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Lucio phenomenon: a case report on an overlooked reaction in lepromatous leprosy

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Abstract

Our patient presented with a 5-year history of chronic, asymptomatic papulonodular lesions on the extremities. The lesions spread to the face and earlobes, with new ulcerative lesions on both legs for the past 8 months. Skin biopsy was compatible with lepromatous leprosy with Lucio phenomenon. Lucio phenomenon is a rare type of leprosy reaction found mostly in neglected lepromatous leprosy cases. Unfortunately, the patient developed pulmonary embolism and passed away. This case report focuses on the clinicopathological characteristics and management of Lucio phenomenon, which is an unusual form of leprosy reaction that often carries a poorer prognosis. Importantly, physicians should be able to differentiate Lucio phenomenon from other types of leprosy reactions for prompt management.

Introduction

Leprosy is a chronic granulomatous infectious disease caused by the bacteria *Mycobacterium leprae*, which primarily affects the skin and nerves. It follows a chronic, indolent course, often complicated by the host immunological reactions known as the leprosy reactions.[1] Leprosy reactions can occur before, during, or after leprosy treatment and are classified into three variants: reversal reaction (type 1 reaction), erythema nodosum leprosum (type 2 reaction), and Lucio phenomenon (type 3 reaction). Type 1 reaction results from an increase in cell-mediated immunity against the mycobacteria, whereas type 2 reaction is an immune complex-mediated humoral hypersensitivity reaction. Lucio phenomenon is considered the rarest reaction, occurring only in lepromatous leprosy and mostly in untreated patients.[2] In this report, we present the second case of Lucio phenomenon in Thailand, following the initial report in 2020.[3]

Case Report

A 26-year-old Thai female presented with multiple asymptomatic reddish papules and nodules on the extremities for 5 years. Initially, she sought multiple medical treatments, but her rash did not improve. Because there were no symptoms associated with the lesions, no further action was taken. Eight months prior to her visit to the Institute of Dermatology, she developed more of the same rashes on the face and ears, with non-painful ulcerations emerging on her legs. She denied any constitutional symptoms and was otherwise healthy, with no underlying disease reported. Upon physical examination, her vital signs were normal. Skin examination showed multiple ill-defined, non-scaly, skin-colored to erythematous papules and nodules on the face (Figure 1A), earlobes, and extremities. Particularly, the lesions on both of her legs

demonstrated crusted, necrotic, and jagged-edged ulcerations (Figure 1 B,C). Madarosis was present. Her motor and sensory functions were intact, and there were no thickened nerves. Cardiovascular and respiratory systems were normal, with no lymphadenopathy, hepatomegaly, or peripheral edema detected.

Skin biopsy from the right leg showed dense granulomatous infiltration with central necrosis in the dermis (Figure 1D). Several foamy histiocytes and globi were present. Leukocytoclastic vasculitis (Figure 1E) and endothelial proliferation of medium-sized vessels resulted in luminal obliteration. Ziehl-Neelson stain showed numerous acid-fast bacilli (AFB) in the dermis, within histiocytes, and within the small and medium-sized vascular endothelium (Figure 1F). Polymerase chain reaction was positive for *M. leprae*. Complete blood count, creatinine, and liver function tests were within normal limits. Anti-HIV was negative, rapid plasma reagin was reactive with a 1:8 titer, and treponemal pallidum hemagglutination was non-reactive. A false positive non-treponemal test was explained by lepromatous leprosy.

The final diagnosis of lepromatous leprosy with Lucio phenomenon was made. The patient was started on multidrug therapy for multibacillary leprosy based on WHO's recommendation,[4] which is composed of rifampin 600 mg once monthly, clofazimine 300 mg once monthly, clofazimine 50 mg daily, and dapsone 100 mg daily. The ulcerative lesions on the legs healed within 1 month after therapy, and there were no new lesions. Five weeks later, she sought medical care at a local hospital due to fever, right upper quadrant abdominal pain, and acute dyspnea. CT angiography of the chest was done and revealed a small intraluminal filling defect within the anterior branch of the right pulmonary artery and posterior branches of both pulmonary arteries compatible with acute pulmonary embolism. The patient was diagnosed with acute pulmonary embolism and was treated with subcutaneous enoxaparin 60 mg every 12 hours. Meanwhile, the laboratory investigation showed leukocytosis and a mixed pattern of liver injury with direct bilirubinemia. The sonographic murphy sign was positive, and computerized tomography (CT) revealed gallstone and gallbladder wall thickening compatible with acute cholecystitis. She was diagnosed with acute cholecystitis and treated with intravenous antibiotics, and cholecystectomy was performed a week later. Two days after surgery, she passed away from postoperative acute respiratory distress syndrome and sepsis.

Discussion

Lucio phenomenon is caused by direct invasion of AFB into the vascular endothelium, triggering immune complex and vascular damage.[5,6] In the past, Lucio phenomenon was limited to diffuse non-nodular lepromatous leprosy (also known as Lucio leprosy), and it was

believed to be related to the species *Mycobacterium lepromatosis*.[7] Newer reports have shown that lepromatous leprosy caused by *M. leprae* can also develop Lucio phenomenon.[5,8] Lucio phenomenon is endemic to Mexico and Brazil, with sporadic cases reported from Asia, including India, Indonesia, Malaysia, China, and South Korea.[5]

The diagnosis of Lucio phenomenon requires both relevant clinical and histopathologic features. The clinical manifestation begins with erythematous to violaceous macules and slightly infiltrated plaques, mainly affecting the lower extremities.[5] Other notable characteristic features include purpuric, hemorrhagic blisters, and net-like cyanotic pattern with a burning sensation.[6] These lesions subsequently turned into variable-sized necrotic ulcers with jagged-edges, leading to an atrophic scar as a sequalae.[6] Lucio phenomenon is known to have two histological patterns; the first one is leukocytoclastic vasculitis due to antigen-induced immune complex, whereas the second pattern is characterized by endothelial cell proliferation, thrombosis, and ischemic epidermal necrosis. The hallmark of both patterns is the presence of AFB in the vascular endothelium.[3,5,6] Our patient's histopathology showed AFB in the vascular endothelium, with both leukocytoclastic vasculitis and endothelial cell proliferation, accompanied by dermal necrosis, suggesting a potential explanation through vascular occlusion.[9]

When physicians encounter ulcerative lesions in multibacillary leprosy, it is crucial to differentiate between Lucio phenomenon and vasculonecrotic erythema nodosum leprosum. The latter will present with painful necrotic ulcers over preceding nodules, accompanied by constitutional symptoms, lymphadenopathy, neuritis, and visceral organ inflammation. These systemic involvements are uncommon for Lucio phenomenon. Vasculonecrotic erythema nodosum leprosum is often observed after treatment initiation, and the histopathology reveals leukocytoclastic vasculitis with prominent neutrophilic infiltration involving the dermis and lobular panniculitis.[6,8,10]

Lucio phenomenon has a high mortality rate, mostly associated with secondary infection and sepsis. Our patient's condition deteriorated from pulmonary embolism and sepsis, coinciding with acute cholecystitis. Notably, Costa *et al.* documented a case of lepromatous leprosy with Lucio phenomenon, resulting in a fatal pulmonary embolism. However, the cause of the pulmonary embolism was not specified.[8] It is worth knowing that lepromatous leprosy patients may develop a hypercoagulable state attributed to elevated levels of anti-cardiolipin IgM, soluble tissue factors, and von Willebrand factors, which may be predisposed to thrombus formation.[11] Previous reports have suggested an association between Lucio phenomenon and antiphospholipid syndromes. Both Nunzie *et al*. and Patel *et al.* described cases of Lucio

phenomenon complicated by antiphospholipid syndrome and thrombosis of digital arteries.[12,13] Additionally, Kumar *et al*. reported an association between Lucio phenomenon and ischemic stroke in the context of antiphospholipid syndrome.[14] These findings suggest that antiphospholipid syndrome may be involved in some cases of Lucio phenomenon. In our case, it was possible that the pulmonary embolism was related either to the hypercoagulable state associated with lepromatous leprosy or to a secondary antiphospholipid syndrome. Unfortunately, antiphospholipid antibodies were not tested in our patient due to limited awareness at the time.

Treatment for Lucio phenomenon is not standardized and is largely derived from case reposts. The mainstay treatment involves multibacillary multidrug therapy,[2] given in the same dosage as our patient, for 2 years.[15] A short course of high-dose corticosteroids (1 mg/kg/day) has shown benefit in severe immune reactions and hasten ulcer healing.[3,16] Systemic antibiotics should be given to prevent secondary bacterial infection.[8] In cases associated with antiphospholipid syndrome, anticoagulants, aspirin, and prednisolone have been shown to be effective.[12-14] However, thalidomide demonstrates no benefit in Lucio phenomenon.[2,6]

Thailand is recognized as an endemic region for leprosy, yet awareness of the Lucio phenomenon and its related complications remains limited. The prevalence of leprosy in Thailand is 0.03 persons per 10,000 population. In 2023, the detection rate is 0.12 persons per 100,000 population.[17] While leprosy cases in Thailand have decreased over the years, the slow-onset nature of the disease and the rise in expatriate workers from border countries have made the elimination of leprosy a persistent challenge.

Conclusions

Lucio phenomenon has unique characteristics and is associated with poorer outcomes. Early recognition and differentiation of Lucio phenomenon from other leprosy reactions will tailor the management approach accordingly. Close monitoring for complications, such as pulmonary embolism, secondary infection, and phospholipid syndrome, is crucial to optimizing patient outcomes.

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Figure 1. A) Multiple skin-colored and erythematous papules and nodules on the face; **B)** bilateral crusted and necrotic ulcers on the thighs; **C)** crusted, necrotic, and jagged-edged ulceration on the left thigh; **D)** low magnification of a skin biopsy taken from the right thigh showed dense granulomatous infiltration with central necrosis in the dermis (H&E stain, x 20); **E)** high magnification showed fibrinoid necrosis, karyorrhexis, and intravascular infiltration with neutrophils, compatible with leukocytoclastic vasculitis (H&E stain, x 400); **F)** high magnification showed endothelial proliferation of medium-sized vessels in the dermis resulted in luminal obliteration with AFB within the vascular endothelium (Ziehl-Neelson stain, x 400).