Lucio phenomenon and antiphospholipid antibodies in leprosy mimicking rheumatologic disorders: a case report

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Summary

Hansen's disease, also known as leprosy, is often termed "the great imitator" due to its diverse clinical presentations that can mimic various rheumatologic disorders. We present the case of a 34-year-old female who developed extensive purpuric rashes, initially raising suspicion of vasculitis. Laboratory investigations revealed triple-positive antiphospholipid antibodies. However, skin smears and histopathological examination confirmed a diagnosis of diffuse lepromatous leprosy complicated by Lucio phenomenon. This case highlights the importance of considering infectious etiologies, such as leprosy, in the differential diagnosis of vasculitis and rheumatologic diseases. Given the overlapping clinical features, a comprehensive patient history and careful interpretation of autoantibody tests are essential for achieving an accurate diagnosis.

Introduction

Hansen's disease, also known as leprosy, is a chronic granulomatous infectious disease caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*. It primarily affects the skin, peripheral nerves, and musculoskeletal system (1). According to the World Health Organization, approximately 182,815 new cases of leprosy were reported globally in 2023 (2). The disease is predominantly found in developing countries, particularly in Indonesia (17,251 cases; prevalence 0.06‰), Brazil (25,720 cases; prevalence 0.12‰), and India (85,276 cases; prevalence 0.06‰). Leprosy is often referred to as "the great imitator" due to its varied clinical manifestations, which can mimic autoimmune diseases such as rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus (SLE), and vasculitis (1, 3). Herein, we report the case of a 34-year-old female with diffuse lepromatous leprosy complicated by Lucio phenomenon, which presented similarly to vasculitis, with triple-positive antiphospholipid (aPL) antibodies.

Case Report

A 34-year-old Indonesian woman was initially referred to our hospital with red-purplish rashes, vesicles, and skin erosions (defined as loss of the superficial layers of the skin) on both arms, extending to the palms, abdomen, buttocks, and both lower limbs, which had worsened 6 days before admission. Five months before admission, she noticed a spontaneous wound on her leg that progressively worsened, resulting in multiple ulcers on both feet. She was initially suspected of having vasculitis and referred to rheumatology. Upon further evaluation, the symptoms were found to have begun 6 years before admission, initially presenting as a burning sensation and numbness in both soles, accompanied by foot swelling and loss of eyebrow, eyelash, and pubic hair. The patient lived in crowded housing in an endemic rural area in Indonesia but denied any contact history with a leprosy patient.

On physical examination, there was madarosis of the bilateral eyebrows and eyelashes. Diffuse multiple infiltrations were observed on both ears and the face. The arms, palms, abdomen, buttocks, legs, and soles of the feet displayed multiple purpuric plaques in a reticulate pattern, with a solitary bulla on the left knee. Multiple ulcers, each measuring approximately 2 cm by 4 cm, were noted on both feet, with raised borders surrounded by callus, a base of granulation tissue, and some areas covered with necrotic tissue (Figure 1). There was enlargement of the bilateral ulnar, common peroneal, and posterior tibial nerves, and the left greater auricular nerve, without pain or tenderness. Sensory function was decreased in both palmar digits and plantar surfaces of the feet. Electroneuromyography was not performed, as sensory impairment was clinically evident and further testing was therefore not pursued. Given the constellation of findings, including madarosis, nerve enlargement, sensory impairment, and skin lesions, the patient was also referred to the dermatology department for further evaluation.

A complete blood count revealed anemia with a hemoglobin level of 8.2 g/dL and leukocytosis at 17,289/mm^3. D-dimer was elevated at 1860 G/L (normal range: <440). An aPL antibody panel showed a low to medium positive immunoglobulin G (IgG)

anticardiolipin antibody (ACA) (24.5 GPL, normal range: <15), high positive immunoglobulin M (IgM) ACA (352.1 MPL, normal range: <12.5), negative IgG β-2-glycoprotein I (6.9, normal range: ≤20), positive IgM β-2-glycoprotein I (265.6, normal range: ≤20), and medium positive lupus anticoagulant (2.0, normal range: <1.2). Skin smears obtained from both earlobes, the left forearm, and bilateral lower limbs revealed positive acid-fast bacilli (AFB), with a bacteriological index of +4 and a morphological index of 3%. Histopathological examination of the skin showed granulomas dominated by foam cells with a few lymphocytes. Blood vessels exhibited signs of vasculitis, fibrinoid necrosis of the walls, and erythrocyte extravasation (Figure 2). Fite-Faraco staining detected AFB infiltrating the walls of blood vessels and nerve bundles (Figure 3). The patient was diagnosed with diffuse lepromatous leprosy with Lucio phenomenon and secondary vasculitis. She was started on intravenous methylprednisolone and multidrug therapy for multibacillary (MB) leprosy, which consists of rifampicin 600 mg and clofazimine 300 mg once per month, and dapsone 100 mg and clofazimine 50 mg daily. Due to aPL positivity and elevated D-dimer levels, which indicated an increased risk of both arterial and venous thrombosis, warfarin and aspirin were also initiated. Proper wound care, including normal saline compresses and antibiotic tulle dressings, was provided for her ulcers. Initially, her red-purplish rashes eroded and bled during the first week, but then progressively healed. By the 27th day of hospitalization, her wounds had dried, skin erosions had reduced, and no new wounds had formed. She was discharged and scheduled for outpatient follow-up. A repeat aPL antibody testing was planned 12 weeks after the initial test; however, the patient did not return for follow-up testing.

Discussion

Leprosy is a slow-progressing disease with a wide range of clinical manifestations, as well as diverse immunological and histopathological patterns. The Lucio phenomenon is a rare form of leprosy reaction, considered a variant of a type II leprosy reaction, typically seen in untreated lepromatous leprosy, characterized by uncontrolled proliferation of bacilli (4). Clinically, it manifests as diffuse skin infiltration, erythematous macules, hemorrhagic necrotic lesions that can ulcerate, complete loss of eyebrows and eyelashes, and peripheral neuropathy. The lesions are extensive, primarily affecting the extremities, though the buttocks and trunk may also be involved (5). Constitutional symptoms are uncommon. The pathogenesis of the Lucio phenomenon remains unclear;

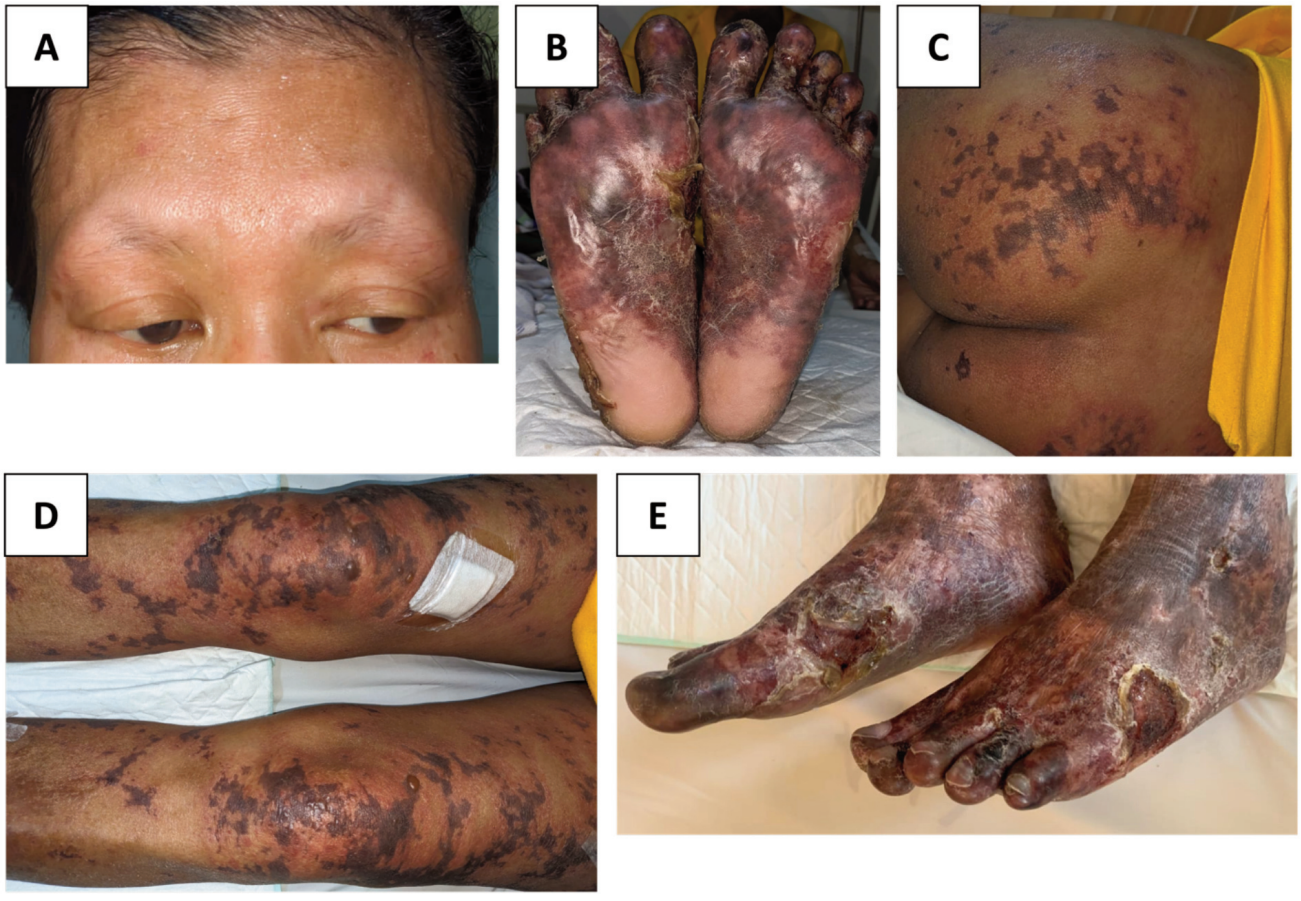

Figure 1. Clinical presentation of the patient. **A)** Madarosis of the eyebrows and eyelashes; **B-D**) multiple purpuric rashes on the soles, buttocks, and legs; **E)** ulcers on both feet.

however, the deposition of immunoglobulin and complement in the vasculature suggests an immune complex involvement (6). Histopathological features include Hansen bacilli invasion of blood vessel walls and lumina, leukocytoclastic vasculitis, vascular thrombosis, fibrinoid necrosis, and epidermal ischemic necrosis (4). Leprosy mimicking vasculitis and other rheumatologic diseases has been documented in several studies (7, 8). Differential diagnoses of the Lucio phenomenon include aPL syndrome (APS), SLE, cryoglobulinemia, polyarteritis nodosa, and other connective tissue disorders (4, 9). Sadeghinia *et al.* reported a case of lepromatous leprosy misdiagnosed as vasculitis for 8 years, presenting with erythematous lesions, recurrent extremity ulcers, and peripheral neuropathy, and treated with immunosuppressants (9). Another differential diagnosis for necrotic lesions in leprosy is vasculonecrotic erythema nodosum leprosum (ENL), typically observed in MB leprosy patients undergoing treatment, usually without AFB findings at histopathology (10). Additionally, a case of leprosy with the Lucio phenomenon, presenting with cutaneous infarcts and mimicking cutaneous vasculitis, has been reported (11). Autoantibodies associated with rheumatological diseases are frequently tested and may yield positive results in leprosy, complicating the clinical picture and making differentiation from autoimmune diseases challenging. aPL antibodies, typically associated with thrombotic events in APS, have been found in several infectious diseases, including leprosy, without thromboembolic manifestations (12). De Larranaga *et al.* found that 68.6%, 60.8%, and 56.9% of their leprosy patients tested positive for lupus anticoagulant, ACA, and anti-β2-glycoprotein I, respectively, without APS clinical features (13). Unlike other infections, these aPL antibodies may persist in leprosy patients even years after treatment (12). IgM was the predominant isotype in leprosy, in contrast to APS, where thrombotic events are more associated with IgG (12, 13). Nevertheless, thrombotic complications in leprosy patients with aPL positivity have also been documented (14). Nunzie *et al*. presented a case with manifestations of both the Lucio phenomenon and APS, showing hemorrhagic skin lesions, digital gangrene, and positive ACA (15). Other case reports have documented patients with leprosy and aPL positivity presenting with deep vein thrombosis or arterial thrombosis (14, 16, 17). Therefore, whether the presence of aPL antibodies in leprosy increases the risk of thrombotic events warrants further investigation. In our patient, given the aPL positivity, elevated D-dimer levels, and reports of thrombotic complications in similar cases, a decision was made to initiate anticoagulation therapy.

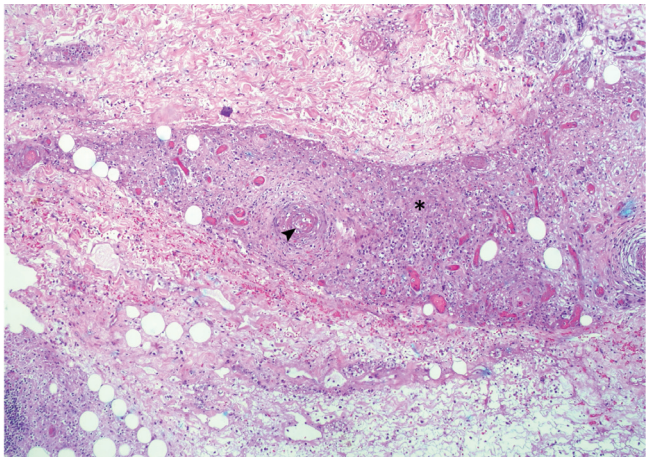

Figure 2. Histopathological examination of the skin (hematoxylin and eosin, 100×) showing areas of granuloma in the dermal layer (star) and vasculitis (arrowhead).

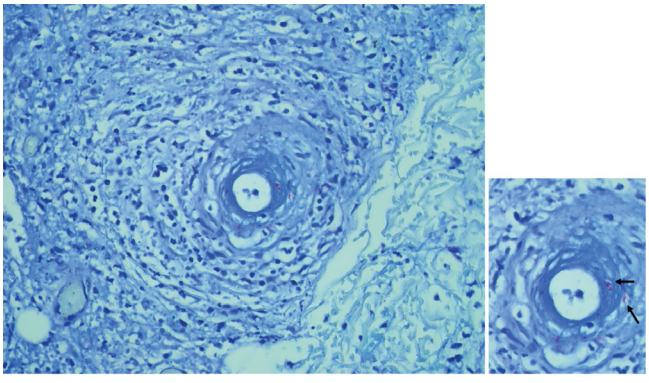

Figure 3. Fite-Faraco staining (400×) showing acid-fast bacilli in the walls of blood vessels (arrows).

Our patient presented with extensive erythematous-violaceous lesions with multiple ulcers and triple aPL antibody positivity, raising initial suspicion of primary vasculitis or vasculitis-associated APS. However, upon careful evaluation, including the presence of madarosis, nerve enlargement, and hypoesthesia, a diagnosis of leprosy with Lucio phenomenon was considered and subsequently confirmed by histopathological examination. Additional autoantibody testing was not pursued following the positive skin smear results and the patient's favorable response to leprosy therapy. Although antineutrophil cytoplasmic antibodies (ANCA) and antinuclear antibodies (ANA) are often tested in suspected vasculitis cases, ANCA is not routinely performed for secondary vasculitis at our center, and ANA is known to lack specificity and may test positive in leprosy.

Infectious etiologies, such as leprosy, should always be considered in the differential diagnosis of vasculitis and rheumatologic diseases, as the primary treatment involves antibiotics rather than the immunosuppressive therapies used for autoimmune conditions. Although the Lucio phenomenon is a rare form of leprosy, maintaining a high index of suspicion is essential, particularly in endemic regions like Indonesia, and even in non-endemic countries where an increase in leprosy cases has been reported, especially among immigrants. A thorough patient history and careful interpretation of autoantibody tests are crucial to reach an accurate diagnosis.

Conclusions

Hansen's disease can present as vasculitis, which is often mistaken for a manifestation of autoimmune diseases. It is crucial to carefully evaluate the patient's clinical data to make an accurate diagnosis, as the clinical manifestations of leprosy can closely resemble those of autoimmune diseases.

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