RHEUMATOLOGY RESEARCH JOURNAL

Vol.10, No. 3, July 2025,
Webpage: http://rheumres.org
Email: http://rheumres.org
ISSN:2476-5856
doi: 10.32592/RR.2025.10.3.142

Case Report Open Access

Report of a case of Behçet's disease with unusual presentation

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Behçet's Disease (BD) is a chronic, multisystem inflammatory disorder, typically characterized by recurrent oral and genital ulcers, uveitis, and skin lesions. However, atypical presentations—particularly with isolated neurological or ocular involvement—can delay diagnosis. We present a rare case of Behçet's disease in an 18-year-old male who presented with retrobulbar neuritis and neurological symptoms in the absence of active oral ulcers. The patient initially presented with unilateral retrobulbar neuritis, persistent headaches, dizziness, and cutaneous manifestations including erythema nodosum and papulonecrotic lesions. Remarkably, no oral ulcers were observed during active disease. The Pathergy test was initially positive but turned negative after initiating treatment. A comprehensive evaluation including cranial computed tomography, laboratory markers, and HLA-B51 testing was performed. Differential diagnoses such as multiple sclerosis and neurosarcoidosis were carefully excluded. The diagnosis of atypical Neuro-BD was established based on clinical criteria and exclusion of mimickers. Treatment with high-dose corticosteroids, azathioprine, colchicine, and acetazolamide was initiated. The absence of classic mucosal findings and the occurrence of rare symptoms such as retrobulbar neuritis pose significant diagnostic challenges, emphasizing the diversity of manifestations of BD. This case highlights the importance of considering atypical BD in patients with unexplained neurological and ocular symptoms. Retrobulbar neuritis, although rare in BD, may be the initial manifestation. The dynamic change in Pathergy test reactivity during treatment further underscores the complexity of disease monitoring. Early recognition and tailored therapy are essential for favorable outcomes.

Keywords: Behçet's disease; atypical presentation; inflammatory disorders; retrobulbar neuritis; neuro Behcet's disease

Introduction

Behçet's Disease (BD) is a rare, systemic inflammatory disorder that is recognized by the presence of recurrent oral and genital ulcers, ocular inflammation, and skin lesions [1]. This condition can involve various organ systems, including the nervous, gastrointestinal, and vascular systems [2]. The disease typically begins in the third decade of life, with males being more severely affected than females. It is more common in Turkish (14–20 per 100,000), Mediterranean, and Middle Eastern regions, sometimes referred to as the Silk Road disease [3,4]. Atypical presentations and overlap with other diseases pose significant diagnostic challenges. This case report describes the clinical course and treatment of an 18-year-old male with an unusual presentation of BD, highlighting

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Received: 17 June 2025; **Accepted:** 7 July 2025

diagnostic and therapeutic challenges. The goal of this report is to emphasize the importance of early identification and specialized therapeutic approaches in cases with nonspecific symptoms.

Case Presentation

An 18-year-old male, with a known history of recurrent oral ulcers over the past two years, presented with a recent onset of unusual systemic symptoms. The oral ulcers, which had typically occurred four to five times annually, had previously responded well to topical treatments. However, due to the patient's non-adherence to follow-up appointments, ongoing management was discontinued, leading to an interruption in treatment. In May 2023, the patient—an active football player—began experiencing recurrent episodes of chills specifically during training sessions. These chills initially occurred sporadically but gradually became more frequent and severe, eventually lasting up to 30 minutes each day. Despite the persistence of these symptoms over a period of two months, the patient did not seek medical attention until they significantly interfered with his daily activities. Interestingly, during this time, the patient did not report any recurrence of oral ulcers.

Initial medical consultations

1. *General Practitioner:* Initially suspected brucellosis, but test results were negative.

2. Infectious Disease Specialist: Suspected malaria and tularemia, but tests for these diseases were also negative.

3. Internal Medicine Specialist: Considered COVID-19, pneumonia, EBV, and thyroid issues, but the patient did not exhibit clear pneumonia symptoms, and COVID-19 and EBV tests were negative. Thyroid function tests were also normal.

4***.*** *Traditional Medicine****:*** Suspected renal failure, and herbal treatments were prescribed, providing temporary improvement for three weeks. However, the patient ultimately experienced severe muscle cramps.

5. *Rheumatology***:** Based on fatigue, headaches, and inability to exercise (COPD), inflammatory diseases were considered.

Diagnostic evaluation

The following conditions were considered given the patient's clinical and paraclinical findings.

Table1: Differential diagnoses excluded and supporting evidence

Condition	Reasons for Exclusion
Sarcoidosis	Normal serum ACE levels Absence of granulomas on biopsy No hilar lymphadenopathy or pulmonary involvement on CT
Systemic lupus erythematosus	Negative ANA and anti-dsDNA No renal/hematologic involvement (e.g., lupus nephritis, cytopenia)
Systemic vasculitis	Negative ANCA (cANCA/ pANCA) Lack of clinical features of granulomatosis with polyangiitis or polyarteritis nodosa
IBD	• Normal colonoscopy without mucosal ulcers/inflammation • Poor response to IBD-specific therapy

ACE, angiotensin converting enzyme; CT, computed tomography; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; IBD, Inflammatory bowel disease

Confirmation of BD diagnosis

Atypical BD was diagnosed according to the International Criteria for Behçet's Disease (ICBD 2014):

1. Recurrent oral ulcers (confirmed by patient history, though inactive during admission).
2. Ocular involvement: Unilateral retro-bulbar neuritis.
3. Skin lesions: Papulonecrotic lesions and erythema nodosum.
4. Positive pathergy test at initial presentation (prior to treatment).

Note:

- The pathergy test was positive at diagnosis, fulfilling an ICBD criterion.
- Its subsequent negativity after initiating therapy reflects treatment response, not diagnostic invalidity.

Supportive features

- Elevated inflammatory markers [C-

reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin].
- HLA-B51 positivity.
- Clinical response to therapy (cortico-steroids + colchicine).

Table 2: Laboratory tests supporting the diagnosis of BD

Normalized test	Reported result	Interpretation of result
CRP	Elevated	Supports active inflammation: Indicates systemic inflammation consistent with active Behcet's disease.
ESR	Elevated	Supports active inflammation: Reflects an ongoing inflammatory process, aligning with Behcet's flares.
Serum Ferritin	Elevated	Confirms systemic symptoms: Elevated levels suggest severe inflammation or macrophage activation, correlating with fever/body aches in BD.
HLA-B51 (Genetic Marker)	Positive	Strong genetic risk factor: A known susceptibility marker for Behcet's; supports diagnosis (though not diagnostic alone; negative result does not exclude BD).
Anti-gliadin IgA antibodies	Positive	Differential evaluation (IBD mimic): Ordered due to GI symptoms resembling IBD; positivity suggests celiac disease/gluten sensitivity, aiding exclusion of IBD as primary cause.
c-ANCA	Negative	Excludes systemic vasculitis: Negativity helps rule out ANCA-associated vasculitis (e.g., Granulomatosis with Polyangiitis).
p-ANCA	Negative	Excludes ulcerative colitis/other vasculitis: Negativity aids in excluding ulcerative colitis (often p-ANCA positive) and certain vasculitis.

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IBD, Inflammatory bowel disease; GI, gastro intestinal; ANCA, c-ANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; p-ANCA perinuclear anti-neutrophil cytoplasmic antibody

Therapeutic approach & justification:

i) *Acetazolamide (250 mg 6 × daily):* Empirically initiated for symptomatic management of elevated intracranial pressure (ICP) secondary to neuro-BD involvement.

Rationale: Patient presented with severe headaches, dizziness, and radiological signs suggestive of elevated ICP. While typically used for glaucoma, acetazolamide was chosen as a bridging therapy to mitigate ICP-related symptoms while immunosuppressants took effect.

Evidence of response: Headache and dizziness resolved within 72 hours of initiation.

ii) Gluten-free diet + Mesalazine/Sulfasalazine: Empirical trial for refractory gastrointestinal symptoms mimicking IBD.

Rationale: Despite negative endoscopic findings, persistent GI symptoms (pain, diarrhea) and positive gliadin IgA antibodies prompted a diagnostic-therapeutic trial of gluten exclusion. Mesalazine/sulfasalazine were added for potential gut-specific anti-inflammatory effects in BD.

Evidence of response: Symptomatic improvement (reduced pain/ frequency of stools) after 4 weeks.

iii) High-dose corticosteroids (prednisone 50 mg/day): First-line therapy for acute severe BD (ocular/CNS involvement).

iv) Methotrexate + Azathioprine: Steroid-sparing agents for CNS/ocular disease refractory to monotherapy [5].

v) Colchicine (1.5 mg/day): For mucocutaneous and articular symptoms [6].

Initial clinical response

Rapid symptom control (Week 1): Headaches resolved within 72 hours of acetazolamide + colchicine. Visual disturbances improved by the seventh day.

1. Oral Ulcer Dynamics:

Baseline: History of recurrent ulcers (inactive at admission)

Recurrence:

"Oral ulcers reactivated exclusively during prednisone taper (when reduced to 5 mg/day at Month 3)."

Intervention: Increased prednisone to 20 mg/day + colchicine maintenance → ulcers resolved within 2 weeks.

2. Pathergy Test:

The pathergy test was initially positive but became negative after initiating treatment. This

shift not only confirmed the correct diagnosis but also demonstrated proper therapeutic management of the disease trajectory.

6-Month follow-up:

1. Clinical Status:

- Asymptomatic (no oral/genital ulcers, skin lesions, headaches, or visual/GI symptoms)
- Normal inflammatory markers (CRP 2.1 mg/L, ESR 8 mm/hr)

2. Patient Outcome:

"At 6-month follow-up, the patient reported full satisfaction with treatment outcomes. All medications were discontinued following shared decision-making due to sustained remission."

Discussion

Behçet's Disease (BD) is a systemic vasculitis characterized by heterogeneous manifestations, rendering diagnosis particularly challenging in atypical presentations. While typically emerging in the third and fourth decades of life with a male predominance, this case exemplifies the diagnostic complexities encountered when faced with an unusual constellation of symptoms. The observed male preponderance and potentially more severe disease course in males may be linked to testosterone's role in activating neutrophils and Th-1 cells, key players in BD pathogenesis [7]. This case is especially significant and unusual due to the simultaneous development of severe neurological, gastro-intestinal, *and* dermatological manifesta-tions early in the disease course, a combination less commonly reported concurrently at presentation. The patient's symptoms—including pseudotumor cerebri-like features, retrobulbar neuritis, strabismus, IBD-like GI symptoms (abdominal pain, diarrhea, mucus-laden stools), alongside classic oral ulcers and papulo-necrotic/erythema nodosum skin lesions—represent a profound multisystemic challenge [8].

The diagnostic Odyssey in this case underscores the formidable challenge posed by atypical BD presentations. Initial symptoms like persistent headaches, dizziness, visual disturbances, and GI complaints readily mimicked more common conditions such as multiple sclerosis, idiopathic intracranial hypertension, primary gastrointestinal inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), or even CNS infections or malignancies [9, 10]. This broad differential diagnosis inevitably led to extensive investigations (imaging, lumbar puncture, endoscopy) and consultations across neurology, gastroenterology, and ophthalmology, potentially contributing to diagnostic delay. Our experience aligns with studies highlighting that BD patients presenting with predominant neurological or GI symptoms experience significantly longer diagnostic delays compared to those with recurrent oral-genital ulcers as the initial complaint [10, 11]. The absence of pathognomonic tests further compounds this difficulty. The dynamic nature of the pathergy test in this patient, turning positive during symptom recurrence upon steroid taper and negative post-treatment, provides compelling evidence supporting its utility as a disease activity marker rather than merely a diagnostic tool, a correlation increasingly recognized in recent literature [12].

Comparing our findings to the literature emphasizes the rarity and complexity of this presentation. While neurological involvement (neuro-BD) occurs in 5-50% of patients and GI involvement (intestinal BD) in 3-25%, the concurrent, severe presentation of both, alongside pseudotumor cerebri-like features and classic mucocutaneous lesions at onset, is highly atypical [9, 13]. Our patient's neurological picture (headache, papilledema/pseudotumor, retrobulbar neuritis) shares similarities with cases reported by emphasizing intracranial hypertension in neuro-BD. Similarly, the IBD-like presentation (abdominal pain, diarrhea, mucus) reflects the known overlap between intestinal BD and Crohn's disease, often requiring careful histological differentiation [11, 13]. This case vividly illustrates how BD can act as a "great mimicker," reinforcing the critical importance of considering it in young patients with unexplained multisystem inflammation, even when classic symptoms like genital ulcers are absent initially.

Treatment required a multifaceted approach: high-dose corticosteroids for acute severe

inflammation (especially neurological and ocular), azathioprine for long-term immunosuppression, acetazolamide for intracranial hypertension, colchicine for mucocutaneous lesions, and a gluten-free diet trialed empirically for GI symptoms. The recurrence of oral ulcers upon corticosteroid reduction is a well-documented challenge in BD management, highlighting the disease's chronicity and the frequent need for sustained immunosuppression or steroid-sparing agents [14]. The transient hypertension, resolving without specific antihypertensives, was likely a manifestation of active vasculitis impacting vascular tone or renal perfusion [8]. This case underscores the necessity for personalized treatment strategies tailored to the dominant organ systems involved and close monitoring for relapse, particularly during medication tapering.

The paramount importance of early diagnosis cannot be overstated. Delays, as potentially encountered here due to the unusual presentation, increase the risk of irreversible damage, particularly in neuro-BD (e.g., vision loss, cognitive decline) or from vascular complications [9, 10]. This case strongly advocates for the rigorous application of the ICBD in patients with complex multisystem symptoms and the strategic use of supportive tests like HLA-B51 genotyping. While HLA-B51 positivity, as seen in this patient, is neither necessary nor sufficient for diagnosis, it significantly increases the pre-test probability in the appropriate clinical context, especially in non-endemic regions or atypical cases [15]. A high index of suspicion and early rheumatology consultation are crucial for mitigating diagnostic delay and improving long-term outcomes in complex BD presentations like this one.

Conclusion

This case report underscores the need to consider Behçet's Disease in the differential diagnosis of young patients with multisystemic symptoms. Early diagnosis and personalized treatment approaches can significantly improve clinical outcomes. Long-term management and close monitoring are crucial to prevent disease recurrence.

Acknowledgment

Not applicable.

Conflict of Interest

The author reports no conflicts of interest in this work.

Funding

There is no funding for this report.

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