

Lepromatous Leprosy in a Patient with B-Cell Lymphoma and Tubulointerstitial Nephritis

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Leprosy is an ancient disease, and although the treatment for leprosy has been available for several decades, the number of cases of leprosy worldwide was recently estimated to be approximately 5.5 million.¹ Most cases of leprosy occur in tropical countries. In the United States, indigenous transmission has been recorded in Hawaii, Pacific island territories, and sporadically along the Gulf Coast.²

Generally, patients with leprosy do not experience increased morbidity as a result of viral, fungal, or protozoal infections, for which cellular immunity is an important defense mechanism. *Mycobacterium leprae* infection has not been shown to predispose patients to an increased risk for neoplasia,² and Hodgkin's lymphoma has rarely been reported in a patient with leprosy.³ In contrast, several cases of leprosy have been reported in patients with non-Hodgkin's T-cell lymphoma.⁴ This article reports the case of a patient with lepromatous leprosy and B-cell lymphoma whose clinical presentation with inguinal and axillary lesions preceded the development of cutaneous lesions by 1 week.

CASE PRESENTATION

A 54-year-old white man presents to an ambulatory medicine clinic with an approximately 7-week history of worsening diffuse erythematous rash that has become more pruritic, dry, and scaly.

History

The patient reports progressive swelling in his left groin over the past 8 weeks. He also reports a 30-lb weight loss and episodes of night sweats over the same time period. The patient denies fever and chills but admits to bilateral paresthesia in the lower extremities. He is taking no medications, but reports using antibiotics 1 month before presentation.

The patient previously worked in the logging business. He lives in a small town in southeast Texas and denies international travel or exposure to patients with leprosy. He admits to occasionally seeing armadillos scurrying near his home.

Physical Examination

On physical examination, the patient's vital signs are normal. His pupils are equal in size and reactive to light, and bilateral accommodation and extraocular movements are intact. Left posterior cervical and right submandibular lymphadenopathy is noted and is mobile, firm, nontender, and approximately 1 to 2 cm in diameter. On pulmonary examination, the patient's breath sounds are vesicular bilaterally. His heart rhythm is regular, the first heart sound and second heart sound are normal, and no murmurs, gallops, or rubs are detected.

The patient's abdomen is unremarkable. An approximately 6- by 10-cm confluent mass in the left inguinal area is noted and is minimally tender. Axillary lymphadenopathy is noted and measures 1 to 2 cm in diameter. The extremities are without edema.

Cranial nerves appear grossly intact. Peroneal, ulnar, and greater auricular nerves are not enlarged. Motor strength is normal in all muscles. Diminished sensation to light touch is found in the lower extremities. Diffuse erythematous skin lesions with sparing of the axillary, groin, palms, soles, and suprapubic areas are noted (**Figure 1**).

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Figure 1. Photograph of a patient with skin lesions caused by lepromatous leprosy. Diffuse, erythematous, papular skin lesions with sparing of the warmer axillary region are evident.

Laboratory Evaluation

Laboratory examination reveals the following values:

- Leukocyte count, 8000/mm³, no atypical lymphocytes noted
- Hemoglobin, 11.5 g/dL
- Hematocrit, 34.3%
- Platelets, 358,000/mm³
- Serum electrolytes, normal range
- Serum creatinine, 3.2 mg/dL
- Glucose, 75 mg/dL

Urinalysis is significant for the following values:

- Protein concentration, 100 mg/24 hr
- Glucose, 250 mg/dL

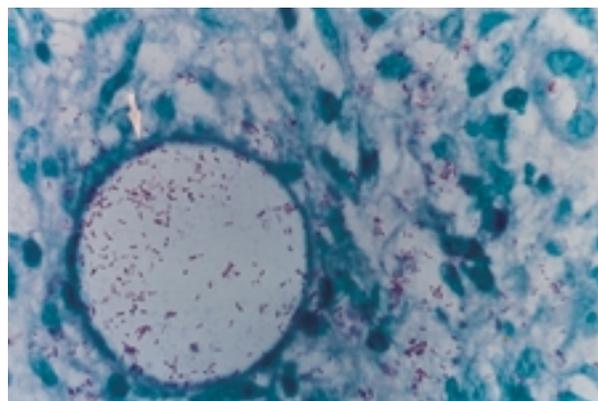


Figure 2. Skin biopsy specimen from a patient with lepromatous leprosy shows multiple acid-fast positive bacilli in the subcutaneous tissue.

- Sodium, 101 mEq/L
- Creatinine, 38 mg/kg/24 hr
- Osmolality, 359 mOsm/kg
- Protein, 918 mg/24 hr
- Creatinine clearance, 18 mL/min
- Erythrocytes, 2 cells/high power field

In addition, rare leukocyte casts are observed on urine microscopy. Chest radiography reveals numerous calcified nodes in the right hilum and small calcified granulomas in the right lung field. The remaining lung fields and cardiovascular silhouettes are normal. HIV serology is negative.

Hospital Admission and Further Evaluation

The patient is admitted to the hospital for evaluation of diffuse erythroderma, generalized lymphadenopathy, and renal insufficiency. Skin biopsies with Fite-Faraco staining reveal acid-fast bacilli with morphology that is consistent with *M. leprae* (**Figure 2**). Fine-needle aspiration of the left inguinal lymph node reveals non-Hodgkin's lymphoma, large-cell type. Histopathology of an excisional biopsy later confirms this finding. Flow cytometry confirms that, phenotypically, these cells are of B-cell lineage. Computed tomography of the thorax and abdomen is performed for staging and demonstrates diffuse adenopathy that involves the mediastinal, mesenteric, retroperitoneal, inguinal, and iliac nodes bilaterally. Bone marrow biopsy reveals acid-fast bacilli, without malignant cell infiltration.

Evaluation of the patient's non-oliguric renal insufficiency demonstrates a creatinine clearance of 18 mL/min. A renal ultrasound is unremarkable, and

renal biopsy shows tubulointerstitial nephritis with no evidence of acid-fast bacilli or lymphocyte infiltration.

Treatment

The patient is treated with dapsone (100 mg/day), rifampin (600 mg/day), clofazimine (50 mg/day), and prednisone (40 mg/day). He is also treated with combination chemotherapy consisting of cyclophosphamide (750 mg/m²), doxorubicin (50 mg/m²), and vincristine (1.4 mg/m²). During 5 days of chemotherapy, the dose of prednisone is increased to 100 mg/day.

Outcome

Significant improvement of the patient's diffuse erythroderma is noted after 1 week of therapy. The patient is discharged after 2 weeks of hospitalization. The patient's serum creatinine value significantly improves from 3.2 mg/dL on the day of hospital admission to 2.5 mg/dL on the day of hospital discharge. Out-patient follow-up is arranged for oncology and infectious disease visits. The patient's serum creatinine value is normal (1.1 mg/dL) after several months of therapy, but the patient is later lost to follow-up.

DISCUSSION

Overview of Leprosy

Leprosy, also termed *Hansen's disease*, is a granulomatous infection caused by *M. leprae*, an acid-fast bacillus that involves the skin and peripheral nerves. Leprosy is an ancient, communicable disease that occurs with an increased incidence in tropical climates, including the Gulf Coast of the United States. Transmission of *M. leprae* can occur from one individual to another after prolonged contact and appears to occur from the nasal mucosa of infected humans, non-human primates, and armadillos to the skin or upper respiratory tract of the host. The incubation period can range from 6 months to several decades, and the disease manifests as early leprosy in 20% to 30% of infected individuals.

Types of leprosy. Infection with *M. leprae* has been classified into four types: early or indeterminate, tuberculoid, borderline, and lepromatous leprosy.

Early or indeterminate leprosy. Early or indeterminate leprosy commonly presents with a subtle cutaneous lesion that may or may not be paresthetic.

Tuberculoid leprosy. Tuberculoid leprosy may present with a hypopigmented macule that later enlarges and becomes raised and anesthetic. This form of leprosy leads to the loss of dermal structures. Frequent involvement of the ulnar, peroneal, and greater auricular

nerves may lead to atrophy, contracture, and pain. Facial nerve involvement can result in corneal ulceration and blindness. Histologic findings include noncaseating granulomas with lymphocytes and giant cells, although acid-fast bacilli are infrequently demonstrated.

Borderline leprosy. Borderline leprosy commonly presents with an increased number and variability of skin lesions. The involved nerves are less anesthetic than in other forms of leprosy. Microscopically, there is a pre-dominance of macrophages within the granulomas.

Lepromatous leprosy. Lepromatous leprosy presents with extensive cutaneous involvement, sparing warmer sites of the body (ie, axilla, groin, palms, and plantar surfaces). Nerve involvement is less pronounced than in other forms of leprosy. Histologically, extensive granulomas with macrophages, foam cells, and many intracellular bacilli are present.

Clinical Presentation and Diagnosis

Lepromatous leprosy commonly presents with an extensive symmetrical distribution of macules, papules, and nodules involving the face, ears, wrist, elbows, knees, and buttocks. Clinical manifestations include epistaxis, nasal congestion, septal perforation with collapse (saddle nose), loss of lateral eyebrows, laryngitis, painless inguinal and axillary lymphadenopathy, sterility, gynecomastia, hypoesthesia of peripheral extremities, and invasion of the eye resulting in keratitis and iridocyclitis. The diagnosis of lepromatous leprosy can be made by demonstrating acid-fast bacilli in skin smears or biopsy. Histologic involvement of peripheral nerves is pathognomonic, even in the absence of bacilli.

Case Discussion

The emergence of leprosy in patients with T-cell lymphoma and mycosis fungoides has been reported.⁴ The development of lymphoma in patients with established leprosy has also been documented, although leprosy in patients with B-cell lymphoma is a rare occurrence.⁵ Whereas patients with cellular immunodeficiency may be susceptible to protozoal, fungal, and certain mycobacterial infections, patients who have defects in humoral immunity (ie, B-cell lymphoma in this case) are thought to be less prone to *M. leprae* infection. Patients with leprosy have defects in their cell-mediated immunity against *M. leprae*,² and this defect is hypothesized to be a generalized depression of cellular immunity.⁶ Studies have shown that the incidence of cancer in patients with leprosy is not significantly higher than the incidence in the general population.⁷

Based on the history of the patient in this case, it is tempting to postulate that his B-cell lymphoma occurred first and then lepromatous leprosy followed. Temporally significant was the documentation of lymphadenopathy and weight loss prior to the appearance of a generalized skin eruption. Although these authors believe that the patient may have been exposed to *M. leprae* at some point in the past, immunodeficiency associated with lymphoma may have allowed multiplication of dormant *M. leprae* and resulted in this patient's current presentation. A variety of renal lesions, such as glomerulonephritis, acute tubular necrosis, and tubulointerstitial nephritis, have been reported as manifestations of leprosy.⁸ Renal biopsy in this patient showed tubulointerstitial nephritis. No acid-fast bacilli were found, but a significant neutrophil infiltration was suggestive of an infectious or inflammatory etiology. An improvement of the patient's kidney function after intensive anti-leprosy therapy suggested that *M. leprae* played a key role in the pathogenesis of his reversible renal insufficiency.

Treatment

Recommended therapy for leprosy consists of dapsone (50 to 100 mg/day), rifampin (600 mg/day), clofazimine (50 to 200 mg/day), and a tapering dose of prednisone added to prevent erythema nodosum leprosum, a reactional state characterized by painful erythematous skin nodules, iridocyclitis, neuritis, fever, and other systemic manifestations.

A modified schedule of therapy for developing countries was established by World Health Organization (WHO) in 1982, based on practical considerations such as financial constraint and the availability of slit smear facilities. For multibacillary disease with a bacillary index of more than 2+ at all six skin sites, WHO recommends unsupervised administration of 100 mg/day of dapsone and 50 mg/day of clofazimine, as well as administration of 600 mg of rifampin and 300 mg of clofazimine once monthly with supervision.

SUMMARY

A combination of leprosy and lymphoma as seen in the patient in this case study is rare. Nonetheless, a case of cutaneous lymphoma masquerading as lepromatous leprosy has been reported.⁹ Also noted is the common presentation of painless inguinal and axillary lymphadenopathy associated with lepromatous leprosy, which can easily mask underlying lymphoma. Such cases stress the importance of making a histopathologic diagnosis, particularly in patients who present with atypical skin lesions. HP

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