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A challenging case of Behçet's disease with late diagnosis in a 49-year-old female

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Abstract
Behçet's Disease (BD) is a rare, chronic, multi-system vasculitis with a complex and variable clinical presentation, making early diagnosis difficult. We report a case of a 49-year-old female of Middle Eastern descent with a history of recurrent oral ulcers, arthralgias, and erythema nodosum, ultimately diagnosed with BD after years of misdiagnosis. The patient's response to biologic therapy, specifically Etanercept, highlights the importance of individualized treatment. This case report addresses the diagnostic challenges of BD and emphasizes the importance of early recognition and a multidisciplinary approach to treatment.

Keywords: Behçet's disease, late diagnosis, vasculitis

Introduction
Behçet's Disease (BD) is a rare but severely debilitating vasculitis, characterized by relapsing and remitting inflammation that can affect multiple organ systems. Although BD often presents with mucocutaneous symptoms such as recurrent oral and genital ulcers and skin lesions, the disease can involve the musculoskeletal system, eyes, nervous system, gastrointestinal tract, vascular beds, and cardiopulmonary system, leading to significant morbidity and mortality [1]. BD is particularly prevalent along the Silk Road, with the highest occurrence rates in countries like Turkey (80–370 cases per 100,000), Iran, and Japan, although it is less common in North America and Northern Europe [2, 3].
The pathophysiology of BD involves both autoinflammatory and autoimmune mechanisms, with a strong genetic predisposition. The HLA-B51 allele is present in approximately 60% of BD patients, especially in regions with a higher prevalence of the disease, suggesting a significant role of genetic factors in its development [2]. Environmental triggers, such as microbial exposures, are also thought to play a role in disease onset in genetically susceptible individuals [1].
Diagnosing BD is challenging due to the complex nature of the disease and the lack of a specific diagnostic test. Instead, diagnosis is based on clinical criteria and the exclusion of other diseases with similar presentations, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and inflammatory bowel disease (IBD) [4]. The International Study Group (ISG) and International Criteria for Behçet's Disease (ICBD) are commonly used for classification, though they vary in sensitivity and specificity [5]. Given the potential for serious complications, such as vascular involvement or neuro-Behçet's, early recognition and treatment are crucial to improving outcomes.
In this case report, we present a 49-year-old female who experienced a long delay in diagnosis, with symptoms of BD being initially misattributed to other conditions. Her successful response to Etanercept, a TNF-α inhibitor, demonstrates the importance of tailored therapeutic strategies in managing refractory BD.

Case Presentation
A 49-year-old female of Middle Eastern descent presented to the clinic with a 10-year history of chronic arthralgias, recurring erythematous rashes, oral ulcers, and persistent fatigue. She had a complex medical history, including severe endometriosis, recurrent gout, and multiple

surgical procedures, such as two cesarean sections, a partial hysterectomy, bilateral oophorectomies, thyroidectomy, and cholecystectomy. Previous diagnoses of chronic fatigue syndrome (CFS) and fibromyalgia had been made, and the patient had been treated with gabapentin and duloxetine without significant relief, contributing to her frustration and diminished quality of life.

On examination, erythema nodosum was noted on both lower and upper extremities, as well as active oral aphthous ulcers. Given her recurrent symptoms and poor response to prior treatments, a comprehensive workup was initiated. Initial laboratory tests revealed elevated inflammatory markers, including an elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), suggestive of a systemic inflammatory process [1].

Autoimmune serological tests, including antinuclear antibodies (ANA), anti-double stranded DNA (anti-dsDNA), and rheumatoid factor (RF), were negative, ruling out more common autoimmune conditions. The combination of clinical findings, including the presence of oral ulcers, erythema nodosum, and arthralgias, alongside the positive HLA-B51 test, led to the diagnosis of Behçet's Disease [2, 3].

Initial treatment with oral prednisone was started, aiming to reduce inflammation. However, after six weeks of therapy, the patient's symptoms had only minimally improved, and the decision was made to begin treatment with Etanercept, a biologic TNF-α inhibitor that has shown efficacy in controlling BD symptoms [7]. The patient was instructed on proper self-administration techniques for Etanercept injections and was monitored for potential adverse effects. Etanercept was administered weekly, in conjunction with duloxetine and dexamethasone for breakthrough flares.

At a follow-up visit two months later, the patient reported significant improvement in her fatigue, joint pain, oral ulcers, and rashes. She was referred to ophthalmology for evaluation of possible ocular complications, such as uveitis, and to cardiology for assessment of any underlying cardiovascular involvement, as BD is known to increase the risk of vascular complications, including thrombosis and aneurysms [1, 6].

Discussion

This case illustrates several challenges in diagnosing and managing Behçet's Disease. The long delay in the patient's diagnosis, attributed to prior misdiagnoses of chronic fatigue syndrome and fibromyalgia, reflects how BD's symptoms can mimic other more common autoimmune conditions, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and inflammatory bowel disease (IBD). The intermittent nature of BD's symptoms further complicates diagnosis, leading to extended periods of mismanagement [1, 4].

Although the patient did not present with the severe organ manifestations often associated with poor outcomes in BD, such as uveitis or vascular involvement, her chronic, unexplained fatigue, recurrent mucocutaneous ulcers, and arthralgias significantly affected her quality of life. A high index of suspicion is necessary to differentiate BD from other diseases, especially in patients with recurrent mucocutaneous symptoms and elevated inflammatory markers [5].

Etanercept, a TNF-α inhibitor, was chosen after the patient failed to respond to prednisone. Although not FDA-approved for BD, Etanercept has demonstrated efficacy in controlling inflammation in various autoimmune diseases, and its off-label use for BD is supported by studies showing its ability to reduce symptoms in patients with refractory disease [7, 8]. The patient's positive response to Etanercept, with notable improvement in fatigue, joint pain, and mucocutaneous lesions, highlights the potential benefit of biologics in managing difficult cases of BD. However, the use of biologics carries risks, including increased susceptibility to infections, reactivation of latent tuberculosis, and the potential development of malignancies [9].

The multidisciplinary approach in managing this patient, involving rheumatology, dermatology, ophthalmology, and cardiology, was essential for monitoring the systemic nature of BD. This collaborative approach helped ensure that complications, such as uveitis and cardiovascular involvement, were promptly identified and managed. Regular follow-up is necessary, given the long-term nature of BD and the risks associated with both the disease and its treatments.

The successful use of Etanercept in this case supports the growing role of biologics in the treatment of refractory BD. However, ongoing monitoring for adverse effects and further research into the long-term safety and efficacy of biologics in BD are necessary.

Conclusion

This case emphasizes the diagnostic and therapeutic complexities of Behçet's Disease, particularly in patients with a long history of misdiagnosed autoimmune conditions. The patient's significant improvement following treatment with Etanercept, a TNF-α inhibitor, highlights the potential of biologic therapies in managing refractory BD. Early diagnosis, personalized treatment plans, and a multidisciplinary approach are critical for optimizing outcomes in patients with BD. Increased awareness and further research into BD are necessary to improve diagnostic accuracy and therapeutic strategies.

Conflict of Interest

Not available

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