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CHRONIC NON-HEALING LEG ULCER AS A MANIFESTATION OF UNDIAGNOSED BEHÇET'S DISEASE

JEYARAMAN SAI PRITAM[1], C. SARANYA[2*], R. KANNAN[3]
[1]POST GRADUATE STUDENT, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI. INDIA
[2]PROFESSOR, DEPARTMENT OF RHEUMATOLOGY, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI. INDIA
[3]PROFESSOR, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI. INDIA CORRESPONDING AUTHOR: C. SARANYA

Abstract
Chronic ulcerations constitute a considerable clinical challenge, frequently requiring individualized, multidisciplinary therapeutic strategies and rigorous adherence to treatment regimens. Precise diagnosis and effective management are predicated upon a comprehensive understanding of the ulcer's underlying etiology and associated systemic pathologies. This case report delineates the clinical course of a 35-year-old male patient presenting with a chronic, non-healing leg ulcer complicated by a history of deep vein thrombosis (DVT) and pulmonary thromboembolism. Although initial investigations for common vasculitic and prothrombotic profiles yielded negative results, histopathological analysis of a biopsy specimen revealed leukocytoclastic vasculitis. Subsequent genetic testing for HLA-B51 positivity confirmed the diagnosis of Behçet's disease. The patient was managed with a therapeutic regimen comprising prednisolone, mycophenolate mofetil, and rivaroxaban, which resulted in significant clinical improvement and regression of the ulceration. This report underscores the clinical imperative to include Behçet's disease in the differential diagnosis for young male patients who present with chronic non-healing ulcerations in conjunction with thromboembolic phenomena. Prompt diagnosis and vigilant, multidisciplinary management are crucial for mitigating severe complications, including pulmonary artery hemorrhage and neuro-Behçet's disease. This case report accentuates the necessity for comprehensive diagnostic evaluations and sustained long-term surveillance to avert irreversible organ damage and enhance patient prognoses.

Keywords: Behçet's syndrome, non-healing leg ulcer, deep vein thrombosis, pulmonary thromboembolism, leukocytoclastic vasculitis.

1. INTRODUCTION

Chronic non-healing ulcers, characterized as cutaneous wounds that fail to proceed through the orderly phases of physiological healing despite appropriate therapeutic intervention, represent a substantial clinical challenge. These lesions typically persist for a duration exceeding 12 weeks and are frequently associated with considerable morbidity, a recurrence rate surpassing 66%, functional impairment, and a significant reduction in quality of life. While this pathology is more prevalent among geriatric populations, the manifestation of chronic ulcerations in younger individuals mandates a thorough evaluation for underlying systemic etiologies.

In India, the prevalence of chronic wounds is notable, affecting an estimated 4.5 per 1,000 individuals. Although the predominant etiologies of chronic ulcers include diabetes mellitus, arterial insufficiency, and venous stasis disease, a diverse spectrum of other conditions, including autoimmune disorders and infectious processes, contributes to their diagnostic and therapeutic complexity. Notwithstanding advancements in wound care modalities, such as the development of dermal substitutes, therapeutic management remains arduous, especially in cases refractory to standard interventions.

The clinical presentation of non-healing leg ulcers in young male patients warrants investigation for underlying connective tissue disorders, vasculitis, and other autoimmune pathologies. While venous and diabetic ulcers represent the more common etiologies, rare conditions such as Behçet's disease must be included in the differential diagnosis, particularly in the context of concurrent thromboembolic events. Behçet's disease is a chronic, relapsing, multisystemic inflammatory disorder characterized by a constellation of clinical features, including recurrent oral aphthae, genital ulcerations, cutaneous lesions, and vasculopathy. The disease predominantly affects populations in the Mediterranean, the Middle East, and East Asia; however, its global incidence is increasing, though prevalence rates in other regions remain lower.

This report delineates the diagnostic and therapeutic complexities encountered in the management of a 35-year-old male who presented with a non-healing leg ulcer and a history of deep vein thrombosis (DVT) and pulmonary

thromboembolism. Histopathological examination of a biopsy specimen confirmed leukocytoclastic vasculitis, and subsequent HLA-B51 genotyping facilitated the diagnosis of Behçet's disease. This case highlights the clinical importance of considering Behçet's disease in the differential diagnosis of young patients presenting with chronic ulcerations and thromboembolic phenomena, thereby emphasizing the necessity for a comprehensive and multidisciplinary management strategy.

2. CASE PRESENTATION

A 35-year-old male was referred to the rheumatology outpatient department for evaluation of a chronic, non-healing ulcer on the right lower extremity, which had been present for approximately one year. The patient had previously received management from the vascular surgery service; however, he was subsequently referred to the rheumatology department due to the ulcer's recalcitrance to conventional wound care protocols.

The patient's past medical history was significant for a deep vein thrombosis (DVT) in 2017, for which oral anticoagulation therapy was initiated. In 2018, the patient sustained a pulmonary thromboembolism, which prompted an investigation for a potential underlying hypercoagulable state. Comprehensive evaluations performed at that time, encompassing autoimmune and coagulation profiles, did not reveal evidence of vasculitis or a prothrombotic disorder. In 2019, the patient developed a non-healing ulcer over the medial aspect of the right lower leg, with no antecedent history of trauma, pyrexia, or significant algia. The patient denied any history of oral or genital ulcerations, recurrent febrile episodes, or a familial predisposition to autoimmune conditions.

On physical examination, an 8 × 6 cm shallow ulceration with flat margins and focal areas of necrosis was located over the right medial malleolus. The peri-ulcer skin exhibited signs of inflammation, but there was no significant exudate. The affected lower limb was well-perfused, with palpable distal pulses. Examination of the oral and genital areas was negative for ulcerations, and the remainder of the systemic examination, including cardiovascular, neurological, and musculoskeletal assessments, was within normal limits. Additionally, follicular lesions were noted on the the left hand; however, there were no other systemic manifestations suggestive of active vasculitis.

In 2018, a comprehensive serological evaluation for autoimmune and coagulation disorders, including assays for antineutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), and antiphospholipid antibodies (APLA), yielded negative results. The patient was initially managed with oral anticoagulation.

In 2019, routine laboratory investigations, including a complete blood count (CBC), renal function tests (RFT), and liver function tests (LFT), were unremarkable. The patient's coagulation profile was within normal parameters. However, inflammatory markers were elevated, with an erythrocyte sedimentation rate (ESR) of 72 mm/hr and a C-reactive protein (CRP) concentration of 12 mg/L.

A biopsy of the ulcer margin was performed, and histopathological analysis revealed findings consistent with leukocytoclastic vasculitis. Furthermore, polymerase chain reaction (PCR) genotyping for the human leukocyte antigen (HLA)-B51 allele was positive, thereby confirming the diagnosis of Behçet's disease.

The patient was diagnosed with Behçet's disease, with clinical manifestations including a chronic non-healing ulcer, leukocytoclastic vasculitis, and a history of thromboembolic events. A treatment regimen was initiated consisting of oral prednisolone at a dose of 30 mg per day, which was subsequently tapered according to the clinical response. Mycophenolate mofetil, at a dosage of 500 mg twice daily, was introduced as an adjunctive immunosuppressive agent. Rivaroxaban 20 mg once daily was continued for anticoagulation to mitigate the risk of recurrent thromboembolic events.

At a three-month follow-up evaluation, the ulcer demonstrated substantial improvement, characterized by reduced necrosis and diminished peri-ulcer inflammation. The patient remains under regular multidisciplinary surveillance to monitor for the development of potential complications, such as pulmonary artery hemorrhage and neuro-Behçet's disease.

3. DISCUSSION

This case report illustrates the diagnostic challenge posed by a young male patient with chronic non-healing leg ulcers and thromboembolic events, who was ultimately diagnosed with Behçet's disease. The patient's history of deep vein thrombosis (DVT) and pulmonary thromboembolism initially suggested a hypercoagulable state or an underlying vasculitis. Despite negative serological findings for antineutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), and antiphospholipid antibodies (APLA), the histopathological evidence of leukocytoclastic vasculitis and a positive HLA-B51 allele test substantiated the diagnosis of Behçet's disease. The finding of leukocytoclastic vasculitis, a common histopathological feature of Behçet's disease, was a critical diagnostic element in this case, affirming the underlying vascular pathology.

Behçet's disease is a multisystemic inflammatory disorder affecting numerous organ systems and is classically characterized by recurrent oral aphthosis, genital ulcerations, ocular inflammation, and vascular manifestations (Alpsoy et al., 2016). The condition exhibits a male predominance and is particularly associated with severe vascular complications, including thrombosis and pulmonary artery aneurysms, which contribute to significant morbidity and

mortality (Alpsoy et al., 2016; Yildirim et al., 2023). The manifestation of vascular Behçet's disease, which involves the venous system in approximately one-third of cases, was evident in this patient's history of thromboembolism and highlights the importance of early recognition of vascular involvement (Alibaz-Oner et al., 2022).

Positivity for the HLA-B51 allele is a strong genetic susceptibility marker for Behçet's disease, present in 50–80% of affected individuals, and is particularly correlated with more severe vascular manifestations (International Team for the Revision of the International Criteria for Behçet's Disease [ITR-ICBD], 2014). This genetic marker was pivotal in confirming the diagnosis in the present case.

The therapeutic management of Behçet's disease is complex, owing to its chronic and relapsing-remitting clinical course. Corticosteroids, such as prednisolone, constitute the first-line therapy for acute inflammatory exacerbations. Whereas immunosuppressive agents like mycophenolate mofetil are utilized for long-term disease modulation and control (Alpsoy et al., 2016; Sevimli Dikicier et al., 2019). In the presented case, prednisolone was administered to suppress acute inflammation, with subsequent introduction of mycophenolate mofetil to prevent disease progression.

The continuation of anticoagulation therapy with rivaroxaban is consistent with contemporary management strategies for patients with recurrent thromboembolic events in the context of Behçet's disease. Although the role of anticoagulation in Behçet's disease remains a subject of debate due to the potential risk of hemorrhage, especially in patients with coexistent pulmonary artery aneurysms, studies such as Alakkas et al. (2021) advocate for its judicious use in select cases under strict clinical surveillance.

Given the chronic trajectory of Behçet's disease and its potential for life-threatening complications, including pulmonary artery hemorrhage and neuro-Behçet's disease, sustained follow-up and multidisciplinary care are imperative (Bettiol et al., 2020). Prompt diagnosis and targeted therapeutic intervention can mitigate severe complications and improve long-term prognoses for patients with vascular Behçet's disease (Mohan et al., 2015).

4. CONCLUSION

This case report reiterates the importance of including Behçet's disease in the differential diagnosis of young male patients who present with chronic non-healing ulcers and concurrent thromboembolic events. The diagnosis of Behçet's disease, particularly in individuals lacking the classic symptomatic triad of oral and genital ulcerations and ocular involvement, remains diagnostically challenging and is frequently delayed. Nevertheless, the presence of vascular involvement, such as deep vein thrombosis and pulmonary thromboembolism, should prompt investigation into less common etiologies, including Behçet's disease.

In the case of this patient, the histopathological finding of leukocytoclastic vasculitis and positive HLA-B51 genotyping were pivotal in establishing a definitive diagnosis. This underscores the diagnostic utility of genetic testing and histopathological evaluation in clinical scenarios where more common autoimmune and prothrombotic disorders have been excluded. Early recognition of Behçet's disease is critical for the prevention of severe, life-threatening complications, including pulmonary artery aneurysm formation, neuro-Behçet's disease, and recurrent thromboembolic events.

The management of Behçet's disease necessitates a multidisciplinary approach, wherein corticosteroids and immunosuppressive agents, such as mycophenolate mofetil, constitute the cornerstone of therapy. In light of the inherent thromboembolic risk, anticoagulation therapy must be considered on an individualized basis, as exemplified by the use of rivaroxaban in this case. Consistent follow-up and vigilant clinical monitoring are essential for the effective management of Behçet's disease, given the substantial risk of relapse and the potential for severe, long-term complications.

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