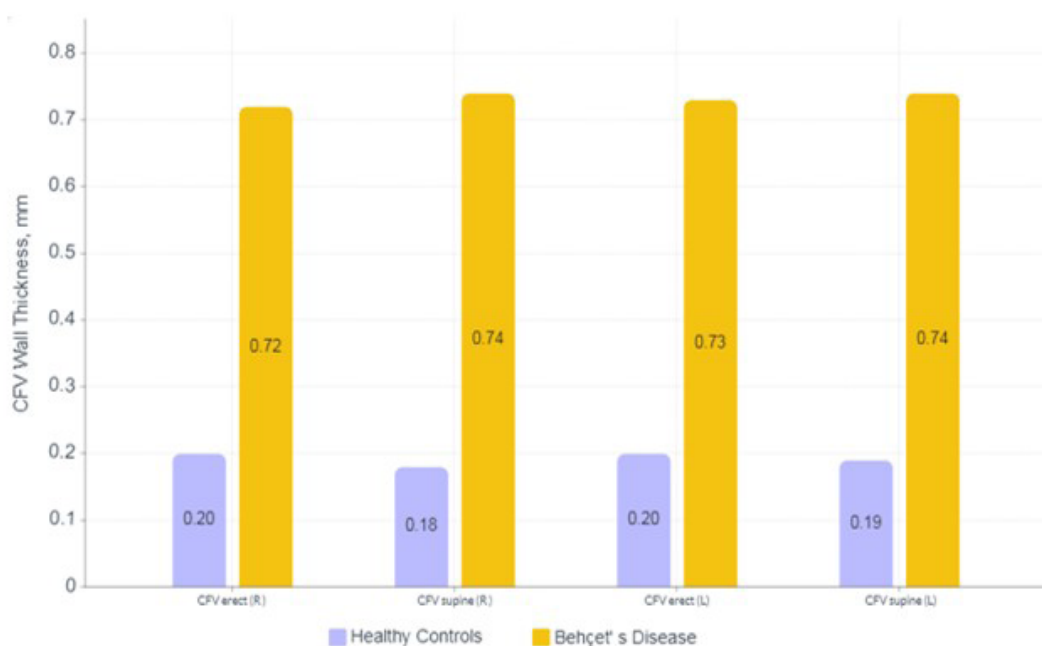
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Table 1. Clinical characteristics of patients with Behçet's Disease.

	Behçet's Patients (n=42)
Age, mean (SD), years	39.8 (10.04)
Gender, male, n (%)	27 (64.3%)
Disease duration, mean (SD), years	9.1 (8.2)
Follow-up time, mean (SD), months	110.1 (98.5)
Family History, n (%)	7 (16.7%)
Pathergy positivity, n (%)	3 (7.1%)
Mucocutaneous Involvement, n(%)	16 (38.1%)
Major Organ Involvement, n (%)	26 (61.9%)
Vascular Involvement, n (%)	24 (57.1%)
Ocular Involvement, n (%)	8 (19%)
Neurological Involvement, n (%)	7 (16.7%)

Figure 1. Measurements of Common Femoral Vein Wall thickness of Behçet's patients and healthy controls in supine and erect positions



P078**IMPACT OF BEHÇET'S DISEASE AND DISEASE ACTIVITY ON PHYSICAL, PSYCHOLOGICAL, SOCIAL AND FINANCIAL WELL-BEING OF PATIENTS**

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Background: Behçet's disease (BD) is a chronic, immune-mediated, systemic vasculitis. The chronic, relapsing nature of BD is associated with significant physical, psychological, social, and financial burden in these patients.

Objectives: To determine the impact of BD, disease activity and clinical phenotypes on physical, psychological/mental, social and financial domains in patients.

Patients and methods: Thirty patients (20 males, 10 females) with BD and 20 age and sex-matched healthy controls (HCs) were enrolled. Demographic data including age, sex, level of education, smoking status, disease duration and employment/work status was collected. Patients were then asked about their most troublesome symptom/s. Complete examination was done. The Multidimensional Assessment of Fatigue (MAF) questionnaire, Hospital Anxiety and Depression (HADS) scale, Health Assessment Questionnaire (HAQ), Fibromyalgia Impact Questionnaire (FIQ) and Pittsburgh sleep quality index (PSQI) were administered. Disease activity was assessed using the Behçet's disease activity form.

Results: Fatigue was the most commonly reported troublesome symptom, followed by ulcers (genital/mouth), arthritis related pain and decreased mobility. Sixty percent of patients reported fatigue. Sexual problems were reported in 50%. Thirty-seven percent reported sleep problems. Fibromyalgia was present in 33 % of patients and was associated with active disease and genital ulcers. BD patients had significantly higher MAF and HADS scores compared to HCs. Patients with ocular involvement reported significant limitations in their daily activities and work capacity. Disease activity was higher in those with genital ulcers, active ocular, neurological and vascular involvement. Patients reported decreased socialization. Fifty percent reported financial negative effects in the form of loss of employment.

Conclusion: BD activity has a negative impact on the physical, psychological/mental, social and financial domains of patients. To improve patient-centered care, targeted initiatives aimed at treating activity, controlling the disease and addressing the specific needs which are most important to BD patients such as fatigue are essential.

Keywords: Behçet's disease, disease activity, physical and psychosocial well-being

P079

CLINICAL COURSE OF PEDIATRIC ONSET BEHÇET'S DISEASE IN YOUNG ADULTHOOD

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Objective: Although onset of Behçet's Disease (BD) is common in the second or third decade, initial symptoms occur under the age of 16 years in 4–26% of the patients.¹ In this study we aimed to assess the clinical course of pediatric onset BD in adulthood period.

Method: The files of 1114 BD patients were reviewed retrospectively. 51 (4.6%) (F/M:21/30) pediatric-onset BD patients were included in the analysis. Demographic and clinical characteristics, follow-up and treatment data of the patients were recorded from files.

Results: The median age at diagnosis was 16 (14-17) years, and the median follow-up duration was 51 (26-96) months. The distribution of disease findings was shown in Table 1. At the end of follow-up, 32 (62.8%) patients had major organ involvement, half of them had at the time of diagnosis.

47 (M:27/F:20) patients had a follow-up with median of 50 (20-82) months in adulthood period. Thirty-one (65.6%) patients had major organ involvement. While 20 (64.5%) patients had major organ involvement in the pediatric period, 11 (35.5%) patients developed major organ involvement in adulthood. Overall, 19 (40.4%) patients had active disease manifestations (relapse and/or new major organ involvement) in adulthood follow-up. Of these patients, 11 (57.9%) had new major organ involvement, 7 (36.8%) had a relapse of the same organ, and one (5.3%) had both new major organ involvement and a relapse. The disease course of patients are seen in Table 2.

Conclusion: Our results show that, about half of the pediatric-onset BD patients has still active disease manifestations (mainly new major organ involvement) in adulthood period.

Disclosures: None

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Table 1. Distribution of disease characteristics of Pediatric Onset Behçet's Disease patients.

	Male (n=31)	Female (n=20)	p	All (n=51)
Oral aphthae	30 (96.8%)	20 (100%)	1	50 (98%)
Genital ulcers	26 (83.9%)	17 (89.5%)	0.695	43 (84.3%)
Patergy positivity	21 (80.8%)	10 (66.7%)	0.453	31 (75.6%)
Papulopustular lesions	21 (67.7%)	10 (50%)	0.205	31 (60.8%)
Erythema nodosum	15 (48.4%)	17 (85%)	0.008	32 (62.7%)
Family history	4 (13.3%)	6 (30%)	0.171	10 (20%)
Arthritis/ arthralgia	-	2	0.149	2 (3.9%)
Major organ involvement	22 (71%)	10 (50%)	0.131	32 (62.7%)
Vascular	12 (38.7%)	2 (10%)	0.025	14 (27.5%)
Ocular	11 (35.5%)	6 (35.3%)	0.685	17 (33.3%)
Neurologic	6 (19.4%)	3 (15%)	1	9 (17.6%)
Gastrointestinal	1 (50%)	1 (50%)	1	2 (3.9%)

Table 2. Disease course of patients followed in adulthood period.

<i>Patients followed in adulthood</i>	n=47 (%)
Major organ involvement in childhood	20 (42.6%)
<i>Relapse or/and new major organ involvement</i>	8 (17%)
<i>No relapse or major organ involvement</i>	12 (25.5%)
Mucocutaneous disease in childhood	27 (57.4%)
<i>New major organ involvement</i>	11 (23.4%)
<i>No major organ involvement</i>	16 (34%)

P080

VENOUS HALO SIGN DETECTED WITH SUPERB MICROVASCULAR IMAGING IN BEHÇET SYNDROME

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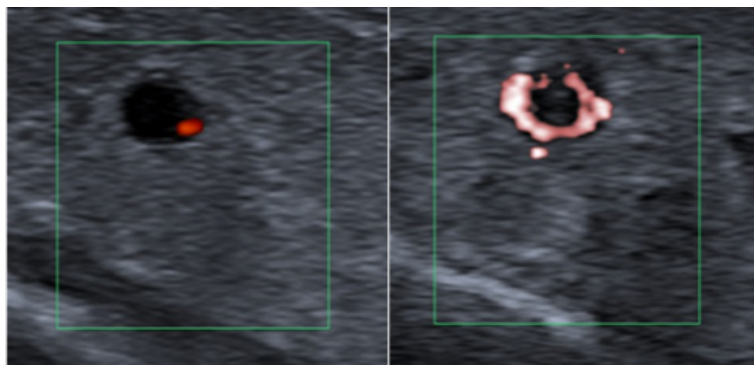
Aim: Superb microvascular imaging (SMI) is a novel technique that provides a more sensitive assessment of small vessels compared to color Doppler US (CDUS), by distinction of low-speed flow signals from motion artifacts. Superficial thrombophlebitis (STM) is a common manifestation in patients with Behçet syndrome (BS) and is thought to be associated with inflammation of the vessel wall rather than a procoagulant state. We aimed to assess STM lesions of patients with BS, together with controls, using SMI.

Methods: We studied 45 BS (16F/29M, mean age:40.0±12.2) patients and 10 non-BS (6F/4M mean age:45.0±10.4) patients with nodular lesions on physical examination. B-mode US, CDUS and SMI were performed and recorded by the same radiologist and images were then evaluated by another radiologist. Both radiologists were blinded to the diagnoses and to each other's assessments.

Results: The nodular lesions of 16 BS and 3 non-BS patients were diagnosed as STM. The diagnosis was phlebitis without thrombosis in 4 patients with BS and 1 patient with non-BS and erythema nodosum in the remaining 20 BS and 6 non-BS patients. A venous halo sign, meaning a halo-shaped lesion on the venous wall was detected with SMI in 13/16 (81%) BS patients with STM, 1 (25%) BS patient with phlebitis and none of the BS patients with erythema nodosum (Figure). Among the 3 non-BS patients with STM, 1 (33%) had venous halo sign. None of the other non-BS patients had a venous halo sign. The interobserver reliability was good ($\kappa=0.96, p<0.001$).

Conclusion: A venous halo sign suggesting inflammation of the vessel wall was detected with SMI in the majority of BS patients with STM. This finding needs to be studied in different vascular lesions of a large number of BS patients together with controls, in order to understand its specificity for BS and its significance.

Figure. A. Color Doppler US. **B.** «Venous halo» sign in SMI in the same patient.



P081

MEASUREMENT OF COMMON FEMORAL VEIN WALL THICKNESS IS A USEFUL DIAGNOSTIC TOOL TO DIFFERENTIATE OCULAR BEHÇET'S DISEASE FROM OTHER INFLAMMATORY UVEITIS

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Background: Diagnosis of Behçet's Disease (BD) can be challenging, especially in patients presenting with single major organ involvement. Our group showed that common femoral vein (CFV) wall thickness measured by Doppler ultrasonography (US) can be a non-invasive diagnostic method¹ and can also be used to diagnose incomplete BD.² Since ocular involvement of BD may result in irreversible vision loss if untreated, it is important to diagnose without delay and initiate immunosuppressive therapy promptly.

Objectives: In this study, we aimed to assess the discriminative role of CFV wall thickness measurement in uveitis associated with BD compared to other inflammatory uveitis.

Methods: Patients with BD uveitis (n=41) and age-gender matched 58 non-BD uveitis patients were included in the study. Demographics, clinical characteristics, and treatment data were recorded during routine visits. CFV wall thickness was measured by an experienced and blinded radiologist on the same day.

Results: Twenty-four (58.5%) of BD patients and 23 (39.7%) of non-BD patients were male. All BD patients had panuveitis. 3 (3.0%), 8 (8.1%), 8 (8.1%) of non-BD patients have anterior uveitis due to sarcoidosis, HLA-B27 positivity, ankylosing spondylitis, respectively, and 7 (7.1%) had idiopathic anterior uveitis. 12 non-BD patients had panuveitis caused by sarcoidosis. The most common complaint was decreased visual acuity in both groups. Right CFV (0.73 mm± 0.08) and left CFV (0.73 mm± 0.07) wall thickness of BD patients was significantly higher than right and left CFV (0.57 mm± 0.1 for both) wall thickness of non-BD patients (p < 001).

Conclusion: Diagnosis of ocular BD can be challenging, especially when there is no other clinical finding or organ involvement specific to BD. Our results suggest that measurement of CFV wall thickness by Doppler US can be helpful for the differentiation of ocular BD from other causes of inflammatory uveitis in daily practice.

Disclosures: None

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P082

INCREASED INFERIOR VENA CAVA WALL THICKNESS AS A SIGN OF EXTENSIVE VENOUS INFLAMMATION IN BEHÇET'S DISEASE

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Background: Vascular involvement of Behçet's disease (BD) affects both arterial and venous vessels.¹ We have previously shown that common femoral vein wall thickness is increased in BD patients and can be used as a diagnostic test.² However, other sites including vena cava inferior/superior and pulmonary arteries may also be involved. Despite the dominance of venous vessel involvement, there is limited data assessing the large veins in BD.

Objectives: In this study, we aimed to assess inferior vena cava wall thickness (IVC) by transthoracic echocardiography (TTE) in BD compared with healthy controls (HC).

Methods: Patients with BD (n=70) and age and sex-matched HC (n=51) were included in this study. Assessment of IVC wall thickness was performed by an experienced cardiologist blinded to cases. Measurement of IVC wall thickness was made at end-expiration and approximately 0.5 to 2.0 cm proximal to the ostium of the right atrium (Figure 1).

Results: IVC wall thickness of patients with BD (0.29 cm (SD: 0.03) was significantly higher than HC (0.26 cm (SD: 0.03) (p <0.01). IVC wall thickness of the patients with only mucocutaneous (0.28 cm (SD:0.03) and major organ involvement (0.29 cm (SD: 0.03) was significantly higher compared with HC (p= 0.006, p <0.01, respectively). In patients with vascular and non-vascular involvement, IVC wall thickness was comparable. While no relationship between IVC wall thickness, disease duration, and BDCAF was detected, however, a positive correlation was observed between age and IVC wall thickness (r=0.3, p <0.01).

Conclusion: We had previously shown the presence of increased wall thickness in lower extremity veins. The present study shows that venous wall inflammation is not limited to only lower extremity veins, also present in the IVC wall. Our results show that there is extensive venous wall inflammation in BD including large venous structures despite not being involved.

Disclosures: None

References:

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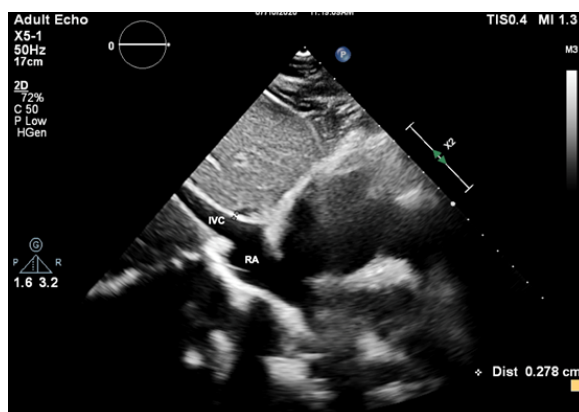


Figure 1: Demonstration of measurement of Inferior Vena Cava Wall Thickness by Transthoracic Echocardiography

P083

PULMONARY ARTERIAL WALL THICKNESS IS INCREASED IN BEHÇET'S DISEASE PATIENTS WITH MAJOR ORGAN INVOLVEMENT: IS IT A SIGN OF SEVERITY?

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Background: Behçet's Disease (BD) is a unique systemic vasculitis that mainly involves veins, in contrast to other vasculitides. Prior studies showed that pulmonary arteries (PA) have a similar structure to systemic veins in terms of thin walls, increased compliance, and low resistance (1). We have recently shown increased venous wall thickness in lower extremity veins of BD patients (2).

Objectives: In this study, we aimed to assess PA wall thickness by transthoracic echocardiography (TTE) in BD compared to healthy controls (HC) and patients with non-inflammatory pulmonary embolism (NIPE).

Methods: Patients with BD (n=77), NIPE (n=33) and HC (n=57) were included in the study. PA wall thickness was measured with TTE by a cardiologist. PA wall thickness was measured from the mid-portion of the main PA (approximately 1 to 2 cm distal to the pulmonary valve) (Figure 1).

Results: PA wall thickness was significantly lower in controls compared to NIPE and BD ($p < 0.001$ for both) (Table 1). PA wall thickness was also found to be significantly higher in BD patients with major organ involvement compared to HC and NIPE ($p < 0.001$ and $p = 0.027$, respectively). PA wall thickness was higher in patients with vascular, ocular, and neurologic involvement compared to BD patients with the mainly mucocutaneous disease ($p < 0.001$ for all).

Conclusion: We found that PA wall thickness was significantly higher in BD with major organ involvement compared to BD patients with the only mucocutaneous disease, regardless of major organ involvement type. It suggests that extensive vascular inflammation in patients with BD, not limited to venous vessels. Increased PA wall thickness is present only in patients with major organ involvement, possibly as a sign of more severe disease in BD, and may be the predictor of the major organ involvement during follow-up.

Disclosures: None

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2. Alibaz-Oner F. et al. Venous vessel wall thickness in lower extremity is increased in male patients with Behçet's disease. Clin Rheumatol. 2019;38(5):1447-51

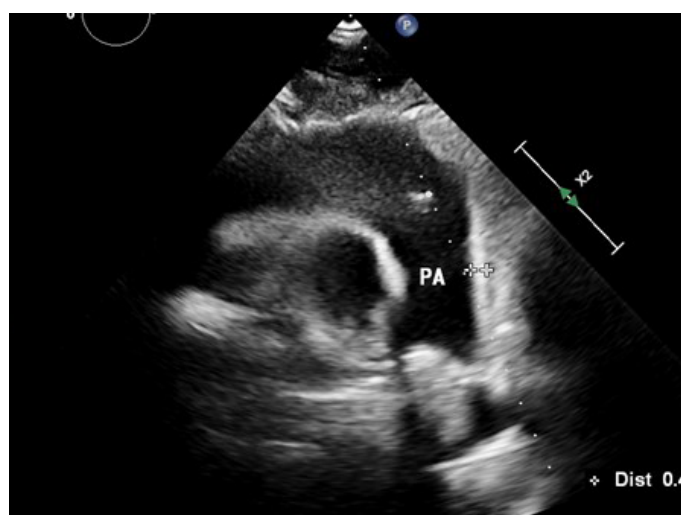


Figure 1. Measurement of pulmonary artery wall thickness by Transthoracic Echocardiography.

P083

Table 1. Measurement of pulmonary artery wall thickness.

Healthy controls, mean (SD), cm	0.36 (0.03)
Patients with BD, mean (SD), cm	0.44 (0.06)
Patients with NIPE, mean (SD), cm	0.44 (0.05)
Patients with major organ involvement, mean (SD), cm	0.46 (0.04)
Patients with vascular involvement, mean (SD), cm	0.46 (0.05)
Patients with ocular involvement, mean (SD), cm	0.47 (0.05)
Patients with neurological involvement, mean (SD), cm	0.49 (0.02)

P084**DOES VEIN WALL THICKNESS HAVE PROGNOSTIC VALUE IN BEHÇET'S DISEASE? A PROSPECTIVE FOLLOW-UP STUDY**

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Background/Objectives: We reported the first controlled ultrasound study showing increased common femoral vein(CFV) thickness in Behçet's Disease(BD),¹ and showed that this is a distinctive feature of BD, rarely present in other inflammatory diseases with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm.² This study aimed to assess the prognostic value of CFV thickness during prospective follow-up BD patients.

Methods: We included 195 patients with BD. Bilateral CFV thickness was measured with ultrasonography by an experienced radiologist. Patients were started to follow up prospectively with 3-6 months intervals and in any urgent visit.

Results: At baseline, 98.6% of patients had CFV wall thickness above the cut-off value of ≥ 0.5 mm (Table 1). 149 patients had prospective follow-up with a mean of 26.03 (16.29) months. New major organ involvement or relapse was seen in 41(27.5%) patients. Among 36 patients with only mucocutaneous disease at baseline, new major organ involvement developed in 9 patients during follow-up. These patients had higher baseline CFV thicknesses compared to patients not developing major organ involvement despite no statistical significance (0.83 mm vs 0.73 mm for right; 0.80 mm vs 0.73 mm for left: $p > 0.05$ for both). In 47 patients, the second CFV thickness measurement was done mean 19.8 months later. First and second measurements were found similar ($p=0.26$, $p=0.26$ respectively). CFV wall thickness didn't change with the treatment.

Conclusions: CFV wall thickness measurement which is a new diagnostic tool for BD, does not change over time with treatment modality, new organ involvement or relapses. However, our preliminary results suggest that mucocutaneous BD patients with higher CFV thickness may have a higher risk for the development of major organ involvement during follow-up. The long-term results of our prospective cohort would clarify the prognostic value of CFV thickness in BD.

Disclosures: None

References

1. Alibaz-Oner F, et al. Clin Rheumatol 2019. 2- Alibaz-Oner F, et al. Rheumatology (Oxford) 2021.

P084

Table 1. The baseline and follow-up clinical characteristics of patients with Behçet's Disease.

	Baseline (n=149)	Last Follow-up (n=149)	Relapses or New Involvement during follow-up
Age mean (SD)	35.36 (8.72)		
Gender F/M ratio	45/104		
Pathergy (positive/negative)	59/55		
Right CFV Wall Thickness mean (SD) mm	0.773 (0.186)		
Left CFV Wall Thickness mean (SD) mm	0.796 (0.206)		
Oral Aphthous Ulcers n (%)	138 (92.6)	141 (94.6)	13 (8.7)
Genital Ulcers n (%)	94 (63.1)	96 (64.4)	7 (4.7)
Folliculitis n (%)	85 (57)	76 (51)	3 (2)
Erythema Nodosum n (%)	67 (45)	72 (48.3)	10 (6.7)
Arthritis (%)	54 (36.2)	50 (33.6)	10 (6.7)
Major Organ Involvement n (%)	112 (75.2)	120 (80.5)	41 (27.5)
Vascular Involvement n (%)	94 (63.1)	105 (70.5)	36 (24.2)
<i>Deep Venous Thrombosis (%)</i>	64 (43)	68 (45.6)	7 (4.7)
<i>Pulmonary Thrombosis n (%)</i>	38 (25.5)	55 (36.9)	22 (14.8)
<i>Sinus Venous Thrombosis n (%)</i>	12 (8.1)	14 (9.4)	2 (1.3)
<i>Thrombophlebitis n (%)</i>	4 (2.7)	6 (4)	5 (3.4)
<i>Vena Cava Thrombosis (%)</i>	3 (2)	3 (2)	0 (0)
<i>Pulmonary Aneurysm n (%)</i>	1 (0.7)	2 (1.3)	2 (1.3)
<i>Other Vascular Involvement n (%)</i>	4 (2)	5 (3.3)	2 (1.3)
Neuro-Behcet n (%)	15 (10.1)	17 (11.4)	2 (1.3)
Uveitis n (%)	38 (25.5)	43 (28.9)	9 (6)
Entero-Behcet n (%)	9 (6)	10 (6.7)	1 (0.7)

P085

FEMORAL VEIN WALL THICKNESS MEASUREMENT CAN BE A DISTINCTIVE DIAGNOSTIC TOOL TO DIFFERENTIATE BEHÇET'S DISEASE FROM CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: Differentiation of gastrointestinal (GI) involvement of Behçet's disease (BD) and inflammatory bowel disease (IBD) can be a diagnostic challenge. We recently showed that common femoral vein (CFV) wall thickness is significantly higher in BD patients compared to Crohn's disease (CD).¹ However, the study has limited number of IBD patients with only CD. Therefore, this study aimed to evaluate the CFV thickness measurement in BD patients compared to IBD patients with both CD and ulcerative colitis (UC).

Methods: Patients with BD(n=117), IBD(n=87, [53 CD, 34 UC]) and healthy gender-matched controls (HC)(n=85) were included in the study. CFV wall thicknesses were measured with Doppler ultrasonography.

Results: The patient characteristics are shown in Table 1. Among BD patients, 70 (59.8%) had major organ (48[41.0%] vascular, 21[30.0%] ocular, 11[15.7%] gastrointestinal, and 8[11.4%] neurological) involvement.

The mean right CFV thickness was 0.75±0.21 mm, 0.32±0.08 mm, and 0.28±0.13 mm for BD, IBD, and HC, respectively (p<0.0001). The mean left CFV thickness was 0.76±0.21 mm, 0.32±0.09 mm, and 0.28±0.13 mm for BD, IBD, and HC, respectively (p<0.0001). Both right and left CFV thicknesses were significantly higher in BD compared to HC and IBD (adj.p<0.0001 for both). Bilateral CFV thicknesses in IBD were similar to HC (adj.p>0.05 for both).

Among BD patients, right and left CFV thicknesses were similar in patients with and without major organ involvement (p=0.53 for right, p=0.21 for left). CFV thicknesses were also similar between BD patients with and without GI involvement (p=0.64 for right, p=0.27 for left).

Among IBD patients, right and left CFV thicknesses were similar in patients with CD and UC (p=0.13 for right, p=0.14 for left).

Conclusions: There was significantly higher CFV thickness in BD patients compared to both CD and UC patients. These results suggest that measurement of CFV thickness can be used in daily practice to differentiate GI-BD and IBD.

Disclosures: The authors have no conflict of interest.

References:

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Table 1. Demographics and patient characteristics.

	Behçet's disease	Crohn's disease	Ulcerative colitis	Healthy controls
Age, years (mean±SD)	34.9 ± 8.2	42.9 ± 12.7	43.6 ± 14.5	32.3 ± 7.2
Gender, (M/F)	75/42	28/25	20/14	59/26
Disease duration, months median (IQR)	97.0 (48.0-159.0)	90.0 (29.5-111.5)	106.7 (48.0-144.0)	-
Immunosuppressive use, n (%)	70 (59.8)	44 (83.0)	9 (26.4)	-
Right CFV thickness, mm (mean±SD)	0.75 ± 0.21	0.33 ± 0.07	0.29 ± 0.09	0.28 ± 0.13
Left CFV thickness, mm (mean±SD)	0.76 ± 0.21	0.33 ± 0.09	0.33 ± 0.06	0.28 ± 0.13

P086

INCREASED INTIMA-MEDIA THICKNESS OF COMMON FEMORAL VEIN IN BEHÇET'S DISEASE:
A SIGN OF FULL LAYER VENOUS WALL INFLAMMATIONGizem Sevik¹, Rabia Ergelen², Seda Kutluğ Ağaçkiran¹, Haner Direskeneli¹, Fatma Alibaz-Oner¹¹Marmara University School of Medicine, Department of Internal Medicine, School of Medicine, Division of Rheumatology, Turkey,²Marmara University School of Medicine, Department of Radiology, Turkey

Introduction: In vascular involvement of Behçet's disease (BD), inflammatory cells infiltrate mainly the adventitia and media, but only a few inflammatory cells were shown in the intima layer during active arteritis.¹ We recently showed that increased common femoral vein (CFV) thickness is a distinctive feature of BD with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm.² In this study, we aim to investigate the localization of inflammation in vein wall in BD patients by measuring both whole wall thickness and the intima-media thickness (IMT) of CFV.

Methods: Patients with BD (n=42, 27M/15F) and age- and sex-matched healthy controls (HC) (n=35, 21M/14F) were included in the study. IMT and venous wall thickness of CFV were measured with Doppler ultrasonography.

Results: The mean age was 39.8 ± 10.0 years in BD patients and 36.8 ± 7.9 years in HC. The median disease duration of BD patients was 72 (28.5-162.0) months and 61.9% of them had major organ involvement. The most common major organ involvement was vascular (57.7%) followed by ocular (34.6%), and neurological (7.7%) involvement. Most (66.7%) BD patients were using immunosuppressive treatment.

Both IMT-R and IMT-L were significantly higher in BD patients than HC ($p < 0.0001$). The measurements of IMT and venous wall thickness of CFV were shown in Table 1.

There was a significant positive correlation between IMT-R and CFV-R, IMT-L and CFV-L measurements ($p < 0.0001$, $r = 0.918$ and $p < 0.0001$, $r = 0.907$, respectively).

There was no significant difference between IMT-R and IMT-L measurements in BD patients with and without major organ involvement ($p > 0.05$ for both).

Conclusions: Intima-media thickness of CFV, as well as CFV wall thickness, is significantly increased in BD patients than HC. Our results suggest that there is a full layer venous wall inflammation including intima-media layer in BD independent of vascular involvement.

References

1. Kobayashi M, et al. Histopathology, 2000.
2. Alibaz-Oner F, et al. Rheumatology (Oxford), 2021.

Disclosures: The authors have no conflict of interest.

Table 1. The measurements of intima-media and venous wall thickness of common femoral vein.

	Behçet's disease	Healthy controls	p
Right CFV wall thickness, mm, (mean \pm sd)	0.74 ± 0.18	0.18 ± 0.04	<0.0001
Left CFV wall thickness, mm, (mean \pm sd)	0.74 ± 0.19	0.19 ± 0.05	<0.0001
Right IMT of CFV, mm, (mean \pm sd)	0.32 ± 0.17	0.10 ± 0.01	<0.0001
Left IMT of CFV, mm, (mean \pm sd)	0.34 ± 0.17	0.10 ± 0.01	<0.0001

P087**CAUSES OF HOSPITALIZATION IN BEHÇET SYNDROME**

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Objectives: The causes of hospitalization may provide important information on the course of diseases and treatment-related adverse effects. We aimed to determine the causes and outcome of hospitalizations in Behçet Syndrome (BS) in a dedicated center.

Methods: We surveyed hospitalization records in our clinic between January 2002 and December 2019 and identified those with a diagnosis of BS. The records were reviewed for demographic and clinical features, causes of hospitalization and outcome. We divided hospitalization causes into 2 as being BS-related (organ involvement/deterioration) and non-BS related (treatment complication/others).

Results: Four-hundred and fourteen BS patients (76%M, mean age 37.4±11.6 years) were hospitalized a total of 536 times during 18 years. The median disease duration was 7(IQR:11) years. Three-hundred and forty-one (64%) patients were using immunosuppressives(±corticosteroids) and 78 (15%) were under biologic treatment at the time of hospitalization. The mean duration of hospitalization was 12.7±10.4 days. The reasons for hospitalization were related to BS in 304 patients (57%) and non-related to BS in 223 (42%). Nine patients were hospitalized for both BS and non-BS related reasons at the same time. The most common reasons were vascular involvement (n=198,37%) for BS-related and infections (n=81,15%) for non-BS related reasons. Patients hospitalized for BS-related causes were younger, had short disease duration, shorter hospitalization duration and less immunosuppressives(±corticosteroids) use compared to non-BS related hospitalizations(Table). There were no differences between the groups regarding gender distribution and use of biologic agents. Three patients died during hospitalization due to malignancy, infection and right heart failure due to pulmonary artery thrombosis and pulmonary hypertension.

Conclusions: Vascular involvement is the leading cause of hospitalization among BS patients, followed by infections. The predominance of men among hospitalized patients underlines the relatively severe course of BS in men. The retrospective design and inclusion of patients who were hospitalized only in the rheumatology unit are limitations of this study.

P087

Table- Distributions and Demographic Features of BS-related and non-BS related Reasons of Hospitalizations		
	BS related reasons (n of hospitalizations=304)*	non-BS related reasons (n of hospitalizations=223)*
Causes of hospitalizations (per hospitalization)	Vascular inv. (n=201, 66%) <i>Pulmonary artery inv. (n=75, 25 %)</i> <i>Deep vein thrombosis (n=42, 14 %)</i> <i>Budd-Chiari synd. (n=32, 11%)</i> <i>Vena cava inf. thrombosis (n=19, 7%)</i> <i>Peripheral artery inv. (n=18, 6 %)</i> <i>Vena cava sup. thrombosis (n=16, 5%)</i> <i>Aorta inv. (n=17, 6%)</i> <i>Coronary artery inv. (n=4, 1%)</i>	Infection (n=74, 33%) <i>Pneumonia (n=22, 10%)</i> <i>Tuberculosis (n=9, 4%)</i> <i>Urinary tract inf (n=8, 4%)</i> <i>Gastroenteritis (n=5, 2%)</i> <i>Osteomyelitis (n=4, 2%)</i> <i>Septic arthritis (n=3, 1%)</i> <i>Aspergillosis (n=2, 1%)</i> <i>Nocardia (n=1, 0.5%)</i> <i>Salmonella (n=1, 0.5%)</i> <i>Others (n=19, 9%)</i>
	Neurologic inv. (n=61, 20%) <i>Parenchymal inv. (n=47, 15%)</i> <i>Dural sinus thrombosis (n=14, 5%)</i>	Drug side effects other than infections (n=29, 15 %) <i>Interferon (n=10, 5%)</i> <i>Azathioprine (n=7, 4%)</i> <i>Cyclosporine (n=5, 3%)</i> <i>Steroid (n=3, 2%)</i> <i>TNF antagonists (n=3, 2%)</i> <i>IVIG (n=1, 1%)</i>
	GI inv. (n=23, 8%)	Additional rheumatologic diseases (n=17, 8%)
	Joint inv. (n=13, 4%)	Renal disease (n=17, 8%)
	Mucocutaneous inv. (n=13, 4%)	Cardiovascular dis. (n=14, 6%)
	Eye inv. (n=9, 3%)	Avascular necrosis (n=6, 3%)
	Others (n=6, 2%)	Malignancy (n=12, 5%)
		Others (n=47, 21%)
Gender	232M/72F	166M/57F
Mean age \pm SD	34.7 \pm 10.6 [†]	41.1 \pm 12.4
Mean disease duration \pm SD (years)	7.1 \pm 7.3 [‡]	11.6 \pm 9.5
Mean duration of hospitalization \pm SD (days)	11.5 \pm 8.2 [§]	14.1 \pm 12.9
Immunosuppressives use (\pm corticosteroids)	59%	70%
Biologic agents use	14%	15%
*Some patients were hospitalized more than one times and for both BS related and non-BS related reasons at different time and had more than one type of BS related and/or non-BS related reasons. [†] p=0.006, [‡] p<0.001, [§] p<0.001, p=0.01		

P088**FACTORS ASSOCIATED WITH THROMBOSIS IN BEHÇET'S SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Although several studies were conducted to highlight the mechanism of thromboinflammation in Behçet syndrome (BS), it is still not fully understood. We performed a systematic review and meta-analysis of studies investigating thrombotic, fibrinolytic, and endothelial factors in BS.

Methods: We searched PubMed and EMBASE with the keyword "Behçet*" in four languages (English, German, French and Turkish) from their inception up to April 2020. Studies comparing BS patients with and without thrombosis and studies comparing BS patients with thrombosis and patients with thrombosis due to other causes were analyzed separately.

Results: Of 15548 articles, 15052 were excluded due to duplication and inappropriate study design. Full text review of the remaining 388 articles yielded 106 papers meeting our predetermined inclusion criteria.

Factors significantly associated with BS thrombosis compared to BS without thrombosis were high frequency of factor V Leiden mutation (15 studies, OR: 2.55, 95% CI 1.66, 3.93), high homocysteine levels (14 studies: 4.27, 95% CI 2.31, 6.22), high protein C levels (5 studies, SMD: 0.80, 95% CI 0.15, 1.45), high VEGF levels (2 studies, SMD: 1.63, 95% CI 0.21, 3.05), high CEC concentrations (2 studies, SMD: 1.00, 95% CI 0.22, 1.77), and high factor 8 levels (4 studies, MD: 17.17, 95% CI 7.79, 26.55).

Factors that were associated with BS thrombosis compared to thrombosis due to other causes including JAK-2 mutation, circulating endothelial cells, activated protein C resistance, tPA, and PAI were assessed in 1 study each. Among these, tPA levels (MD: -6.00, 95% CI -10.99, -1.01), APCR (OR: 0.09, 95% CI 0.01, 0.73) and JAK-2 mutations (OR: 0.01, 95% CI 0.00, 0.06) were significantly less in patients with BS thrombosis.

Conclusions: The cut-offs used for defining the normal level for these factors, time of blood collection and the type of thrombosis were not uniform across the studies. Studies investigating these factors together, in a large number of patients, and together with appropriate controls are needed to confirm these results.

P089

LESION PROBABILITY MAP IN CEREBRAL VEIN THROMBOSIS DUE TO BEHÇET'S DISEASE

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Introduction: Behçet's disease (BD) is a multisystemic inflammatory disease. The second most common clinical form of Neuro-BD is cerebral venous sinus thrombosis (CVST). Most of the previous studies on CVST-BD classified the involved cerebral venous sinuses categorically. The purpose of this study was to construct flow void probability maps of patients with CVST with and without BD to visually illustrate the impacted cerebral venous sinuses and to compare the subgroups of patients.

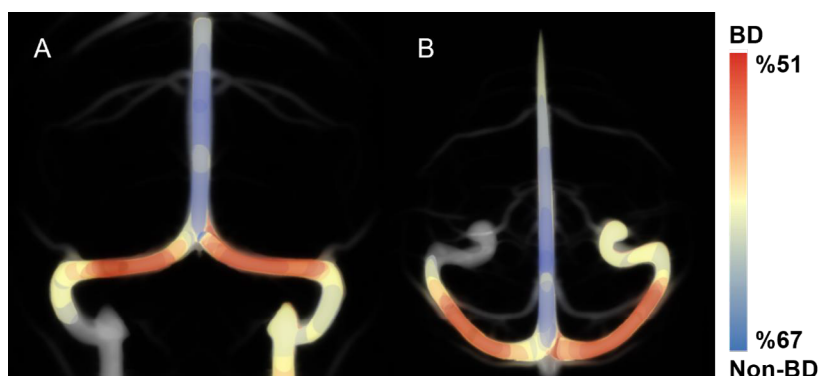
Methods: Seventeen patients with a diagnosis of BD-related CVST (CVST-BD) and 23 patients with a diagnosis of CVST related to other etiologies (CVST-O) were included. We collected clinical data including gender, age at onset of BD and CVST, presenting symptoms, neurological examination findings, and the etiology of CVST-O. High-resolution MR venography examinations obtained during CVST were used to mark and digitalize thrombosed areas using computer-aided design software.

Thrombus probability and subtraction maps were created to reveal the differences between the subgroups.

Results: Focal neurological findings were only found in the CVST-O. Structural brain MRIs were within normal limits except for one patient with BD, while parenchymal pathology was observed in 13 patients (56.5%) in the CVST-O group. Remarkably, all patients with CVST-BD had thrombosis in the TS. However, TS was affected in 73.9% of the CVST-O patients ($p=0.03$). Thrombosis developed mostly in the SSS and TS in the CVST-O group. The frequency of SSS thrombosis was more common in the CVST-O (Figure 1).

Conclusion: Our study showed important clinical and radiological differences in CVST patients with and without BD. Venous infarction and venous hemorrhage were less common in patients with CVST-BD. The only clinical symptom in most of the CSVST patients with BD was headache due to elevated intracranial pressure. Transverse sinus thrombosis was more common in patients with BD than in other CVST patients.

Figure 1. Thrombus probability difference map of patients with and without BD. A. Anteriorposterior view. B. Superior-inferior view. The level of the thrombus probability difference is shown on the red-blue color scale. The maximum thrombus probability difference is expressed as a percentage for each group. BD: Behçet's disease. Non-BD: Non-Behçet's disease.



P090

SEXUAL DYSFUNCTION CAUSED BY BEHÇET'S DISEASE: IS IT AN OVERLOOKED PROBLEM, ESPECIALLY IN MALE BEHÇET'S PATIENTS?

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Objectives: Behçet's disease (BD) is a chronic systemic inflammatory disease characterized by oral and urogenital ulcers, ocular, musculoskeletal, vascular, and neurological involvement. Recent evidence suggests that sexual dysfunction (SD) is prevalent in BD patients.¹ We aimed to determine the frequency of SD in BD and compare the rates of SD in Behçet's patients with neurological involvement (NBD), Behçet's patients without neurological involvement (BDWONI) and healthy controls (HC).

Methods: Age matched, sexually active 59 BD (17 NBD, 42 BDWONI) patients and 36 HC were recruited. All participants were questioned with Short Form-36, Beck Depression Inventory (BDI), Golombok-Rust Inventory of Sexual Satisfaction (GRISS), Female Sexual Function Index (FSFI), International Index of Erectile Function (IIEF-5), in addition, disease activity has been assessed by Behçet Disease Current Activity Form (BDCAF) in all BD patients.

Results: The rate of SD was higher in BD patients (44.2%) compared to HC (14.2%) ($p=0.003$). Male BD patients had lower sexual function scores compared to male HC. Three parameters of GRISS (premature ejaculation, noncommunication, infrequency) were observed more frequently in male BD patients compared with male HC (BD vs HC for 3 parameters respectively: 6.5-4.7, 3.6-2.0, 3.9-2.4 $p<0.05$ for all).

The SD rates were comparable between female BD patients and HC. SD rates were similar in BDWONI (44.2%) and NBD (42.8%) groups ($p>0.05$). BDCAF score was negatively correlated with IIEF scores of male BD patients ($r=-0.437$) and positively correlated with GRISS scores of female BD patients ($r=0.748$) ($p<0.05$). There was no relation between SD and depression in BD patients. ($p=0.284$)

Conclusion: The frequency of SD is increased in BD compared to HC and affects males more frequently than females. Premature ejaculation, infrequency and noncommunication are common sexual problems in male BD patients. In conclusion, BD has a negative effect on sexuality and BD patients should be evaluated in terms of SD during follow up.

Disclosures: None

Reference

1. Hiz O, et al. The Journal of Sexual Medicine 2011; 8(5), 1426–1433.

P091**LATE ONSET BEHÇET'S DISEASE IN IRAN; CLINICAL CHARACTERISTICS AND COMPARISON WITH CLASSIC ONSET FORM**

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Objectives: To report the characteristics of late onset Behçet's disease (LOBD) in a cohort of patients from Iran's registry and compare them with classic onset form (COBD).

Methods: From a cohort of 7797 BD patients two groups were selected: LOBD (disease onset >50 years), and COBD (disease onset between 20-39 years). Their data (demographic, clinical, laboratory) were collected on a standard protocol comprising 105 items. Appropriate statistical comparisons were done, and $p < 0.05$ considered significant.

Results: LOBD was seen in 120 patients (1.5%, CI:0.3). The male/female ratio was 1.1/1. Positive familial history for BD was present in 6.3%. As the first presentation, oral Aphthosis (OA) was the most frequent (74%) followed by ocular lesions (18%) and genital ulcers (GU) in 14%. The prevalence of various manifestations were as follows: OA: 91.7%; GU: 47.5%; skin: 55.8% (pseudofolliculitis: 41.7%, erythema nodosum: 18.3%); ocular: 65% (uveitis 66.7%, retinitis 29.2%); joint: 27.5%; neurological: 2.5%; vascular: 12.5%; gastrointestinal: 6.7%; epididymo-orchitis: 3.2% (men); High ESR (≥ 20): 47.8%; abnormal urine: 15.8%; positive pathergy test: 49.6%; HLA-B5/51: 59.8%. The sensitivities of ISG and ICBD criteria were 65%, and 90% respectively. Comparison with 5073 COBD patients showed no significant difference in any demographic features (sex ratio, familial history, disease duration or follow-up time) between the two groups. As the first presentation, OA rate was lower in LOBD ($p < 0.004$), but ocular lesions were higher ($p < 0.00003$). During the disease course, OA ($p < 0.00001$), GU ($p = 0.00002$) and pseudofolliculitis ($p < 0.04$) were lower in LOBD.

Despite higher prevalence of ocular lesions ($p < 0.03$), severe forms (retinitis, panophthalmitis) were less encountered. Among the minor manifestations, only articular involvement ($p = 0.01$) had lower frequency in LOBD. Laboratory tests showed no statistically significant difference between the two groups.

Conclusion: LOBD in Iran showed a lower frequency of mucocutaneous and joint involvement, while a higher but less severe ocular lesions were seen.

P092**MANAGEMENT OF MUCOCUTANEOUS LESIONS OF BEHÇET'S DISEASE**

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Behçet's disease is an inflammatory disease characterized with oral aphthous ulcers, genital ulcers, skin lesions, and ocular lesions. Vascular-, entero-, neuro- Behçet's disease are also included. Skin lesions are included in acneiform eruptions, erythema nodosum, and thrombophlebitis. The mucocutaneous lesions are the first signs of Behçet's disease, and the internal organ lesions develop several years later the mucocutaneous lesions. The mucocutaneous lesions also recur during clinical course. We developed consensus guideline that provides recommendations on the management of the mucocutaneous lesions of Behçet's disease (J Dermatol 47: 223- 235, 2020). We have designed recommendation and algorithm of each mucocutaneous manifestation of Behçet's disease.

P093

VALIDATION OF BEHÇET'S DISEASE OVERALL DAMAGE INDEX (BODI) FOR RETROSPECTIVE STUDIES AND A PROPOSAL FOR MODIFICATION

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Background: Damage accrual in BS may progress over the years and an index that can be scored using retrospective data may be useful in measuring damage accrual over a long time and comparing different treatment strategies or patient populations. We aimed to assess the construct validity, reproducibility, sensitivity to change and feasibility of Behçet's Disease Overall Damage Index (BODI) for use in retrospective studies, and to identify items that may be missing in BODI.

Material and Method: BODI was translated into Turkish with the principles of scale adaptation and translated backwards by 2 people. The study included 300 patients with at least 2 visits at 1-year intervals out of 712 consecutive BS patients admitted between 2015-2017. Correlation between BODI score of the same patient that was assessed during a face-to-face visit and that was calculated retrospectively using patient charts was evaluated using intraclass correlation coefficient (ICC). Interobserver and intraobserver correlation, correlation with disease activity and feasibility were also evaluated.

Results: The mean BODI score was 1.56 ± 1.44 . There was good correlation between face-to-face and retrospective evaluation (ICC 0.998; %95CI 0.997-0.999), good interobserver agreement (ICC 0.96 (95%CI 0.94-0.98) and intraobserver agreement (ICC 1). No correlation with disease activity was detected ($r = -0.01$, $p = 0.5$). We observed an increase in BODI score in 113 (37.6%) patients during follow-up. The main reasons for increasing BODI scores were eye, vascular and neurological involvement. Items not captured by BODI were hypertension, lymphedema, liver failure, glaucoma, damage due to venous interventions and lung parenchymal involvement. The mean time to complete the form was 1.5 (1-4) minutes.

Conclusion: The validated Turkish version of BODI is convenient and applicable in terms of construct validity and can be used reliably in retrospective studies. Modification of BODI by adding damage items identified in this study may make it an even better scale.

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Table. Demographic features and BODI scores of BS patients.

Sex	140 F/160 M
Mean age (SD), years	33.6 (9.9)
Mean age at the time of fulfilling ISG criteria (SD), years	30 (9.2)
Mean disease duration (SD), years	8.8 (5.9)
Mean follow-up time, years	5.3 (0.8)
Clinical features (%)	
<i>Oral ulceration</i>	99.6
<i>Genital ulceration</i>	81.6
<i>Erythema nodosum</i>	56.6
<i>Papulopustular lesions</i>	88.6
<i>Joint involvement</i>	25.6
<i>Pathergy positivity</i>	26.6
<i>Ocular involvement</i>	46.6
<i>Vascular involvement</i>	20.6
<i>Neurologic involvement</i>	2.6
<i>Gastrointestinal involvement</i>	1.6
N of patients with more than 1 BODI score*(%)	239 (79.6)
Causes for increase in BODI score**(n=113) (%)	
<i>Ocular involvement</i>	79 (69.9)
<i>Vascular involvement</i>	17 (15)
<i>Neurological involvement</i>	8 (7)
<i>Gastrointestinal involvement</i>	3 (2.6)
<i>Mucocutaneous inv.</i>	6 (5.3)
<i>Cardiovascular inv.</i>	1 (0.8)
<i>Diabetes mellitus</i>	4 (3.5)
<i>Avascular necrosis</i>	2 (1.7)
<i>Osteoporosis related fracture</i>	1 (0.8)

*All patients had at least 1 BODI score.

**Some patients had more than 1 type of involvement.

P094**EVIDENCE-BASED BEHÇET'S DISEASE ACTIVITY (EBDA) – A NEW INSTRUMENT FOR DISEASE ACTIVITY AND REMISSION ASSESSMENT**

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Background: Most current Behçet's disease (BD) activity assessment tools strongly focus on patient-reported symptoms and findings. Here we aimed to develop and test a BD-specific disease activity instrument that relies to a high extent on objective findings, dissects the impact of organ-threatening from non-organ-threatening disease, and classifies remission depth.

Methods: We required verification of reported symptoms through findings on physical exam and diagnostic studies and incorporated results of screening and follow-up studies in four minor system categories, including "mucosal", "cutaneous", "cutaneous pathergy", "articular", and four major system categories, including "ocular", "vascular", "CNS", "GI". Evidence of one or more phenotypically eligible findings in any category triggered scoring with major categories receiving a 3-fold weighed score over minor ones. EBDA and Behçet's Disease Current Activity Form (BDCAF) scoring was applied to 135 BD patient encounters comprising a wide range of degrees of BD severity and prototypical manifestations.

Results: There was moderate positive correlation between EBDA and BDCAF across all scores (Pearson's 0.5150, $p < 1e-9$); Kendall's 0.5758 ($p < 1e-10$), Spearman's rho 0.6587, $p < 1e-10$) without a linear relationship (Lin's concordance score 0.1014, 99.9% confidence). On analysis of categorized scores for lower (EBDA < 12, which excludes major organ involvement) vs higher activity (EBDA \geq 12, which allows major organ involvement) there was evidence for moderate positive correlation with BDCAF for lower (Kendall's 0.4745, $p < 1e-6$); Spearman's 0.4745, $p < 1e-6$), but not for higher activity scores (Kendall's 0.3640, $p = 0.064$; Spearman's 0.3700, $p = 0.063$). EBDA detected moderate-severe and severe disease activity 3-4 times more frequently than BDCAF.

Conclusions: EBDA is a new instrument for the finding-based assessment of BD activity which may exhibit improved performance in moderate-severe and severe, potentially organ-threatening BD. Given its strong focus on objectively verifiable findings directly relevant to the time point of assessment, EBDA may be especially suitable in translational research-intensive settings.

P095**PATIENT'S EDUCATION AND BEHÇET'S DISEASE: EMPOWERING PATIENTS, CAREGIVERS AND FAMILIES**

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Background: The specificities of Behçet's disease (BD) and its impact on patients and on their families suggest the need that a specific educational programme dedicated to BD could improve the knowledge and promote the active involvement in the therapeutic decision-making process. Recently, BehçeTalk, an educational program tailored for patients, families and caregivers living with BD, was launched in Italy. The aim of this work is to share good practice in patients' education in BD to disseminate this initiative across the scientific and patients' community.

Methods: BehçeTalk, co-designed with BD patients and caregivers, offers educational webinars on different aspects of the disease, as well support groups for patients and caregivers coordinated by a psychologist with expertise in BD. Some of the topics addressed in the programme include quality of life, workability, sexuality, self-management, adherence to treatment, pregnancy and family planning. Moreover, some of the major points discussed in the patients' support groups are related to the ability to heal the "wound" resulting from the BD diagnosis, interpersonal and social relationships; notably, for BD caregivers being parents/partner/siblings of a BD patient represent the most frequent challenge.

Results: The educational programme produced a wide range of positive feedbacks from the patient community that reported a significant benefit in their coping strategies and in better involving their caregivers and families in their journeys. Different new initiatives were requested by patients and families after the first edition of BehçeTalk: a narrative medicine laboratory was organised and a new edition of BehçeTalk in English will soon be launched to improve the accessibility of the educational programme.

Conclusions: Thanks to the organisation of co-designed educational programmes such as BehçeTalk, patients and families living with BD can bring an important added value in their empowerment, resulting in both increased awareness and improvement of their participation in care.

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VALIDATION OF THE PEDIATRIC BEHÇET DISEASE CRITERIA (PEDBD): A CONSENSUS-BASED APPROACH

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Introduction: Many criteria exist for the diagnosis or classification of BD in adults while in children only classification criteria exist, the PEDBD criteria (2015), created by international Expert consensus.

Objectives: to perform an external validation of the PEDBD criteria

Methods: 210 patients (BD, PFAPA, FMF, MKD, TRAPS, SURF and undefined autoinflammatory diseases, UND) were randomly selected from the Eurofever Registry (patients excluded if they participated in the first PEDBD study). A set of 11 Experts blinded to the original diagnosis, were chosen to evaluate the patients, and reach a consensus defined as > 80%. In the 1st round clinical and serological data were shown; in the 2nd round genetic data were added; in the 3rd round the other Experts' votes and comments were shared with all experts. Using the expert consensus as gold standard, the PEDBD, the ISG and the ICB criteria were applied to BD patients and to the confounding diseases in order to define the sensitivity and specificity.

Results: In the 1st round a consensus was reached in 45/210 (21%) of patients, while in the 2nd round a consensus was reached in another 58/163 (35%) of patients, for a total consensus on 103/210 patients (49%): 31/70 BD, 17/35 FMF, 21/26 MKD, 15/40 PFAPA, 14/22 TRAPS, 3/12 SURF, 2/5 UND. The 3rd round is now ongoing, and data are not available. The next step will consist on the application of the PEDBD, the ISG and the ICB criteria to the cohort of classified BD, and to the other diseases in order to see their performance on BD and confounding diseases

Conclusions: the classification of Behçet disease showed a wide range of opinions among experts. The heterogeneity of the disease is a challenge but a more robust classification can at least allow homogeneous groups of patients for research purpose.

The Authors declare no conflicts of interest

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ACCRUAL OF ORGAN DAMAGE IN BEHÇET'S SYNDROME: TRAJECTORY, ASSOCIATED FACTORS, AND IMPACT ON PATIENTS' QUALITY OF LIFE OVER A 2-YEAR PROSPECTIVE FOLLOW-UP STUDY

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Objectives: To investigate the trajectory of damage accrual, associated factors, and impact on health-related quality of life (HR-QoL) in a multicenter cohort of patients with Behçet's Syndrome (BS) over 2-years of follow-up.

Methods: The patients recruited in the BS Overall Damage Index (BODI) validation study were followed up for two years and assessed for potential damage accrual, defined as an increase ≥ 1 in the BODI score, and HR-QoL changes by the SF-36 questionnaire. Logistic and multiple linear regression models were built to assess the factors associated with damage accrual and impairment in the different SF-36 domains.

Results: During the follow-up, 36 out of 189 (19.0%) patients had an increase ≥ 1 in the BODI score with a mean (SD) difference of 1.7 (0.8). The incidence rate of damage was stable over time regardless of the disease duration. Out of 61 new BODI items, 25 (41.0%) were considered related to glucocorticoid (GC). In the multivariate analysis, the duration of GC therapy (OR per year 1.15, 95%CI 1.07-1.23; $p < 0.001$) and the occurrence of ≥ 1 disease relapse (OR 3.15, 95%CI 1.09 - 9.12; $p = 0.038$) were identified as factors independently associated with damage accrual, whereas the use of immunosuppressants had a protective effect (OR 0.20, 95%CI 0.08-0.54, $p < 0.001$). In addition, damage accrual was independently associated with the impairment in different physical domains and, to a greater extent, in emotional domains of the SF-36 questionnaire. Female gender, higher disease activity, and fibromyalgia were also independently associated with impairment in HR-QoL.

Conclusion: Preventing progressive damage accrual should be the primary target in the management of BS to prevent physical and emotional HR-QoL impairment. Therefore, a timely and adequate immunosuppressive treatment targeted to reducing the risk of disease flares and minimizing the exposure to GCs emerged as the most effective approach.

P098

IMPACT OF BEHÇET'S SYNDROME ON WORK ACTIVITY AND PRODUCTIVITY: RESULTS FROM A SUB-ANALYSIS OF THE BODI PROJECT COHORT

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Objective: To evaluate the impact of Behçet's Syndrome (BS) on the patients' work activity and productivity.

Methods: A sub-cohort of 148 patients was enrolled from the original Behçet's syndrome Overall Damage Index (BODI) study. Demographic and clinical data, as well as the Work Productivity and Activity Impairment: General Health (WPAI:GH) questionnaire results, were recorded in all patients. Multiple regression models were built to investigate the independent effect of BS features on WPAI.

Results: Out of 97 patients working for pay, 22 (27.8%) reported missing work in the past week due to their health (absenteeism), with a mean (SD) proportion of missed working time of 34.4% (17.8). The only factor associated with absenteeism was the BODI ocular damage (β 0.255, p 0.027).

While 93 patients were working, mean 27.3% (30.7) of their actual work productivity was impaired due to their health problem (presenteeism), with only 37 (38.5%) patients denying such loss. Factors associated with work impairment were female gender (β 0.319, p 0.001), higher patient's global assessment (β 0.298, p 0.002), and an increased BODI score in the last 2 years of follow-up (β 0.212 for one-point increased BODI score, p 0.024).

Ninety-nine (66.9%) patients complained of a daily activity impairment, reporting that a mean of 33.3% (30.6) of their regular daily activities had been prevented due to their health problems. Factors significantly associated with patients' daily activity impairment were younger age at enrolment (β 0.187, p 0.021), higher disease activity (β 0.235, p 0.002) and fibromyalgia (β 0.324, p 0.033).

Conclusions: BS can lead to missing work time and significantly affect both the patient's work productivity and daily activities. Active disease seems to be one of the major determinants together with a higher burden of damage and the association of some specific comorbidities.

Table. WPAI:GH questionnaire results (descriptive analysis).

Variables	n*	Mean (SD)
All patients	148	
Patients working for pay	97	
Percent work time missed due to health	97	7.9 (21.7)
Percent work time missed due to health (patients with missed time >0) *	22	34.4 (17.8)
Patients who actually worked in the past seven days**	93	
Percent impairment while working due to health	93	27.3 (30.7)
Percent impairment while working due to health (pts with % impairment while working > 0) ***	56	45.4 (27.2)
Percent activity impairment due to health	148	33.3 (30.6)
Percent activity impairment due to health (those with % activity impairment >0)	99	49.8 (23.9)

*Patients working for pay who missed at least an hour of work, 22/97 = 22.7%.

**Patients working for pay, but who worked for >0 hours in the last week = 93/97.

***Patients with impairment while working >0 among patients who actually worked in the previous 7 days = 56/93.

P099**INTERRELATIONSHIPS BETWEEN HEALTH UTILITY MEASUREMENTS, DISEASE ACTIVITY AND PSYCHOLOGICAL FACTORS IN BEHÇET'S DISEASE**

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Purpose: Behçet's disease (BD) is a chronic, relapsing, systemic inflammatory disease often requiring immunomodulatory therapy. BD also has a profound effect on quality of life including the psychological wellbeing of patients. We have sought to develop a deeper understanding of patients' perception of the personal impact of BD and its influence on their willingness to take risks associated with treatment. Our aims were to measure the direct health utilities Time Trade-Off (TTO) and Standard Gamble (SG) in BD patients and to explore the interrelationships with an indirect measure of health utility EQ-5D-5L, disease activity, depression, anxiety and fatigue.

Methods: TTO, SG, EQ-5D-5L, EQ VAS, depression (PHQ-9), anxiety (GAD-7) and fatigue (MAF) questionnaires were administered to 103 adult BD patients attending the Birmingham Behçet National Centre of Excellence. Disease activity was assessed using the Behçet's Disease Activity Index (BD AI).

Results: Mean TTO was $0.72 \pm \text{SD } 0.27$, mean SG $0.70 \pm \text{SD } 0.34$, and mean EQ-5D-5L $0.519 \pm \text{SD } 0.315$. Moderate to severe depression was identified in 55.2%, moderate to severe anxiety in 35.1% and moderate to high fatigue in 97.7% patients. TTO correlated with SG ($p < 0.01$), EQ-5D-5L ($p < 0.01$) and negatively correlated with depression ($p < 0.01$), anxiety ($p < 0.01$) and fatigue ($p < 0.01$). Multiple linear regression showed SG was the only predictor of TTO ($p = 0.002$). Cluster analysis revealed one cluster where psychological factors rather than disease activity may have influenced TTO and SG scores.

Conclusion: TTO and SG show that BD patients would on average forgo 28% of their remaining life or run a 30% risk of death to avoid the condition. Complex interrelationships with depression, anxiety and fatigue appear to play an important role in their decision making.

There are no conflicts of interest

P100**THE IMPACT OF MULTIFACTORIAL FACTORS ON THE QUALITY OF LIFE OF BEHÇET'S PATIENTS OVER 10 YEARS**

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Introduction: This study analyses the 2020 survey and reviews the 2009, 2014 surveys to ascertain which Behçet's symptoms, personal and family status, patients' lifestyle, and work-related outcomes impacted on Health-Related Quality of Life (HRQoL).

Materials and methods: 459 Behçet's patients submitted an online survey/questionnaire. 326 completed and 133 partially completed the survey. Respondents provided information on socio-demographic characteristics, disease duration, historical and current symptoms, triggers for Behçet's symptoms, systemic and topical medication, health related lifestyle, work-related outcomes regarding employment status and claiming benefits and quality of life measured by EQ-5D index. 419 patients met the inclusion criteria [Males: Females: Others=84:286:2 mean-age=41.1±23.3:38±13.2:40±5].

Results: The main symptoms associated with patients seeking medical care were mouth ulcers 30% and genital ulcers 23%, joint 14% and eye problems 9%. The EQ-5D index for 2009, 2014, 2020 was (mean±SD); 0.47±0.38, 0.42±0.37, 0.34±0.40 respectively p<0.05. Problems reported in 2009, 2014 and 2020 surveys were fatigue (84%, 85.4%; 92%), anxiety and depression (59%, 60%; 72%), difficulty with washing/dressing (35%, 40%; 49%), and problems performing common daily activities (75%, 77.2%; 84%). The symptoms that had significant negative impact on QoL were 2009 (arthropathy, neurological problems, pathergy reaction, and stomach/bowel symptoms), 2014 (arthropathy, headache, neurological problems, pathergy reaction, and skin lesions). 2020 (arthropathy, neurological problems, and stomach/bowel symptoms).

Conclusion: Behçet's symptoms, sociodemographic factors, lifestyle, employment status, and accessing benefits had significant influence on the HRQoL. The 2014 and 2020 surveys reported that QoL is significantly better in patients who continued in employment and not receiving benefits.

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A PILOT STUDY OF BARICITINIB IN TREATING REFRACTORY INTESTINAL BEHÇET'S SYNDROME

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Background and Aims: Intestinal Behçet's Syndrome (BS) is a severe and potentially life-threatening manifestation of BS, characterized by intestinal ulcerations, bleeding, perforation, and bowel obstruction. We conducted a single-center, uncontrolled study to explore the efficacy and safety of baricitinib in refractory intestinal BS.

Methods: We consecutively enrolled 11 patients (five male and six female) with active intestinal BS between October 2020 and March 2022. All the patients received baricitinib (2mg to 4mg daily) combined with glucocorticoids and (or) immunosuppressants tailored to disease activity. The Disease Activity Index (DAIBD) for Intestinal BS, the global gastrointestinal (GI) symptom score and the endoscopic or ultrasound assessment were used for effectiveness evaluation.¹

Results: All the participants had active ulcerative lesions and (or) fistulas despite intensive treatment, including glucocorticoids, multiple immunosuppressants, and biologics. The dosage of baricitinib was escalated from 2mg to 4mg daily in four patients with inadequate response. After a median follow-up of 9 (IQR, 5 – 11) months, 72.73% (8/11) of patients achieved complete remission (CR) on global GI symptom assessments at the last visit. Of the seven patients that were evaluated endoscopically at 5 - 6 months of follow-up, 71.4% (5/7) and 14.3% (1/7) achieved mucosal healing (CR) and marked improvement, respectively. The global GI symptom assessments improved in the two patients with intestinal fistulas, while the fistulas remained stable. Moreover, we found a significant decrease in the DAIBD score, the erythrocyte sedimentation rate, and C-reactive protein level at the last visit compared to baseline. Eight patients managed to taper glucocorticoids, and four had their immunosuppressants dosage decreased. No severe adverse effect or active tuberculosis was observed.

Conclusion: Our pilot study demonstrated that baricitinib is potentially effective and safe in treating refractory intestinal BS.

Competing interests: None declared.

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P102**EFFECTS OF NANOCURCUMIN SUPPLEMENTATION ON T-HELPER 17 CELLS INFLAMMATORY RESPONSE IN PATIENTS WITH BEHÇET'S DISEASE: A RANDOMIZED CONTROLLED TRIAL**Alireza Khabbazi¹, Rojin Farzaneh¹, Mehdi Yousefi²¹Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran, ²Stem Cell Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Aim: Present research was performed to assess the effects of nanocurcumin supplementation on T-helper 17 (Th17) cells inflammatory response in patients with Behçet's disease (BD).

Methods: In this randomized double-blind, placebo-controlled trial, 36 BD subjects were randomly placed into 2 groups to take 80 mg/day nanocurcumin or placebo for 8 weeks. Disease activity, frequency of Th17 cells and expression of related parameters including retinoic acid-related orphan receptor γ (ROR γ t) transcription factor messenger RNA (mRNA), related microRNAs (miRNAs) such as miRNA-155, miRNA-181, and miRNA-326 as well as proinflammatory cytokines including interleukin (IL)-17 and IL-23 were evaluated.

Results: Thirty-two patients (17 in the nanocurcumin and 15 in the placebo groups) completed the trial. Number of Th17 cells decreased significantly in the nanocurcumin group compared to baseline ($P=0.012$) and placebo ($P=0.047$). Moreover, ROR γ t, IL-17, IL-23, miRNA-155, miRNA-181, and miRNA-326 mRNA expression decreased significantly in the nanocurcumin group compared with baseline ($P=0.004$, $P=0.009$, $P<0.001$, $P<0.001$, $P<0.001$, $P<0.001$, respectively) and placebo ($P=0.002$, $P=0.021$, $P=0.006$, $P=0.035$, $P<0.001$, $P=0.017$, respectively). Significant reductions in IL-17 and IL-23 were seen in nanocurcumin group compared with baseline ($P=0.017$ and $P=0.015$) and placebo ($P=0.047$ and $P=0.048$, respectively). Significant reduction in disease activity was observed in nanocurcumin group compared with placebo group ($P=0.035$).

Conclusion: Nanocurcumin supplementation had favorable effects in improving inflammatory factors and disease activity in BD patients. Additional studies are warranted to suggest nanocurcumin as a safe complementary therapy in BD.

Keywords: Behçet's disease, nanocurcumin, T-helper 17 cells, proinflammatory cytokines, microRNA

P103**CANAKINUMAB TREATMENT IN PATIENTS WITH NEURO-BEHÇET'S DISEASE**

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Objective: The objective of this study was to evaluate the efficacy of canakinumab in patients with neuro-Behçet's Disease (NBD).

Background: Exaggerated neutrophil function is a key component in Behçet's disease (BD) pathogenesis. This is associated with IL-1 production by various types of cells including macrophages, monocytes, fibroblasts, lymphocytes, and dendritic cells. In patients with refractory BD, IL-1 suppression appears to be promising, since IL-1 inhibitors are effective in BD-related uveitis. Canakinumab is a fully human anti-IL-1 β monoclonal antibody approved for periodic fever syndromes and Still's disease. No previous study has investigated canakinumab in NBD.

Design/Methods: Patients with NBD were treated with canakinumab 300 mg IV in the acute stage that is followed by five 150 mg IV and six 150 mg SC doses per month. Patients were followed for 12 months with monthly visits and prescheduled brain MRIs.

Results: We treated three male NBD patients with canakinumab; two with parenchymal-NBD (p-NBD) and one with cerebral venous sinus thrombosis (CVST). In the acute stage, two patients received canakinumab 300 mg IV that is followed by five-monthly doses of 150 mg IV and six-monthly doses of 150 mg SC. In the second month, one patient required a second dose of canakinumab 300 mg IV and five days of methylprednisolone 1000 mg IV. After two months, all patients had a complete or almost complete radiological and clinical response to canakinumab (Figure 1-3, attached). Canakinumab had no serious side effects in any of the patients.

Conclusions: Canakinumab resulted in remarkable resolution of parenchymal and vascular lesions, even without prolonged steroid treatment. This alludes to the presence of detrimental IL-1-related pathways in both the acute and chronic phases of NBD. The reappearance of some systemic symptoms after switching from IV to SC administration may indicate the importance of canakinumab serum levels in response to therapy.

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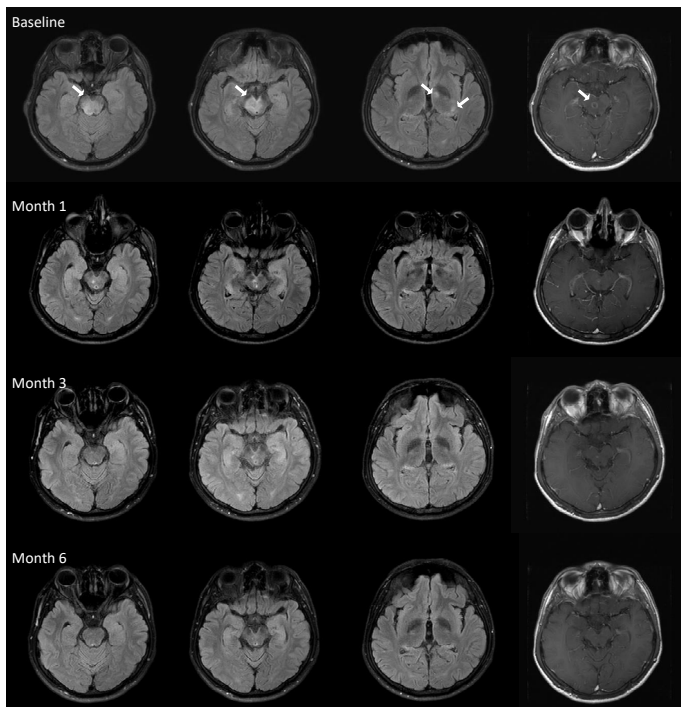


Figure 1. Brain MRI's of patient 1. Axial flair (first three columns) and axial contrast enhanced T1 sections. Baseline MRI shows a ponto-mesencephalic contrast-enhancing lesion that extends to the left thalamus. Note the profound resolution of the perilesional edema after one month and complete resolution of the lesion after six months.

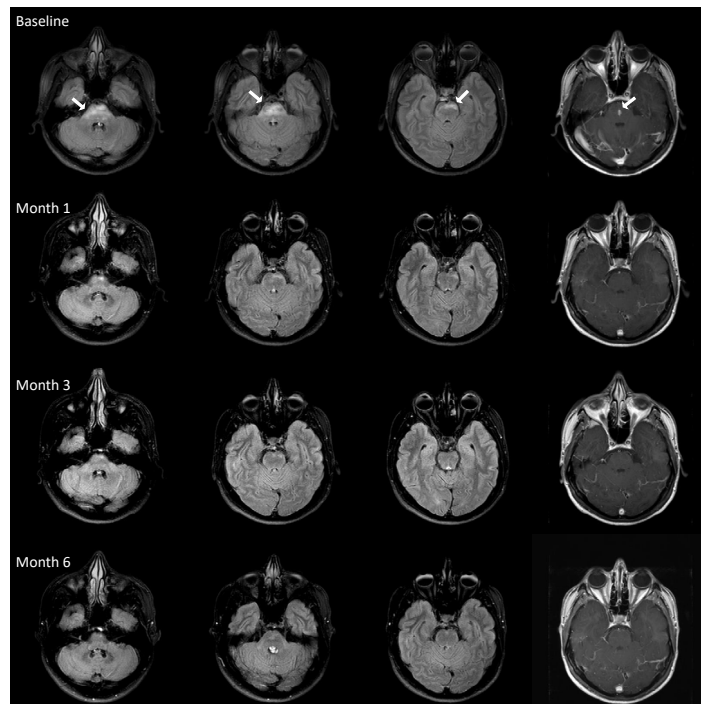


Figure 2. Brain MRIs of patient 2. Axial flair (first three columns) and axial contrast enhanced T1 sections. Baseline MRI shows a contrastenhancing lesion in the pons that resolves completely after six months of canakinumab treatment.

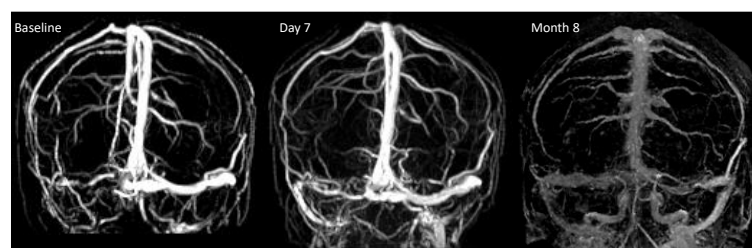


Figure 3. Brain MR venography of patient 3 (Antero-posterior view). Thrombosis and complete occlusion of the right cerebral venous sinus. Note the partial recanalization seven days after canakinumab treatment and complete recanalization after eight months.

P104**INFLIXIMAB FOR VASCULAR INVOLVEMENT IN BEHÇET SYNDROME**

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Background: Vascular involvement is an important cause of morbidity and mortality in patients with Behçet's syndrome (BS). We aimed to survey the efficacy and safety of infliximab (IFX) in BS patients with vascular involvement followed in a dedicated tertiary center.

Methods: Charts of all BS patients who used IFX for vascular involvement between 2004-2021 were reviewed. Primary endpoint was remission at Month 6, defined as lack of new clinical symptoms/findings associated with vascular lesion, lack of worsening of the primary vascular lesion, lack of a new vascular lesion on imaging, and CRP<10 mg/L. Relapse was defined as development of a new vascular lesion or recurrence of preexisting vascular lesion.

Results: Among the 127 patients (102 men, mean age at IFX initiation: 35.8 ± 9 years) treated with IFX, 110 (87%) received IFX for remission induction and 87/110 (79%) were refractory to conventional treatments. Remission rate was 73% (93/127) at Month 6 and 63% (80/127) at Month 12 (Table 1). 17/100 (17%) patients experienced 22 relapses. Adverse events leading to IFX discontinuation were allergic reactions (n=5), tuberculosis, disseminated zona, lung adenocarcinoma, fibromyxoid sarcoma, heart failure, systemic lupus erythematosus, palmoplantar pustulosis, auricular chondritis, and aortic stent graft infection. Four patients had died and reasons for death were lung adenocarcinoma, sepsis, and pulmonary hypertension related right heart failure due to pulmonary artery thrombosis (n=2).

Conclusion: Infliximab seems to be effective in majority of BS patients with vascular involvement, even in those who are refractory to immunosuppressives and corticosteroids.

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Table 1. Concomitant drugs and outcomes

	Venous thrombosis (n=61)	Pulmonary involvement (n=37)	Non-pulmonary involvement (n=16)	Venous ulcers (n=13)	Overall (n=127)
Treatment for remission induction, (n, %)	57 (93)	27 (73)	13 (81)	13 (100)	110 (87)
Number of patients who used concomitant immunosuppressives, (n, %)	48 (79)	25 (68)	14 (88)	8 (62)	95 (75)
Concomitant drugs, (n, %)	58 (47)	34 (94)	15 (100)	9 (75)	116 (94)
Corticosteroid	53 (87)	33 (89)	16 (100)	9 (67)	111 (87)
Corticosteroid dose (mean \pm SD mg)	30 \pm 18.7	28 \pm 22.2	28 \pm 16.6	18 \pm 24.2	28 \pm 20.1
Azathioprine	34 (56)	19 (51)	11 (69)	7 (54)	71 (57)
MMF	7 (11)	2 (5)	0	0	9 (7)
Cyclophosphamide	3 (5)	4 (11)	3 (19)	0	10 (8)
Cyclosporine - A	3 (5)	0	0	0	3 (2) ^a
Methotrexate	1	0	0	1	2 (2)
Duration of IFX use (mean \pm SD months)	26 \pm 19	26 \pm 19	40 \pm 28	25 \pm 24	28 \pm 22
Remission rate at month 6, (n, %)	50 (82)	31 (84)	11 (69)	1 (8)	93 (73)
Remission rate at month 12, (n, %)	43 (70)	25 (68)	10 (63)	2 (15)	80 (63)
Relapse rate during IFX, (n, %)	4 (7)	6 (16)	7 (44)	0	17 (13)
Number of patients who discontinued IFX ^b , (n, %)	31 (51)	23 (62)	6 (37)	9 (69)	69 (54)
Due to remission	15	6	0	1	22 (17)
Due to inefficacy	3	1	3	4	11 (9)
Due to relapse	1	0	1	0	2 (2)
Due to adverse event	7	4	2	1	14 (11)
Due to noncompliance	3	4	0	3	10 (8)
Due to new organ development	1	0	0	0	1
Due to other reasons ^c	1	8	0	0	9 (7)
Death	2	2	0	0	4 (3)

IFX: Infliximab, MMF: Mycophenolate mofetil

a. Two patients used cyclosporine-A in combination with azathioprine.

b. Remission and relapse rates during the second time IFX was used among the 15 patients who restarted IFX are not included here.

c. Other reasons were preparation for surgical operation (n=2), not wanting to come to the infusion frequently during the pandemic (n=2), pregnancy (n=1), willing to get pregnant (n=1), lack of health insurance (n=1), due to prison sentence (n=1), and death (n=1).

P105**SUCCESSFUL TREATMENT OF RECURRENT ORAL AND GENITAL ULCERS IN BEHÇET'S DISEASE WITH RITUXIMAB- A CASE SERIES**

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Introduction: Behçet's disease, also known as malignant aphthosis, is a neutrophilic autoinflammatory dermatosis with multisystem vasculitis. Rituximab acts by inhibiting the entire lineage of B cells containing CD 20 receptors, apart from plasma cells and pre-pro B cells. This, coupled with suppression of antigen presentation and cytokinemia, secondary to T-cell inhibition, is the chief mechanism of action of Rituximab in Behçet's disease, especially useful in recalcitrant disease.

Case Series: Herein, we report a series of 11 cases of Behçet's disease with recalcitrant oral ulcers successfully who were successfully managed with Rituximab. All patients were histopathologically proven cases of Behçet's disease with oral and ocular involvement, on and off treatment for the last 2-3 years with various drugs including systemic steroids, cyclophosphamide, colchicine, dapsone, and apremilast. Two patients had neurological involvement, while one had renal involvement. The patients had experienced multiple recurrences and little to no response with prior treatments. After a thorough analysis to rule out any other systemic illness or infection, the patients were planned for treatment with Rituximab according to rheumatoid arthritis protocol. Two doses of 1 gm Rituximab were given intravenously, one month apart. All the patients experienced clearance in lesions within the next 3 months. The case was kept in follow-up for the next 1 year with the appearance of no new lesions.

Conclusion: Rituximab is a promising and safe modality that can be reliably utilized for the management of cutaneous and systemic symptoms of Behçet's disease with a sustained and prolonged effect.

Keywords: Behçet's disease, rituximab, neurological, renal

P106**EFFICACY AND SAFETY ON APREMILAST IN BEHÇET'S DISEASE PATIENTS**

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Objectives: To evaluate the efficacy and safety of APR(Apremilast) treatment in BD(Behçet Disease)patients.

Methods: Descriptive study of BD patients on APR treatment(2017- 2021). Demographic, clinical and analytical data were collected.

Results: 15 patients(12 women) were included, with a mean age at the beginning of APR treatment of 36±11 years and a median disease evolution of 48(9,145)months. 8 of them showed HLAB51.

Before APR, 8 patients were refractory to DMARDs(3 MTX,4 AZA,1 HQ) and one patient to 2 anti-TNF(ADA, IFX). All patients were under treatment with colchicine and 7 with steroids before APR therapy. The concomitant treatment were: corticosteroids(7), NSAIDs(2), colchicine(8), MTX(2), AZA(2), HQ(1).

The main symptoms at the beginning of the APR treatment were: oral ulcers(93%), genital ulcers(47%) and arthritis(67%). We observed a clinical improvement after 3 months of treatment of 93% of oral ulcers, 100% of genitals and 70% of joint symptoms. The patients had a median follow-up of 12(4,26)months.

Patients presented adverse events: headache(7), diarrhea(8), nausea(5), abdominal pain(2), dysthymia(1), tremors(2), herpes zoster(1) and autolytic ideation(2). The treatment was withdrawn in 10 patients with a median duration of 5(3,12)months. 2 were by autolytic ideation and nausea, 1 for diarrhea, 2 for abdominal pain, 2 for genic desire (1 restarted), 1 primary and 2 for secondary failure. The APR doses were reduced to 30 mg/day in 5 patients, resolving the adverse events and persisting therapy response in patients who continued treatment. Dose reduction of colchicine and prednisone in 5 patients was achieved.

We observed other previous manifestations of BD such as uveitis(4), neurobehçet(3), folliculitis(5), panniculitis(1) and venous thrombosis(1). Cutaneous manifestations were resolved and the rest remain without changes.

Conclusion: We observed an improvement in the most common manifestations of BD and a safety profile similar to those described in other studies.

Disclosure of interest: None declared

P107**CAN GLUCOCORTICOIDS WITHDRAWAL REPRESENT A CHALLENGE IN BEHÇET'S DISEASE? A CATEGORIAL DATA ANALYSIS IN A MONOCENTRIC COHORT**

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Background: When active manifestations occur in Behçet's disease (BD), systemic glucocorticoids (GCs) are essential to induce remission. Scarce evidence is available about how frequently GCs are used in the long-term as well the reason of their withdrawal-failure.

Objective: The aims of the study were: i) to characterize the profile of BD patients taking GCs at the last evaluation, including the reasons behind the withdrawal-failure and ii) to compare their profile with patients not taking GCs.

Methods: One-hundred patients regularly followed-up for at least 24 months were consecutively enrolled. Demographic, clinical and therapeutical data were collected, including GC assumption, daily dosage, and duration; patients were identified as GCs + or GCs -. A categorical data analysis was performed to explore the reasons of non-withdrawal in GCs+: recent BD relapse, inability to reduce current dosage for disease recurrence, and steroid addiction (meant as occurrence of manifestations non-BD-related).

Results: GCs + group included 40 patients, while 60 patients were GCs- at the last evaluation. Both groups were mainly represented by females (75% GCs+, 62% GCs-). Overall mean age was 49 years and disease duration was most commonly 3–10 years. GCs+ group showed higher rates of colchicine and immunosuppressive therapy, while no significant differences were observed in terms of organ involvement.

In the GCs+ 32 patients (80%) assumed a daily prednisone equivalent dose ≤ 5 mg, because of recent relapse in 30% of cases, disease recurrence at tapering in 30% and steroid addiction in 40%. The mean cumulative GC duration in the last 2 years in GCs+ and GCs- was 17.3 and 1.8 months, respectively.

Conclusions: Despite a similar control of disease activity, the main reason for GC assumption seems to be represented by steroid addiction. Such acknowledgement highlights the need to improve the therapeutical approach in BD patients allowing stable steroid discontinuation.

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VALUE OF TDM IN PATIENTS WITH BEHÇET SYNDROME AND TNF-INHIBITOR TREATMENT

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Background: As for the management of Behçet syndrome (BS), TNF-inhibitors (TNFi) such as infliximab (IFX) or adalimumab (ADL) are available on indication (other biologicals are not reimbursed). Incidence of active disease during TNFi-treatment have been described.

Previous studies (1-3) on efficacy of TNFi and antidrug antibodies (ADA) in BS organized the sampling of the serum measurements prospectively in all patients treated (1-3), in some, patients were grouped according to efficacy (2,3). Drug adjustments were guided by the clinical picture.

Objective: The aim of this study is to explore the value of therapeutic drug monitoring (TDM) by utilizing a retrospective analysis of BS-patients with active disease during TNFi-treatment.

Methods: In our BS-cohort of 70 patients, the number of patients treated with TNFi including indications, serum trough level and ADA measurements in patients with active disease, i.e. probable therapy failure, were noted. Patients were assigned to the different failure groups according to the serum trough TNFi levels and ADA in accordance with literature.

Results: Of 16 patients treated with TNFi, 6 had active disease, in whom 9 serum measurements were analyzed (Table 1). ADA were found in 4 (44.4%, 95% Confidence Interval (CI) [18.9,73.3]) and inadequate serum TNFi-levels in 2 (22.2%, 95% CI [6.3,54.7]). The remaining 3 (33.3%, 95% CI [12.1,64.6]) measurements showed active disease despite apparently adequate drug levels.

Conclusion: This study is the first to apply TDM in patients with active BS despite TNFi and describes a new classification of TDM. This corresponding classification helps the physician towards a substantiated treatment decision, although an exact cut-off value between insufficient and adequate TNF trough levels needs to be established. TDM in TNFi is especially useful in BS, considering the context of limited number of (reimbursed) biologicals for BS.

Keywords: Behçet syndrome (BS), tumor necrosis factor inhibitor (TNFi), antidrug antibodies (ADA), therapeutic drug monitoring (TDM)

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Table 1. Blood TNFi trough level/ADA determination of patients with active Behçet during TNFi treatment.

Patient nr.*	Indication TNFi treatment	TNFi	Indication drug serum determination	Result Serum [TNFi] measurement (µg/mL)	Result Serum [ADA] measurement (AE/mL)	
1a	Uveitis with oral aphthae and erythema nodosum	ADL	Persistent erythema nodosum and oral aphthae	-	980	ADA[^] 44.4%, 95% CI
2a	Thrombophlebitis with oral aphthae	ADL	Active orogenital aphthae, thrombophlebitis	0	75	
3	Uveitis, Retinitis with oral aphthae	ADL	Recurrent retinitis as soon as Prednisolone dose was lower than 40 mg/day	2,3 ^{\$}	59	
2c	Thrombophlebitis with oral aphthae	IFX	Active orogenital aphthae and folliculitis	0,4	34	
1b	Uveitis (ocular flare) with regular oral aphthae and erythema nodosum	IFX	Oral aphthae with active anterior uveitis	1,4	-	Insufficient TNFi serum[^] 22.2%, 95% CI
4	Orogenital aphthae, thrombophlebitis with deep vein thrombosis	IFX	Hemoptoe, no infection present	0,8	<12	
5	Retinitis with blindness left eye and oral aphthae	ADL	Grade 1 ocular flare anterior (cells present)	20	<12	Moderate-high TNFi^{#^} 33.3%, 95% CI [12.1,64.6]
6	Orogenital aphthae with severe pustular lesions	ADL	Active with severe folliculitis and high ESR	9,5	-	
2b	Thrombophlebitis with oral aphthae	IFX	Mild active Behçet with oral aphthae, skin abnormalities on the elbows and arthritis	2,8	-	

*The added a, b and c after the patient number is chronological.

#Verboom et al. there was a steady state serum level of 8.78 µg/mL (range: 1.96-16.00) after 6 months follow up.¹

[^]Classification in type of therapy failure has been based on the blood serum [TNFi] and [ADA] measurements

ADL, adalimumab; IFX, infliximab; ADA, antidrug antibodies; TNFi, TNF-inhibitor

^{\$}Therapy failure is based on the inability to taper prednisolone below 40 mg/daily in the presence of a low level of ADL and ADA.

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COMPARATIVE EFFECTIVENESS OF VARIOUS IMMUNOSUPPRESSIVE THERAPY REGIMENS FOR UVEITIS IN PATIENTS WITH BEHÇET'S DISEASE

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Aim: to evaluate the effectiveness of various immunosuppressive therapy schemes for current uveitis in Behçet's disease (BD) patients.

Material and methods: the study included 531 patients with BD, observed in the Institute of Rheumatology from 2006 to 2020. The majority were men (331 (62.3%)). The mean age (M±SD) was 32.9±10.0 years, the median duration of BD (Me [25%; 75%]) – 96 [48; 174] months. 60.4% patients had uveitis, 70.7% - exacerbation of uveitis (EU). Uveitis activity was assessed by the BOS24 index, the total activity of BD - by BDCAF. 68.7% patients with EU received Glucocorticoids (GC); 88.9% - cytotoxics: 33.5% - cyclosporine (CS), 20.7% – azathioprine (AZA), 11.4% - AZA+COL, 8.8% - AZA+CS, 7.5% – colchicine (COL), 3.9% – cyclophosphamide (CPh); 11.9% - Biologics, mainly i-TNF-α (11.4%). The effectiveness of therapy was evaluated on average after 18.0 [8.0; 36.0] months.

Results: the BDCAF to the end of follow-up significantly decreased in all groups except COL-group. A more significant decrease in BDCAF was observed in the combination therapy groups (AZA+CS (ΔBDCAF=-4.08±3.60), AZA+COL (ΔBDCAF=-3.57±2.50)), and in the CS group (ΔBDCAF=-3.57±3.39), without significant differences between the groups. There were no significant differences between patients who received/ didn't receive Biologics (ΔBDCAF=-3.41±3.89/ -3.59±3.23) (Fig. 1).

The most effective for relieving EU were CS (ΔBOS24=-7.0 [-12.0; -3.0]), AZA (ΔBOS24=-7.0 [-15.0; -2.0]), a combination of CS + AZA (ΔBOS24=-5.0 [-8.0; -2.0]) and CPh (ΔBOS24=-4.0 [-14.0; -2.0]). The differences between BOS24 before and after treatment in these groups were significant. Uveitis therapy by CS was more effective compared to AZA+COL and COL; and AZA treatment, compared to COL. Biologics, mainly adalimumab, significantly and rapidly reduce the severity of uveitis (ΔBOS24=-7.0 [-18.0; 0]) compared with GC and cytotoxics (ΔBOS24=-4.0 [-9.0; -1.0]) (Fig. 2).

Conclusion: CS, AZA and their combination, as well as i-TNF-α are more effective for relieving uveitis symptoms in BD patients. BOS24 is a reliable tool for quantifying the activity of uveitis in BD patients and its dynamics against the background of anti-inflammatory and immunosuppressive therapy.

P110**PULMONARY ENDARTERECTOMY FOR BEHÇET'S DISEASE: WHAT IS GOING ON?**

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Background: Behçet's disease is a multisystem disorder and is not known as a risk factor for chronic thromboembolic pulmonary hypertension, for which the treatment of choice is pulmonary endarterectomy. The aim of this study was to review our experience in the surgical treatment of CTEPH in patients with BS.

Methods: Data were collected prospectively for consecutive patients with Behçet's disease who underwent surgery over a 12-year period.

Results: We identified twenty patients (14 males, six females, mean age: 39.8 (20-68 years)) with Behçet's Disease. The mean disease duration before PEA was 81.0±67.2 months. All patients but two received immunosuppressive therapy before the surgery. Exercise-induced dyspnea presented symptoms in 17 patients. One patient had associated intracardiac thrombosis. Pulmonary endarterectomy was bilateral in 16 patients, unilateral in three, and lobar in one. No perioperative mortality was observed; however, one patient died four weeks after PEA due to massive hemoptysis. Morbidity was observed in four patients. The mean pulmonary artery pressure fell significantly from 32.9mm Hg to 24.8 mm Hg after surgery ($p=0.01$). Pulmonary vascular resistance also improved significantly from 514 to 2362 dyn/s/cm⁵ ($p=0.01$). After a median follow-up of 54.8 months, all patients improved to the New York Heart Association (NYHA) functional class I and II. Recurrence was observed in one patient.

Conclusion: Patients with Behçet's disease may suffer recurrent pulmonary thrombosis and develop chronic thrombosis in pulmonary arteries. In patients who do not respond to anticoagulation or immunosuppressive therapy, pulmonary endarterectomy may be a therapeutic option when thrombotic lesions are surgically accessible. Due to the high risk of perioperative mortality, the procedure should be undertaken in centers with experience.

P111**EARLIER AND MORE AGGRESSIVE TREATMENT OF MAJOR ORGAN INVOLVEMENT WITH BIOLOGICS MAY PREVENT RELAPSES OR FURTHER NEW ORGAN INVOLVEMENT IN BEHÇET'S DISEASE**

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Objective: Immunosuppressives (IS) are used for the treatment and the prevention of major organ involvement in Behçet's disease (BD). In this study, we aimed to investigate the rate of relapse/new major organ development in patients under ISs during follow-up and to compare different treatment protocols.

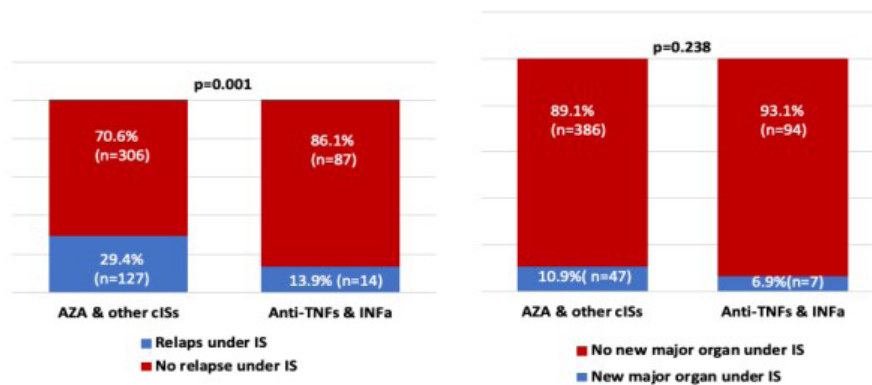
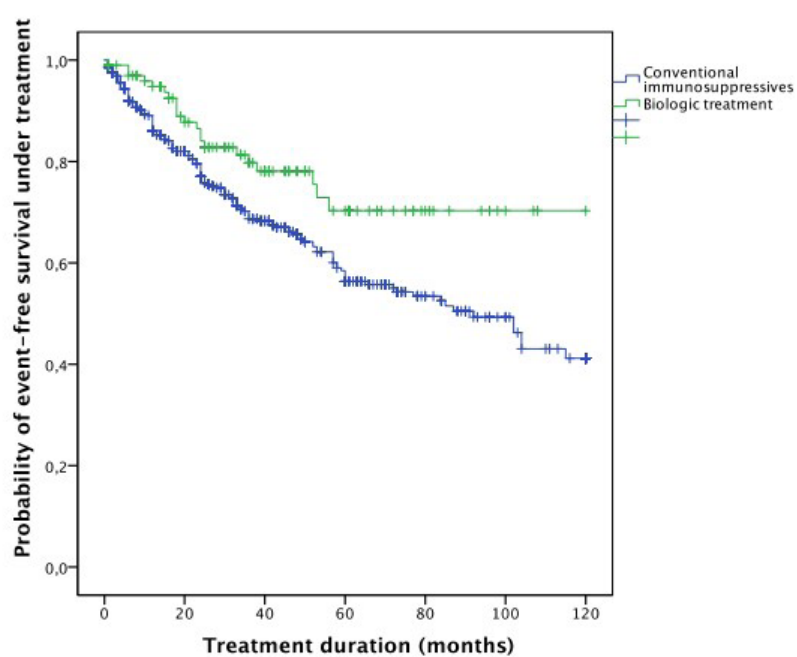
Methods: 1114 patients diagnosed with BD were overviewed retrospectively. Patients with a follow-up period less than 6 months were excluded. All data were acquired from files. Conventional IS (cIS) and biologic treatment courses were compared. Tumor necrosis factor (TNF) inhibitors and interferon-alpha included in biologics. 'Events under IS' defined as relapse of the same organ and/or new major organ development of patients receiving IS.

Results: 806 patients were included in the analysis, of whom 56% were male. Median follow-up time was 68 (6-272) months, median age at diagnosis was 29 (10-65). 232 (50.5%) patients had major organ involvement at diagnosis, 227 (49.5%) patients developed new major organ involvement at follow-up. Major organ involvement developed earlier in males ($p=0.012$) and in patients with a first-degree relative history of BD. The frequency of vascular, ocular, CNS and GIS involvement was 29.8%, 33.5%, 9.7%, and 2%. The majority (86.8%) of 440 patients were received IS due to major organ involvement. 'Events under IS' developed 160 (36.4%) patients. 109 (68.1%) of these 160 patients had a relapse, 24 (15%) had a new major organ involvement, and 27 (16.9 %) had both. 'Events under IS' ($p=0.004$) and relapses ($p=0.001$) were more common under cISs (Figure 1). The cumulative event-free survival was higher with biologics compared to cISs ($p=0.014$) (Figure 2).

Conclusion: Major organ involvement occurred in 57% of the patients. In 36% of the patients had a relapse/new major organ involvement under IS. Events under IS, was less common with biologics compared to cISs. These results suggest that earlier and more aggressive treatment may be an option in patients who had the highest risk for severe disease course.

Disclosures: None

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Figure 1. Events under cIS and biologic treatments.**Figure 2.** Kaplan-Meier curves showing the cumulative event-free survival under treatment.

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IL-6 BLOCKADE FOR BEHÇET'S DISEASE: REVIEW ON 31 ANTI-TNF NAÏVE AND 45 ANTI-TNF EXPERIENCED PATIENTS

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Background: Despite the remarkable efficacy of anti-TNF agents in Behçet's disease (BD), unmet therapeutic needs for refractory or intolerant patients to these drugs still exist. Based on evidence implicating IL-6 in the pathogenesis of BD, we summarize the current experience on the off-label administration of the anti-IL-6 receptor antibody Tocilizumab for BD refractory to disease modifying anti-rheumatic drugs.

Methods: We searched Medline/Pubmed for original articles published through December 2021 reporting on the use of Tocilizumab for BD.

Results: We retrieved 25 articles fulfilling our search criteria, reporting on a total of 74 patients of whom 31 were anti-TNF naïve; 2 additional anti-TNF experienced patients from our center were included. The vast majority (72 of 76) received the standard intravenous dose of tocilizumab, whereas follow-up ranged from 2 to 84 months, without new safety issues. Tocilizumab was given in anti-TNF naïve patients predominantly for vascular (n=16), central nervous system (n=7) and ocular involvement (n=5). On the other hand, anti-TNF experienced patients received tocilizumab predominantly for ocular (n=28), central nervous system (n=8) and mucocutaneous involvement (n=6). Tocilizumab was effective in 87% of anti-TNF naïve (13 and 14 with complete/partial remission, respectively) and in 80% of anti-TNF experienced patients (17 and 19 with complete/partial remission, respectively).

Conclusion: Although preliminary, the current evidence published so far suggests that IL-6 inhibition is a legitimate therapeutic option for BD patients with refractory ocular, CNS and vascular involvement. Controlled studies are clearly needed.

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