Case Letter

Lucio Phenomenon

To the Editor:

Lucio phenomenon is a type of reaction that occurs in a diffuse non-nodular form of lepromatous leprosy, which is chiefly encountered in Mexico. The reaction often is the presenting feature of leprosy. Although all forms of leprosy are common in India, Lucio phenomenon is rare. We report a case of Lucio phenomenon in southern India.

A 65-year-old man from southern India presented with multiple ulcers on the upper and lower extremities of 2 months' duration. He reported pain over the lesions that was moderate in intensity and burning. There was no history of fever, cough, or joint pain. The patient was not taking any medications. His personal and family history did not reveal any abnormalities.

Physical examination revealed masklike facies with loss of the lateral eyebrows. Thinning of the eyelashes was present. Vital signs were normal. Cutaneous examination showed multiple punched-out ulcers of various sizes over the forearms, buttocks, thighs (Figure 1), and dorsal aspects of the hands. Margins of ulcers varied from round to irregular in shape. A few ulcers were covered with a thick crust and a few had slough. Scarring and atrophy were noted over healed ulcers. No purpuric lesions were seen. Glove-and-stocking anesthesia was present. Moderate thickening of the ulnar, radial, and common peroneal nerves was noted. Motor functions were normal. The oral and nasal mucosa was normal. Other systemic examinations revealed no abnormalities. A provisional diagnosis of Lucio phenomenon was made.

Hemogram revealed microcytic hypochromic anemia with a hemoglobin level of 9.5 g/dL (reference range, 14.0–17.5 g/dL) and a total leukocyte count of 22,300/μL (reference range, 4500–11,000/μL). The differential count indicated neutrophils (94% [reference range, 40%–80%]) and lymphocytes (6% [reference range, 20%–40%]). The erythrocyte sedimentation rate was 95 mm/h (reference range, 0–20 mm/h) in the first hour. Urinalysis, liver and renal function tests, coagulation studies, blood sugar agar, antinuclear antibody test, Mantoux test, and chest radiography revealed no abnormalities. Serology for human immunodeficiency virus, syphilis, and hepatitis B surface antigen was negative. Bacterial culture and sensitivity from the lower leg ulcers revealed no growth. Slit-skin smear was positive (bacteriological index, right ear lobe, 6+; left ear lobe, 6+; right eyebrow, 3+; left eyebrow, 4+; normal skin, 2+). Biopsy revealed features of ischemic necrosis in the epidermis with varying degrees of atrophy and loss of rete ridges. The dermis showed foamy histiocytes containing fragmented bacilli with necrotizing vasculitis of vessels in the dermis (Figure 2). Fite-Faraco stain was positive for bacilli (Figure 3). Based on these findings, a diagnosis of Lucio phenomenon was made and the patient was started on a multibacillary dose of multidrug therapy (MDT) and systemic steroids. The patient was followed up for 2 months; initially, he showed improvement but was later lost to follow-up.

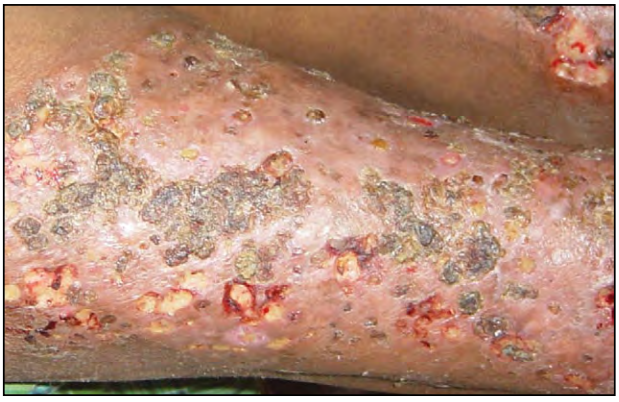

Figure 1. Multiple punched-out ulcers over the thighs.

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The authors report no conflict of interest.

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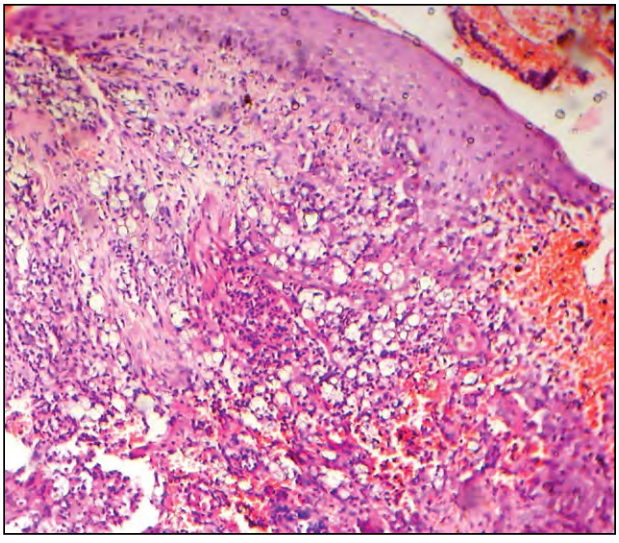

Figure 2. Ischemic necrosis in the epidermis with varying degrees of atrophy and loss of rete ridges. The dermis showed foamy histiocytes containing fragmented bacilli with necrotizing vasculitis of vessels (H&E, original magnification ×10).

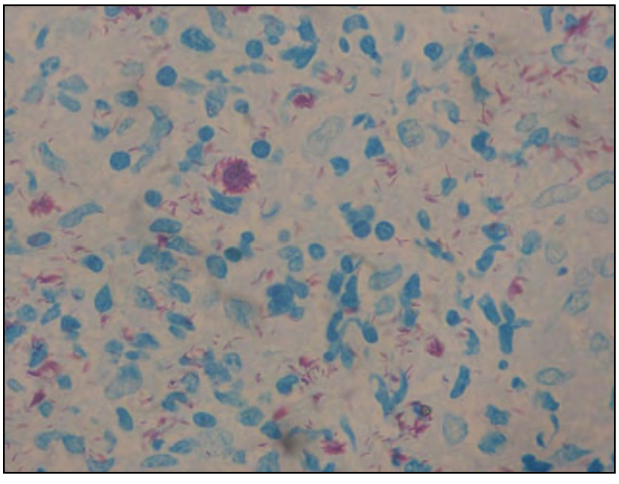

Figure 3. Presence of solid-staining bacilli (Fite-Faraco, original magnification ×100).

Lucio and Alvarado[1] described a diffuse nonnodular form of leprosy (*lepra bonita*) in 1852 that manifested as skin ulcers, which they called spotted leprosy (*lepra manchada*). In 1948, Latapi and Chevez[2] added their observations and recognized vasculitis on histopathology, calling it erythema necroticans or Lucio phenomenon; they referred to the diffuse non-nodular lepromatous form of the disease as pure and primitive diffuse lepromatosis or diffuse lepromatous leprosy.

Lucio leprosy is characterized by shiny thickened skin; loss of body hair including eyebrows and eyelashes, except the scalp hair; and widespread sensory loss giving the patient a myxedematous appearance.[3] It equally occurs in men and women, with a mean age of 34 years at the time of diagnosis. The first sign in the majority of patients is alopecia.[4]

Lucio phenomenon is a reactional state that takes place. It manifests 3 to 4 years after onset of the disease and is mainly seen in untreated patients.[5] Lucio phenomenon chiefly is encountered in the Sinaloa and Jalisco provinces of Mexico but also has been reported in other parts of the world.[2,6,7]

Han et al[8] discovered that the etiologic agent of diffuse lepromatous leprosy is not the usual *Mycobacterium leprae*. In patients with Lucio phenomenon, they found that the 16S ribosomal RNA gene, the signature gene for mycobacteria species, had evolved and had a 3% sequence divergence from the 16S ribosomal RNA gene of M *leprae*. This divergence indicated that this new strain FJ924 had descended from M *leprae* and warranted designation as a novel species called *Mycobacterium lepromatosis*. They further analyzed the genetic differences and phylogenetic distance between M *lepromatosis* and M *leprae*, reporting that the 2 organisms likely diverged approximately 10 million years ago,[8] which implies that the new agent M *lepromatosis* is actually old.[9]

The exact pathogenesis of Lucio phenomenon is unclear. It probably develops due to a deficient defense mechanism, which permits unhindered multiplication of bacilli and exposure of bacterial antigens to circulating antibodies.[10] It also is believed to occur either through the usual or the alternate pathway of complement activation in the natural history of erythema nodosum leprosum.[11] Anoxia is the basic pathogenic mechanism causing tissue necrosis in Lucio phenomenon, which may be due to endothelial proliferation with luminal occlusion with or without thrombosis occurring in the midsized vessels of the dermis, swelling and parasitization of the capillary endothelium, or subcuticular or deep dermal lepromatous granulomatous vasculitis.[4]

Because Lucio phenomenon is a vasculitic process caused by macrophagic infiltration of vessel walls, it can be considered as a type of granulomatous necrotizing vasculitis.[6] Lesions are characterized by painful, tender, red patches over the skin that become purpuric, followed by necrotic areas that are covered by brown-black eschar and fall off within 2 to 4 weeks, leaving a superficial atrophic scar. Ulcers are painful, recurrent, or cyclical for a duration ranging from 2 months to 10 years.[5] Lesions are seen over the legs, thighs, forearms, and buttocks, sparing the trunk and face. Glove-and-stocking anesthesia may be associated with motor abnormality with rhinitis.[4] Glove-and-stocking anesthesia was present in

our patient. Fever, splenomegaly, lymphadenopathy, glomerulonephritis, microcytic anemia, hypoalbuminemia, polyclonal gammopathy, and hypocalcemia have been described.[5]

Differential diagnoses include cutaneous vasculitis (eg, leukocytoclastic vasculitis, pyoderma gangrenosum), infections (eg, subcutaneous fungal infections, ulcerative variant of lupus vulgaris, atypical mycobacterial infection, necrotizing fasciitis), vasculopathy resulting from paraproteinemia (eg, myeloma, cryoglobulinemia), venous or arterial ulcers, and malignant conditions such as squamous cell carcinomas.

Histopathologically, it is characterized by ischemic epidermal necrosis, necrotizing vasculitis of small blood vessels in the upper dermis, severe focal endothelial proliferation of the midsized vessels in the dermis and subcutis, and a large number of bacilli in endothelial cells. Similar features of vasculitis are seen in Arthus reaction, thereby differentiating it from erythema nodosum leprosum where vasculitis does not play a primary role; this differentiation also is strengthened by the fact that erythema nodosum leprosum responds to thalidomide, unlike Arthus reaction and Lucio phenomenon.[12] It is believed to be a distinct type of granulomatous vasculitis that has an excess of antigen, which leads to ischemic necrosis of the depending tissues, and it is responsible for the clinical findings such as cutaneous hemorrhagic infarcts.[4,6]

There is no specific treatment protocol for Lucio phenomenon. Along with a multibacillary dose of MDT, steroids can be given. The response to treatment varies, with few cases showing good response to steroids with rifampicin, and in many cases treatment is associated with long-term morbidity.[4,5,7] Long-term morbidity may be due to glove-and-stocking anesthesia, venous insufficiency, and scar formation, resulting in physical impairment of the hands from fissures, ulcers, and resorption of bone.[4] Few cases have been reported in the literature, making the prognosis and mortality difficult to predict.[5,7] Our patient initially showed good response to steroids and MDT but later was lost to follow-up.

In tropical countries such as India where subcutaneous fungal infections and cutaneous tuberculosis are relatively common, Lucio phenomenon may masquerade as these conditions; therefore, a high index of suspicion is required. Our case represents the classic presentation of Lucio phenomenon, which is rare.

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REFERENCES

1. Lucio R, Alvarado Y. Opusculo sobre el mal de San Lazaro o elefanciasis de los Griegos. M *Murgia y Cia*. 1852:53.
2. Latapi F, Chevez ZA. The "spotted" leprosy of Lucio (la lepra "manchada" de Lucio): an introduction to its clinical and histological study. *Int J Lepr*. 1948;16:421-437.
3. Donner RS, Shively JA. The "Lucio phenomenon" in diffuse leprosy. *Ann Intern Med*. 1967;67:831-836.
4. Rea TH, Jerskey RS. Clinical and histologic variations among thirty patients with Lucio's phenomenon and pure and primitive diffuse lepromatosis (Latapi's lepromatosis). *Int J Lepr Other Mycobact Dis*. 2005;73:169-188.
5. Rea TH, Levan NE. Lucio's phenomenon and diffuse nonnodular lepromatous leprosy. *Arch Dermatol*. 1978;114:1023-1028.
6. Magaña M, Fernández-Díez J, Magaña ML. Lucio's phenomenon is a necrotizing panvasculitis: mostly a medium-sized granulomatous arteritis. *Am J Dermatopathol*. 2008;30:555-560.
7. Ang P, Tay YK, Ng SK, et al. Fatal Lucio's phenomenon in 2 patients with previously undiagnosed leprosy. *J Am Acad Dermatol*. 2003;48:958-961.
8. Han XY, Seo YH, Sizer KC, et al. A new *Mycobacterium* species causing diffuse lepromatous leprosy. *Am J Clin Pathol*. 2008;130:856-864.
9. Han XY, Sizer KC, Thompson EJ, et al. Comparative sequence analysis of *Mycobacterium leprae* and the new leprosy-causing *Mycobacterium lepromatosis* [published online ahead of print July 24, 2009]. *J Bacteriol*. 2009;191:6067-6074.
10. Rea TH. Lucio's phenomenon: an overview. *Lpr Rev*. 1979;50:107-112.
11. Sehgal VN. Lucio's phenomenon/erythema necroticans. *Int J Dermatol*. 2005;44:602-605.
12. Rea TH, Ridley DS. Lucio's phenomenon: a comparative histological study. *Int J Lepr Other Mycobact Dis*. 1979;47:161-166.