Letters to the Editors

Serum CXCL13 is not elevated in ocular Behçet's disease: a brief report

Dear Editors,

Between September 2025 and February 2026, we carried out a cross-sectional study to compare serum levels among Behçet's disease (BD) patients with and without ocular involvement.

Serum CXCL13 levels were measured by ELISA (Sunred 201-12-5345) in 37 BD patients with ocular involvement, 23 BD patients without ocular involvement, and 28 age- and sex-matched healthy controls at a tertiary referral centre. All BD patients met the International Study Group criteria (1), and ocular disease activity was assessed using the Behçet's Disease Ocular Attack Score 24 (BOS24) (2). Non-parametric tests were used with Benjamini-Hochberg false discovery rate (FDR) correction.

Median serum CXCL13 did not differ across the three groups: 198.0 pg/mL (IQR 168.4–303.3) in ocular BD, 237.5 (203.7–355.1) in non-ocular BD, and 267.7 (202.9–307.6) in controls (Kruskal-Wallis p=0.292). No correlation was found between CXCL13 and BOS24 (ϱ= -0.006, p=0.963), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or anterior chamber cell grade. The study had 89% power to detect $\varrho \geq 0.50$. Within the ocular BD subgroup, the six patients on anti-TNF therapy showed numerically higher CXCL13 than untreated patients (388.6 *vs*. 192.6 pg/mL; unadjusted p=0.037), although this did not survive FDR correction (adjusted p=0.203) and should be regarded as hypothesis-generating only. BOS24 behaved as expected, with strong correlations with anterior chamber cells (ϱ=0.758) and posterior segment involvement (r=0.924; both FDR p=0.011) (2).

It is fair to ask why CXCL13, a B-cell chemoattractant central to lymphoid neogenesis and to several classical autoimmune disorders (3), should be considered in BD, an MHC-I-opathy (4) driven by neutrophils and T cells without recognised autoantibodies. Our rationale was more focused on the uveal inflammation side rather than BD itself. First, the only previous serum measurement in BD reported a non-significant trend (p=0.161) and was not stratified by ocular phenotype or compared against a validated ocular activity index (5). Second, aqueous humor data show CXCL13 enrichment in granulomatous uveitis (Vogt-Koyanagi-Harada disease, idiopathic granulomatous uveitis) but not in BD-associated uveitis (6, 7), a compartment-specific signal that warranted systemic verification. Third, Pay *et al*. previously reported elevated CXCL13 in BD synovial fluid (8), raising the possibility that local lymphoid neogenetic activity could appear in the circulation under heavy ocular inflammation. Furthermore, transcriptomic profiling of BD blood mononuclear cells confirmed a predominantly innate-immune signature (9) but did not formally exclude a minor adaptive contribution. From this point of view, our null systemic data complement rather than contradict the prevailing model and add the missing ocular-stratified piece.

Our cross-sectional design captured CXCL13 at a single time point; we plan to recall a subgroup during the next active attack and after treatment escalation for longitudinal sampling. Non-BD uveitis disease controls (HLA-B27-associated, sarcoidosis, VKH) were not enrolled. Given our negative result, parallel inclusion would have served mainly to demonstrate assay dynamic range, which our high outliers (up to 9366 pg/mL) and previous aqueous humour work (6, 7) already establish, although prospective multicentre studies should incorporate them.

In light of the current data, serum CXCL13 does not distinguish BD patients, with or without ocular involvement, from healthy controls and shows no relationship with BOS24 or systemic inflammatory markers. The result is biologically consistent with the neutrophilic, MHC-I-restricted phenotype of BD (4, 9) and with the absence of CXCL13 enrichment in non-granulomatous aqueous humour (6, 7). Further prospective longitudinal studies are warranted to evaluate the anti-TNF signal observed in our small subgroup.

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References

1. INTERNATIONAL STUDY GROUP FOR BEHÇET'S DISEASE: Criteria for diagnosis of Behçet's disease. *Lancet* 1990; 335: 1078-80. https://doi.org/10.1016/0140-6736(90)92643-v
2. KABURAKI T, NAMBA K, SONODA K-H *et al*.: Behçet's disease ocular attack score 24: evaluation of ocular disease activity before and after initiation of infliximab. *Jpn J Ophthalmol* 2014; 58: 120-30. https://doi.org/10.1007/s10384-013-0294-0
3. PAN Z, ZHU T, LIU Y, ZHANG N: Role of the CXCL13/CXCR5 axis in autoimmune diseases. *Front Immunol* 2022; 13: 850998. https://doi.org/10.3389/fimmu.2022.850998
4. LECCESE P, ALPSOY E: Behçet's disease: an overview of etiopathogenesis. *Front Immunol* 2019; 10: 1067. https://doi.org/10.3389/fimmu.2019.01067
5. LEE SJ, KANG SE, KANG EH *et al*.: CXCL10/CXCR3 axis is associated with disease activity and the development of mucocutaneous lesions in patients with Behçet's disease. *Sci Rep* 2017; 7: 14720. https://doi.org/10.1038/s41598-017-15189-9
6. ABU EL-ASRAR AM, BERGHMANS N, AL-OBEIDAN SA *et al*.: The cytokine interleukin-6 and the chemokines CCL20 and CXCL13 are novel biomarkers of specific endogenous uveitic entities. *Invest Ophthalmol Vis Sci* 2016; 57: 4606-13. https://doi.org/10.1167/iovs.16-19758
7. ABU EL-ASRAR AM, BERGHMANS N, AL-OBEIDAN SA *et al*.: Differential CXC and CX3C chemokine expression profiles in aqueous humor of patients with specific endogenous uveitic entities. *Invest Ophthalmol Vis Sci* 2018; 59: 2222-28. https://doi.org/10.1167/iovs.17-23225
8. PAY S, MUSABAK U, SIMSEK I *et al*.: Synovial lymphoid neogenetic factors in Behçet's synovitis: do they play a role in self-limiting and subacute course of arthritis? *Clin Exp Rheumatol* 2007; 25 (Suppl. 45): S21-26.
9. VERROU K-M, VLACHOGIANNIS NI, AMPATZIADIS-MICHAILIDIS G *et al*.: Distinct transcriptional profile of blood mononuclear cells in Behçet's disease: insights into the central role of neutrophil chemotaxis. *Rheumatology* (Oxford) 2021; 60: 4910-19. https://doi.org/10.1093/rheumatology/keab052