Vasculonecrotic Erythema Nodosum Leprosum in a Case of Lepromatous Leprosy: A Rare and Severe Presentation

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ABSTRACT:
Lepromatous leprosy, caused by *Mycobacterium leprae* or *Mycobacterium lepromatosis*, is a progressive, multi-systemic infection affecting the skin and peripheral nerves. Erythema nodosum leprosum (ENL) is a severe immunological complication in lepromatous and borderline leprosy, presenting with inflamed skin nodules. Vasculonecrotic ENL, a rare form, involves deep ulcerations, necrosis, and systemic effects. We report a 40-year-old Myanmarese male with multibacillary leprosy presenting with erythematous patches, nodules, and vesiculopustular bullous eruptions on the trunk and extremities, with bilateral median nerve enlargement and sensory loss. Histopathology confirmed lepromatous leprosy with necrotizing vasculitis and neutrophil infiltration, leading to a diagnosis of vasculonecrotic ENL. Despite initial improvement with multidrug therapy and oral corticosteroids, the patient experienced a relapse of bullous lesions and neuritis following prednisolone tapering. Treatment was intensified with high-dose corticosteroids, leading to the resolution of his bullous lesions.
Key words: Leprosy, Erythema nodosum leprosum, Lepra reaction, Vasculonecrotic phenomenon

Introduction

Leprosy, or Hansen's disease, is a chronic infectious condition caused by *Mycobacterium leprae*, or *Mycobacterium lepromatosis*, which primarily infect macrophages, endothelial cells, and Schwann cells[1]. The disease presents along a clinical spectrum, ranging from tuberculoid leprosy, which involves a strong immune response, to lepromatous leprosy (LL), where severely weakened cell-mediated immunity allows for uncontrolled bacilli multiplication and highly positive acid-fast bacilli tests. LL manifests with widespread erythematous macules, papules, and plaques[2]. One of the significant complications of LL is erythema nodosum leprosum (ENL), a type 2 hypersensitivity reaction observed in nearly half of LL patients[3]. ENL presents with painful erythematous nodules, systemic symptoms, and in severe cases, ulcerative or necrotic lesions. The occurrence of bullous lesions in leprosy is rare, usually reported in Lucio phenomenon or bullous ENL, signaling a severe reaction[4-5]. Bullous ENL, in particular, may appear in patients with high bacillary loads or during corticosteroid tapering, indicating a heightened severity of the condition[6]. This case report highlights a rare instance of vasculonecrotic ENL in a 40-year-old Myanmarese male, emphasizing the challenges of managing this aggressive form of ENL and the critical role of early diagnosis and multidrug therapy in controlling disease progression.

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Case report

A 40-year-old male from Myanmar presented with multiple discrete, painful erythematous patches and nodules on his trunk and extremities for 5 months. He also exhibited bilateral median nerve enlargement and decreased sensation over the palmar aspects in the ulnar and median nerve distributions, the dorsal feet supplied by the superficial peroneal nerve, and the plantar surfaces innervated by the posterior tibial nerve bilaterally. A slit skin smear showed a bacillary index of 2+, and a skin biopsy confirmed a diagnosis of lepromatous leprosy with erythema nodosum leprosum. He was started on multidrug therapy for multibacillary leprosy. Systemic corticosteroid therapy with oral prednisolone 40 mg/day was initiated due to clinical evidence of severe ENL, characterized by painful nodules, bilateral median nerve enlargement, and nerve function impairment manifesting as sensory loss in the distal extremities.

After one month, his cutaneous lesions showed partial improvement, with reduced pain and sensory impairment. The prednisolone dose was tapered to 30 mg per day for 2 weeks and then to 20 mg per day for another 2 weeks. However, two weeks after tapering off prednisolone, he developed multiple new tense vesiculopustular bullous eruptions with crusted erosions on the trunk and extremities. He also experienced fever and pain on his arms along median nerves territory.

The patient has a significant past medical history of tuberculous lymphadenitis, for which he completed a six-month treatment regimen (2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by 4 months of isoniazid and rifampicin) eight months ago. He has worked in a wild animal shop in Thailand's Bang Khun Thian district, with reported contact with armadillos three years prior. There is no family history of leprosy or similar conditions.

On examination, his vital signs indicated fever and tachycardia. Tender lymph nodes were palpable in the right axilla and both groins. Neurological examination showed motor power of grade IV in the distal part of the right upper extremity and both lower extremities, with normal strength in the left upper extremity. Affected motor nerves included the median and ulnar nerves in the right upper limb, and the common peroneal and posterior tibial nerves in both lower limbs, with bilateral median nerve enlargement, tenderness, and decreased sensation in a glove-and-stocking distribution.

Figure 1 Multiple ill-defined, partially blanchable erythematous patches with some necrotic scale crusts (A-B) and multiple tense vesiculopustular bullous eruptions on trunk and extremities.(C-D)

Dermatologic examination showed multiple ill-defined erythematous patches and nodules (Figure 1A and 1B), along with vesiculopustular bullous eruptions and crusted erosions on the trunk and extremities (Figure 1C and 1D). Hair and nails were normal, and mucosal surfaces showed no ulcers or erosions.

Laboratory results revealed leukocytosis with neutrophil predominance (WBC 13,640 cells/uL, neutrophils 88%). Liver function tests were within normal limits, and anti-HIV testing was negative. Slit skin smears from the right ear, left ear, right forearm, and left forearm showed an average bacteriological index of 4. The highest AFB positivity was 5+ at the left ear. The morphological index revealed that approximately 80% of bacilli were fragmented forms. Tzanck smear showed no multinucleated giant cells or acantholytic cells. Chest X-ray findings were unremarkable.

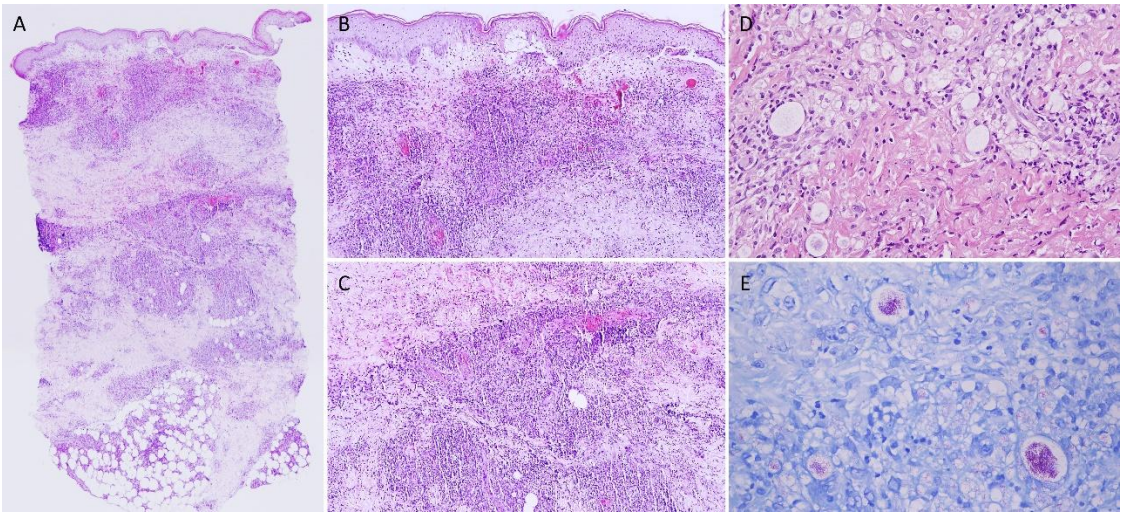

Figure 2 Dense granulomatous infiltrations throughout the dermis and subcutaneous tissue.(A) Perivascular infiltration of neutrophils and nuclear dust, along with extravasated red blood cells and fibrinoid necrosis of the vessel wall.(B-C) The inflammatory cell infiltration is composed of histiocytes, lymphocytes, and some neutrophils.(D) AFB staining shows short, fragmented bacilli within vacuolated histiocytes.(E)

Histopathological examination of the incisional biopsy taken from a bullous lesion on the right forearm revealed dense granulomatous infiltrations throughout the dermis and subcutaneous tissue (Figure 2A). Perivascular infiltration of neutrophils and nuclear dust, along with extravasated red blood cells and fibrinoid necrosis of the vessel wall, were present (Figure 2B and 2C). The inflammatory cell infiltration is composed of histiocytes, lymphocytes, and some neutrophils. Most of the histiocytes are vacuolated, containing short, fragmented bacilli (Figure 2D). AFB staining shows short, fragmented bacilli within vacuolated histiocytes (Figure 2E).

Based on these findings, the patient was diagnosed with lepromatous leprosy complicated by vasculonecrotic ENL. He continued multidrug therapy for multibacillary leprosy (dapsone, rifampicin, and clofazimine), and prednisolone 40 mg/day, along with pentoxifylline 400 mg twice daily, was added to his treatment regimen.Two weeks after adjusting the medication, there was a marked improvement in his vesiculopustular bullous eruptions and fever.

Discussion

Bullous lesions in leprosy were rare which previously reported in Lucio phenomenon, bullous ENL, and bullous drug eruptions related to leprosy treatment like dapsone or rifampicin[4,6]. Atypical ENL presentations include vesiculobullous, ulcero-necrotic, erythema multiforme-like, Sweet's syndrome–like, and polyarthritis- or rheumatoid arthritis–like lesions[5,7]. The presence of bullous lesions in ENL indicates a severe form of the reaction, particularly in patients with high bacillary loads or those tapering systemic corticosteroids.[6] In our patient, the bullous lesions appeared during treatment, initially presenting as vesiculopustular eruptions that later ruptured and progressed to ulceration. This was accompanied by fever and neuritis. Histopathology revealed necrotizing vasculitis within the background of erythema nodosum leprosum, leading to the diagnosis of lepromatous leprosy with vasculonecrotic ENL.

Vasculonecrotic ENL, an uncommon form of ENL, is marked by severe, deep, painful ulcers that heal with atrophic scarring and is often accompanied by systemic symptoms, visceral involvement, and neuritis[8]. The small number of reported cases of vasculonecrotic ENL in the world literature suggests that it is fairly uncommon. Vashisht et al. described a rare presentation of bullous ENL on the trunk in a case of multibacillary leprosy on MB-MDT, similar to our patient[6]. Fogangolo et al. reported one case of necrotic ENL among two cases of vasculonecrotic reactions in lepromatous leprosy[9].

The pathogenesis involves immune complex deposition, which activates the classical complement pathway, triggering tissue damage through a proteolytic cascade. Anaphylatoxins recruit neutrophils and macrophages that produce TNF-α and reactive oxygen species, further damaging tissues. This leads to phagocyte infiltration, extensive platelet deposition on endothelial and vascular tissues, and ultimately necrotizing vasculitis, contributing to the characteristic bullous and necrotic lesions of vasculonecrotic ENL[10].

Treatment of vasculonecrotic ENL primarily focuses on controlling inflammation, relieving pain, and preventing further episodes. According to WHO technical guidance, severe ENL is best managed initially with moderate doses of prednisolone 30-40 mg per day, which are gradually tapered. Thalidomide, known for its strong anti-inflammatory effects, is indicated for steroid non-responders or those with serious comorbidities. Second-line treatments such as clofazimine or methotrexate may also be considered[11]. Aspirin is a commonly used anti-inflammatory agent, and other options like NSAIDs, colchicine, oral zinc and chloroquine have also been utilized. Pentoxifylline has also been reported as a beneficial adjunct in the treatment of ENL. Its therapeutic effect is attributed to the inhibition of TNF-α, leading to a reduction in inflammatory response. It helps alleviate both cutaneous and neurological manifestations and may reduce steroid dependency in patients with chronic or steroid-refractory ENL[12]. Continued multidrug therapy remains essential for the overall management of leprosy[13].

The prognosis of vasculonecrotic ENL varies depending on the severity and duration of the condition. While the ulcers may heal with treatment, they often leave behind extensive linear hypopigmented and hypertrophic scars, particularly over the extremities[14]. Additionally, vasculonecrotic ENL can lead to systemic complications such as lymphadenopathy, arthritis, neuritis, and other immune complex-mediated damages. Early diagnosis and treatment are critical to prevent permanent nerve damage and to manage the systemic manifestations[13]. Chronic or recurrent ENL can persist for months, requiring prolonged treatment and posing a significant burden on the patient[11].

In conclusion, we present a case of lepromatous leprosy with vasculonecrotic erythema nodosum leprosum, characterized by vesiculopustular bullous eruptions that progressed to necrotic ulcer. The patient responded well to treatment with multibacillary multidrug therapy, high-dose systemic corticosteroids, and oral pentoxifylline.

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