Hidden Diagnosis - Chronic Non-Healing Leg Ulcer

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ABSTRACT
Chronic ulcers present a significant clinical challenge, often necessitating tailored, multi-faceted interventions and strict adherence to treatment protocols. Accurate diagnosis and management require a thorough understanding of the ulcer's etiology and associated systemic conditions. This case report highlights a 35-year-old male with a chronic non-healing leg ulcer, compounded by a history of deep vein thrombosis (DVT) and pulmonary thromboembolism. Despite negative findings for common vasculitic and procoagulant profiles, a biopsy revealed leukocytoclastic vasculitis, and subsequent HLA-B51 testing confirmed the diagnosis of Behçet's disease. The patient was treated with a combination of prednisolone, mycophenolate mofetil, and rivaroxaban, resulting in notable regression of the ulcer. This case underscores the importance of considering Behçet's disease in young male patients presenting with chronic non-healing ulcers and thromboembolic events. Early diagnosis and vigilant, multidisciplinary management are essential to mitigate complications such as pulmonary artery hemorrhage and neuro-Behçet's disease. This report emphasizes the need for comprehensive diagnostic approaches and long-term follow-up to prevent irreversible organ damage and improve patient outcomes.

1. Introduction

Chronic non-healing ulcers, defined as wounds that fail to progress through the normal phases of healing despite adequate treatment, present a significant clinical challenge. These ulcers persist for more than 12 weeks and often result in considerable morbidity, with a recurrence rate of over 66%, causing loss of function and a diminished quality of life. This issue is more prevalent in older populations, but the appearance of chronic ulcers in younger patients necessitates the evaluation of underlying systemic conditions.

In India, chronic wounds are prevalent, affecting approximately 4.5 per 1,000 individuals. While the most common causes of chronic ulcers include diabetes, arterial insufficiency, and venous disease, a range of other etiologies, such as autoimmune disorders and infections, contribute to their complexity. Despite advancements in wound management, such as dermal substitutes, treatment remains challenging, particularly when standard therapies fail.

Young males with non-healing leg ulcers should be investigated for connective tissue disorders, vasculitis, and autoimmune conditions. Although venous and diabetic ulcers are more common, rare conditions like Behçet's disease must be considered, particularly when accompanied by thromboembolic events. Behçet's disease is a chronic, relapsing, multisystem inflammatory disorder, characterized by oral and genital ulcers, skin lesions, and vascular involvement. It predominantly affects populations in the Mediterranean, Middle East, and East Asia, but global cases are increasing, albeit with lower prevalence rates.

This case report details the diagnostic and therapeutic challenges faced in treating a 35-year-old male with a non-healing leg ulcer and a history of deep vein thrombosis (DVT) and pulmonary thromboembolism. Biopsy results confirmed leukocytoclastic vasculitis, and further testing for HLA-B51 led to a diagnosis of Behçet's disease. This case underscores the importance of considering Behçet's disease in young patients presenting with chronic ulcers and thromboembolic phenomena, emphasizing the necessity of a comprehensive, multidisciplinary approach.

2. Case Presentation

A 35-year-old male presented to the rheumatology outpatient department with a chronic non-healing ulcer on his right lower leg, persisting for nearly one year. The patient had previously been under the care of vascular surgery but was referred to rheumatology when traditional wound care approaches failed to improve his condition.

The patient's medical history revealed a deep vein thrombosis (DVT) in 2017, for which he was placed on oral anticoagulation therapy. In 2018, he experienced a pulmonary thromboembolism, raising concerns about an underlying prothrombotic condition. Extensive evaluations, including autoimmune profiles and coagulation tests, conducted at that time were negative for vasculitis and prothrombotic disorders. The patient developed a non-healing ulcer over the medial aspect of his right lower leg in 2019, without any history of trauma, fever, or significant pain. There was no history of oral or genital ulcers, recurrent fevers, or family history of autoimmune conditions.

On examination, an 8 × 6 cm shallow ulcer with flat margins and areas of necrosis was noted on the right medial malleolus. The surrounding skin was inflamed but without significant discharge. Palpation revealed a well-perfused lower limb with palpable pulses. No oral or genital ulcers were observed, and the remainder of the physical exam, including cardiovascular, neurological, and musculoskeletal assessments, was unremarkable. Additionally, the patient presented with follicular lesions on the left hand, although no systemic signs of active vasculitis were detected.

In 2018, a thorough evaluation for autoimmune and coagulation disorders, including antineutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), and antiphospholipid antibody (APLA) profiles, yielded negative results. The patient was initially maintained on oral anticoagulants.

In 2019, routine laboratory tests revealed no abnormalities in the complete blood count (CBC), renal function tests (RFT), or liver function tests (LFT). The patient's coagulation profile remained normal. However, inflammatory markers were elevated, with an erythrocyte sedimentation rate (ESR) of 72 mm/h and a C-reactive protein (CRP) level of 12 mg/L.

A biopsy of the ulcer was performed, revealing leukocytoclastic vasculitis. Additionally, polymerase chain reaction (PCR) testing for HLA-B51 was positive, confirming a diagnosis of Behçet's disease.

The patient was diagnosed with Behçet's disease, presenting with chronic non-healing ulcers, leukocytoclastic vasculitis, and a history of thromboembolic events. He was initiated on oral prednisolone at 30 mg daily, which was gradually tapered based on clinical response. Mycophenolate mofetil 500 mg twice daily was added as an immunosuppressive agent. Rivaroxaban 20 mg daily was continued as anticoagulation therapy to prevent further thromboembolic events.

At a follow-up appointment three months later, the ulcer showed significant improvement, with reduced necrosis and decreased inflammation around the margins. The patient remained under regular multidisciplinary care to monitor for potential complications, including pulmonary artery hemorrhage and neuro-Behçet's disease.

3. Discussion

This case presents the diagnostic challenge of a young male with chronic non-healing leg ulcers and thromboembolic events, ultimately diagnosed with Behçet's disease. The patient's history of deep vein thrombosis (DVT) and pulmonary thromboembolism raised suspicion of a procoagulant disorder or vasculitis. Despite negative results for antineutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), and antiphospholipid antibody (APLA), the presence of leukocytoclastic vasculitis on biopsy and a positive HLA-B51 test confirmed Behçet's disease. Leukocytoclastic vasculitis, commonly associated with Behçet's, was a critical finding in this case, supporting its vascular pathology.

Behçet's disease, a multisystem disorder, affects various organ systems and is characterized by oral ulcers, genital ulcers, ocular inflammation, and vascular involvement, as noted by Alpsoy et al. (2016). The condition is more common in males and is particularly associated with severe vascular complications such as thrombosis and pulmonary artery aneurysms, contributing to increased morbidity and mortality (Alpsoy et al., 2016; Yildirim et al., 2023). Vascular Behçet's, which affects veins in nearly one-third of cases, was evident in this patient's thromboembolic history and underlines the importance of recognizing vascular involvement early (Alibaz-Oner et al., 2022).

HLA-B51 positivity is a genetic marker strongly associated with Behçet's disease and is present in 50–80% of affected individuals, particularly in those with more severe vascular manifestations, as highlighted by International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD, 2014). This genetic predisposition played a crucial role in solidifying the diagnosis in our patient.

The therapeutic approach in Behçet's disease remains complex due to its chronic and relapsing nature.

Corticosteroids, such as prednisolone, are the first line of treatment for acute exacerbations, while immunosuppressants like mycophenolate mofetil are employed for long-term disease control, as suggested by Alpsoy et al. (2016) and Sevimli Dikicier et al. (2019). In this case, prednisolone was administered to control inflammation, followed by mycophenolate mofetil to prevent further progression.

The decision to continue anticoagulation therapy with rivaroxaban in this case aligns with current management strategies for patients with recurrent thromboembolic events in Behçet's disease. While anticoagulation in Behçet's remains controversial due to potential risks of hemorrhage, particularly in patients with pulmonary artery aneurysms, studies such as Alakkas et al. (2021) support its use in selected cases with close monitoring.

Given the chronic nature of Behçet's disease and its potential for life-threatening complications such as pulmonary artery hemorrhage and neuro-Behçet's disease, ongoing follow-up and multidisciplinary management are essential, as underscored by Bettiol et al. (2020). Early diagnosis and targeted treatment can mitigate severe complications and improve long-term outcomes in patients with vascular Behçet's disease (Mohan et al., 2015).

4. Conclusion:

This case underscores the importance of considering Behçet's disease in young male patients presenting with chronic non-healing ulcers and thromboembolic events. The diagnosis of Behçet's, particularly in patients without the classic triad of symptoms (oral ulcers, genital ulcers, and ocular involvement), remains challenging and often delayed. However, the presence of vascular involvement, such as deep vein thrombosis and pulmonary thromboembolism, should prompt further investigation into rare causes like Behçet's disease.

In this patient, leukocytoclastic vasculitis on biopsy and positive HLA-B51 testing were pivotal in reaching a definitive diagnosis. This highlights the significance of utilizing genetic testing and histopathological evaluation in cases where common autoimmune and prothrombotic disorders have been ruled out. Early recognition of Behçet's disease is crucial to preventing severe, life-threatening complications such as pulmonary artery aneurysm, neuro-Behçet's disease, and further thromboembolic events.

Management of Behçet's disease requires a multidisciplinary approach, with corticosteroids and immunosuppressive agents like mycophenolate mofetil forming the cornerstone of therapy. Given the risk of thromboembolism, anticoagulation therapy should be carefully considered on a case-by-case basis, as illustrated in this case with the use of rivaroxaban. Regular follow-up and vigilant monitoring are essential to managing Behçet's disease, as the risk of relapse and the potential for severe complications remain high.

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