Acral Erythema, Edema, and Scaly Plaques in a Patient With Polyneuropathy

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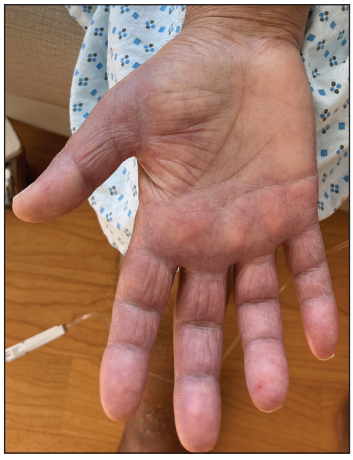

A 67-year-old man presented to his primary care physician with scaly plaques on the extensor surfaces along with distal neuropathy that had been slowly worsening over the past 6 months. The patient was prescribed triamcinolone cream 0.1% twice daily for presumed atopic dermatitis. Three months later, his symptoms rapidly worsened and he developed edema of the hands and feet. He was seen by neurology, and electromyography revealed severe distal sensorimotor neuropathy, prompting hospital admission for further evaluation of a potential rapidly progressive autoimmune disease. Laboratory workup and imaging were ordered, and the patient began an intravenous course of methylprednisolone. Minimal improvement in his symptoms was noted after 1 day, at which time dermatology was consulted.

Physical examination by dermatology revealed well-defined plaques with annular scale on extensor surfaces of the arms and legs, and edema on the hands and feet as well as distal sensorimotor neuropathy. The patient reported associated unspecified weight loss but denied any chest pain, shortness of breath, fevers, chills, cough, night sweats, exposure to chemicals, or recent travel. He reported that he had immigrated from India 37 years prior; his last visit to India was 6 years ago. He currently was taking famotidine for gastrointestinal reflux disease and losartan for hypertension. There was no personal or family history of autoimmune diseases. A complete workup for hematologic, thyroid, liver, and renal function was unremarkable. Initial autoimmune workup was negative for antinuclear antibodies and rheumatoid factor. Serum protein electrophoresis was normal. Results of testing for HIV, hepatitis B, and hepatitis C were negative. Chest radiography was unremarkable. Erythrocyte sedimentation rate and C-reactive protein level were elevated.

WHAT'S YOUR **DIAGNOSIS?**

a. borderline-borderline leprosy with type 1 lepra reaction
b. cutaneous tuberculosis
c. Lucio phenomenon
d. psoriasis vulgaris with associated psoriatic arthritis
e. sarcoidosis

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THE **DIAGNOSIS:** Borderline-Borderline Leprosy With Type 1 Lepra Reaction

Punch biopsies from plaques on the right elbow and right shin revealed diffuse granulomatous dermatitis (Figure 1) with a narrow Grenz zone in the superficial dermis. The upper dermis contained a dense band-like infiltrate of histiocytes with abundant foamy-gray cytoplasm and a moderate admixture of lymphocytes. The mid and deep dermis contained a nodular, perivascular, periadnexal, and perineural infiltrate of histiocytes and a dense admixture of lymphocytes. Periodic acid-Schiff and Gram stains were negative for microorganisms. Fite stain was positive for numerous organisms in histiocytes and small dermal nerves (Figure 2). These findings and the clinical examination confirmed a diagnosis of borderline-borderline leprosy with type 1 lepra reaction. The patient was started on dapsone 100 mg, rifampin 600 mg, and clofazimine 100 mg once daily and experienced clinical improvement within 6 months.

The World Health Organization reported more than 200,000 new leprosy cases globally in 2019, with most occurring in India, Brazil, and Indonesia.[1] About 150 to 250 new cases are detected in the United States annually.[1] The Ridley-Jopling classification of leprosy divides the condition into 5 categories: tuberculoid, borderline tuberculoid, borderline-borderline (BB), borderline lepromatous, and lepromatous. At one end of the spectrum, tuberculoid leprosy—a predominant Th1 immune response mediated by CD4 lymphocytes, interleukin (IL) 2, and interferon gamma[2]—is characterized by sharply demarcated erythematous and hypopigmented plaques with raised borders and an annular appearance.[2,3] Lesions typically have atrophic and hypopigmented centers that often appear in an asymmetric distribution on the arms and legs.[2,3] Histologic features include dermal tuberculoid granulomas with epithelioid cells—some located directly beneath the epidermis and others around deep vessels and nerves[3]—multinucleated Langerhans giant cells, thickened peripheral nerves with intraneural lymphocytic infiltrates, and granulomas with central necrosis. Fite-Faraco staining exhibits few bacteria.[2]

Lepromatous leprosy occurs in individuals with impaired T-cell immunity, leading to multiple red-brown nodular infiltrates in the skin and mucous membranes.[2,3] Lesions typically are symmetric and favor the face and auricle of the ear.[2,3] Histologically, there are bluish-gray foamy macrophages that form diffuse or nodular infiltrates with few lymphocytes,[2] with a Grenz zone between the epidermis and dermis. Nerves may show lamination of the perineurium resembling an onion skin.[2,3] Immunohistochemistry shows predominant CD8-positive infiltrates with a Th2 response and positive IL-4 and IL-10. Fite-Faraco stain shows numerous mycobacteria arranged in clusters and in histiocytes.[2]

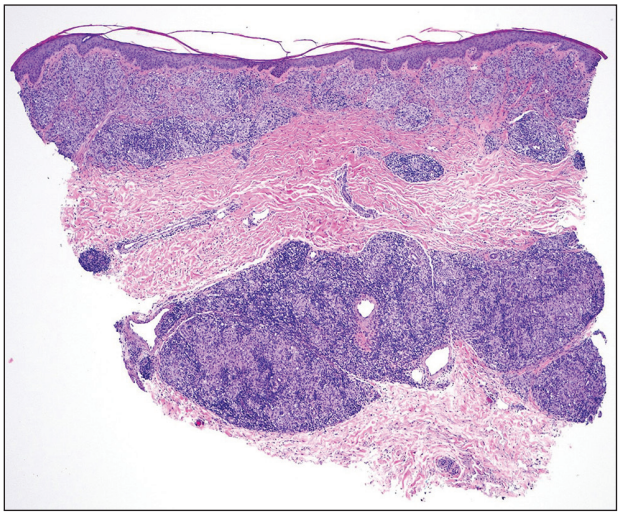

FIGURE 1. Histopathology revealed diffuse granulomatous dermatitis with a narrow Grenz zone in the superficial dermis (H&E, original magnification ×2).

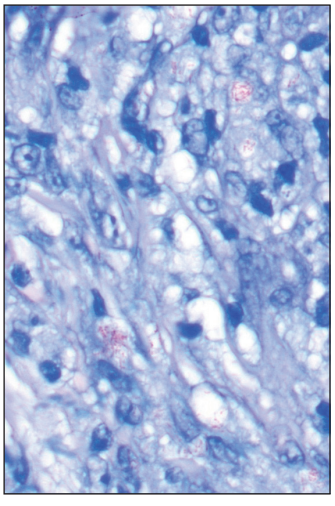

FIGURE 2. Fite stain was positive for numerous organisms in histiocytes and small dermal nerves (original magnification ×40).

Tuberculoid leprosy is treated with dapsone 100 mg and rifampin 600 mg once daily for 6 months,[4] and lepromatous leprosy is treated with dapsone 100 mg, rifampin 600 mg, and clofazimine 50 mg once daily for 12 months.[4] The prognosis for both is good with treatment; erythema and induration of skin lesions may improve within a few months, but residual nerve damage is common, especially in those with advanced disease prior to treatment.[2] For direct contacts, a single dose of rifampin may be given.[4]

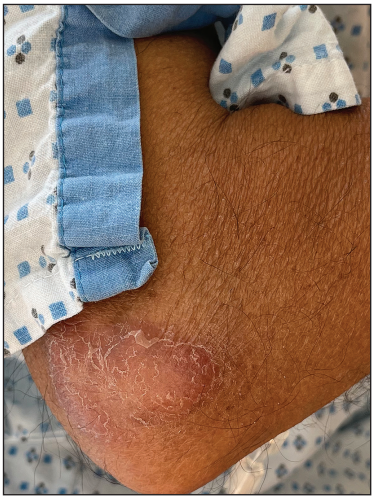

FIGURE 3. Asymmetric annular plaques as seen in our case patient are common in borderline-borderline leprosy.

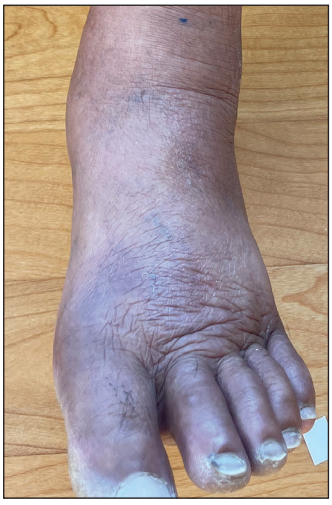

FIGURE 4. The patient had significant edema and erythema of the hands and feet.

Borderline-borderline leprosy manifests with numerous asymmetric annular plaques, as seen in our patient (Figure 3). Histology findings can be variable and often overlap with other forms of leprosy. There can be epithelioid granulomas and only a few acid-fast bacilli (AFB) or diffuse histiocytic aggregates with foamy histiocytes containing large numbers of AFB.[3] Nerve involvement is variable but can be severe in the setting of type 1 lepra reaction, which was present in our patient. Type 1 lepra reaction—a type IV cell-mediated allergic hypersensitivity reaction to *Mycobacterium leprae* antigens—manifests clinically with hyperesthesia, erythema, edema, and subsequent scaling.[2] It occurs in up to 30% of patients with borderline leprosy, usually within 12 months of treatment initiation.[2] Our patient had considerable edema and erythema of the hands and feet (Figure 4) along with extensive polyneuropathy prior to starting therapy.

Lucio phenomenon is a rare leprosy reaction found in patients with untreated lepromatous leprosy characterized by erythematous to violaceous macules that lead to ulceronecrotic lesions.[5] Histologically, there are many AFB in the vascular endothelium, leukocytoclastic vasculitis, and ischemic epidermal necrosis.[5] Our patient did not have ulcerative or necrotic lesions.

The classic skin lesions of psoriasis vulgaris can be described as well-demarcated pink plaques with white or silvery scales that usually are distributed symmetrically and often are found on extensor surfaces.[6] Rapidly progressive lesions can be annular with normal skin in the center, mimicking the lesions seen in tuberculoid leprosy. Clinically, both psoriasis and tuberculoid forms of leprosy are sharply demarcated; however, psoriatic lesions often have micaceous overlying scale that is not present in leprosy. Characteristic histologic findings of psoriasis are hyperkeratosis, parakeratosis, and acanthosis of the epidermis with dilated blood vessels and a lymphocytic infiltrate, predominantly into the dermis.[7] Psoriatic arthritis has a variable clinical course but tends to emerge 5 to 12 years after initial skin manifestation.[8] Classic clinical symptoms include swelling, tenderness, stiffness, and pain in joints and surrounding tissues.[8] Other than edema, our patient did not exhibit signs of psoriatic arthritis.

Sarcoidosis is a systemic autoimmune disease characterized by noncaseating epithelioid granulomas affecting various organs, with cutaneous manifestations present in approximately 30% of all cases. Cutaneous manifestations can be variable, including maculopapular lesions, plaques, and nodules.[9] Differentiating between cutaneous sarcoidosis and tuberculoid leprosy can be challenging, as both are granulomatous processes; however, histology of sarcoidosis demonstrates noncaseating granulomas in the dermis and/or subcutaneous tissues without AFB[9] compared to granulomas with necrotic centers in tuberculoid leprosy.

Cutaneous tuberculosis has variable morphologies. One subtype, lupus vulgaris, can manifest with violaceous, scaly, eroded plaques that could be confused for leprosy. Lupus vulgaris usually results from hematogenous or lymphatic seeding in individuals with high or moderate immunity to *M tuberculosis*.[10] Histologically, the dermis has tuberculoid granulomas containing multinucleated giant cells,[10] which can mimic those seen in BB leprosy. Tuberculin skin test results often are positive[10]; while this test was not performed in our patient, chest radiography was unremarkable, making this diagnosis less likely.

Mycobacterium leprae infections should be considered in a patient with a worsening rash and progressive polyneuropathy. Clinical diagnosis can be challenging due to similarities with other diseases; however, histopathologic findings can help differentiate *M leprae* from other conditions. This infection is treatable, and early detection can minimize long-term patient morbidity.

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