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Case Report
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Type II Reaction Erythema Nodosum Leprosum: A Case Report

Jonas K[1] and Naqvi S[2]*

[1]University of Missouri, School of Medicine, USA

[2]CoxHealth Medical Center, Springfield, Infectious Disease, USA

Abstract

Leprosy, or Hansen's disease, is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*. This is a case of a 25-year-old male from Micronesia who presented to a hospital in the Midwest with a two-week history of a widespread, nodular, erythematous, painful rash most severe on his lower extremities and sparing only his hands and feet. In addition to the cutaneous manifestations, the patient met the criteria for Systemic Inflammatory Response Syndrome (SIRS) due to his presentation of tachycardia, tachypnea, leukocytosis, and elevated inflammatory markers. A short course of antibiotics, including Piperacillin-Tazobactam and Vancomycin, and IV steroids were started on admission. A skin biopsy taken from the center and edge of a lesion on the patient's right arm demonstrated acute and chronic granulomatous superficial and deep inflammation with abundant acid-fast bacilli consistent with lepromatous leprosy from a *Mycobacterium leprae* infection. Once the National Hansen's Disease Center was contacted previous therapies were stopped and a multidrug therapy, consisting of Rifampin, Moxifloxacin, Minocycline, Methotrexate, and Prednisone was started. The multidrug therapy promptly resulting in substantial clinical improvement over the subsequent months. This case emphasizes the significance of early recognition, accurate diagnosis, and timely initiation of appropriate treatment in leprosy management, even in unlikely regions such as the Midwestern United States.

Introduction

Leprosy, or Hansen's disease, is a chronic granulomatous infectious disease caused by *Mycobacterium leprae* a weakly acid-fast rod that is an obligate intracellular organism. The nasal mucosa is the main entry or exit route of *M. leprae*. The temperature required for survival and proliferation is between 27°C and 30°C. This explains its higher incidence in surface areas, such as skin, peripheral nerves, testicles, and upper airways, and lower visceral involvement. *M. leprae* remains viable for 9 days in the environment [1].

Case Presentation

A 25-year-old male from originally from Micronesia, moved to Hawaii in 2020 and then to Springfield, MO, in 2021. In Hawaii, the patient was diagnosed with Hansen's disease based off skin biopsy findings of granulomatous dermatitis consistent with borderline lepromatous leprosy. The patient was prescribed medication by the National Hansen's Disease Center physicians for the treatment of Hansen's disease, but he had stopped taking them in 2021 due to his move to the contiguous 48 states.

In 2022, the patient presented to an urgent care clinic with a two-week history of a widespread, nodular, erythematous, painful rash most severe on his lower extremities and sparing only his hands and feet. Besides the cutaneous manifestations, the patient endorsed systemic symptoms such as myalgia, arthritis, fatigue, nausea, vomiting, and nasal congestion.

His physical exam findings included lesions described as discrete raised wheals and extensive nodular formations with a central scale that are violaceous in color with erythematous perimeter. For the most part, the lesions were circular in shape but there were areas of confluence, ulceration, and necrotic appearing dry lesions with extensive peeling on his lower extremities. Concurrently, he displayed peripheral neuropathy of his left index and middle finger characterized by numbness in the affected area (Figure 1).

The patient was sent to the emergency department where he was admitted for signs of Systemic

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Correspondence:
Kenlee Jonas, University of Missouri, School of Medicine, 1 Hospital Dr, Columbia, MO 65212, USA

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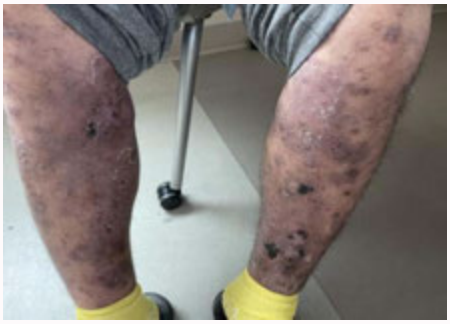

Figure 1: Severely affected areas of tender nodules, scarring, ulceration, and necrotic appearing dry lesions with extensive peeling present on the patient's lower extremities.

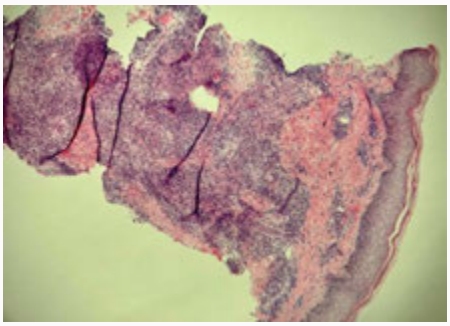

Figure 2: Gram stain of a right arm lesion biopsy demonstrating an impressively high mycobacterial load supporting the diagnosis of Type II Erythema Nodosum Leprosum.

Inflammatory Response Syndrome (SIRS), such as tachycardia (117 bmp), tachypnea (20 bpm), fever (only low grade at 99.2°F), impressive leukocytosis (32.8 thou/mm^3 with a peak of peak of 35.1), and elevated inflammatory markers (CRP of 20.90 mg/dL).

A skin biopsy was then obtained taken from the center and edge of a lesion on the patient's right arm. The histopathological report revealed acute and chronic granulomatous superficial and deep inflammation with high mycobacterial load of acid-fast bacilli consistent with lepromatous leprosy from a *Mycobacterium leprae* infection (Figure 2).

Upon the patient's admission, a short course of empiric antibiotics, including Piperacillin-Tazobactam and Vancomycin, and IV steroids were initiated. However, once the National Hansen's Disease Center was contacted for recommendations following the skin biopsy results, previous therapies were stopped, and a multidrug therapy was started. The dose packs of medications, known as blister packs, were initiated for a treatment plan of 12 to 24 months. The three main medications included once monthly antibiotics of Rifampin, Moxifloxacin, and Minocycline [2]. In addition to antibiotics, methotrexate and low tapered dose of prednisone was added weekly for the management of inflammation [3]. Over his hospital course, the patient showed substantial improvement with a decrease in pain, erythematous lesions, and inflammatory markers, as well as systemic symptoms.

The patient was scheduled to return to clinic in the following months, however missed his next two appointments. Six months after his hospitalization, he presented to the infectious disease clinic with the re-emergence of painful nodular lesions on his lower extremities as well as severe myalgias. The patient divulged that he was inconsistent in taking his blister pack regimen and did not continue

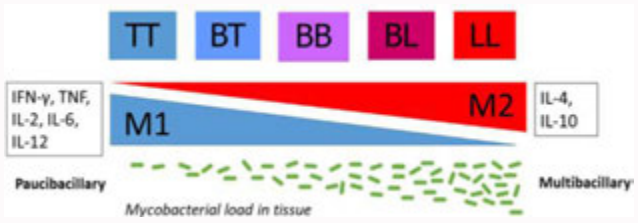

Figure 3: Diagram depicting the pathogenesis and immunologic response in relation to the mycobacterial load and appropriate cytokines responsible for different stages using the Ridley and Joplin classification system of Leprosy [7].

taking prednisone following his hospital stay. The infectious disease physician discussed with the patient the importance of compliance with his medication regimen in relation to his disease. Additionally, the physician helped the patient establish care at a medical facility closer to his home two hours away and scheduled zoom calls with the National Hansen's Disease Center for monthly check-ups. The goals of this extensive therapy are to minimize nerve damage, muscle weakness, and physical deformity while attempting to control the body's immune mediated reactions while eradicating the disease. Compliance is a challenged faced by many with leprosy due to this extended therapy regimen; therefore, follow-up and support are crucial for treating Hansen's disease.

Discussion

Immunological reactions in response to Leprosy are typically divided into two categories (1) Type 1 reversal reaction, which is an acute exacerbation of cell-mediated response possibly triggered by bacilli in Schwann cells leading to peripheral/dermal nerve damage and (2) Type 2 Erythema Nodosum Leprosum reaction, which is a delayed immune-complex mediated response to the large amount of anti-mycobacterial antibodies leading to fever, malaise, arthritis, neuritis, vasculitis, uveitis, lymphadenopathy, SIRS, and tender/painful nodules [4] (Figure3). Our patient demonstrated the more severe and chronic immunologic response to *M. leprae* resulting in extensive disease burden affecting his health, compliance with treatment, and even contributing to his perceived societal isolation experienced by many with Lepromatous Leprosy [5].

By 2000, the World Health Organization (WHO) declared leprosy, also known as Hansen's disease (HD), eliminated as a public health threat. Despite this declaration, to this day, leprosy remains a formidable public health challenge due to the significant cause of neurologic dysfunction and disability, with more than 4 million new cases identified from 2000 to 2020 [2]. Classic endemic regions like Brazil, India, and Indonesia may not be the only endemic regions as of the present. Within the past decade, regions within the United States have become "endemic" to *Mycobacterium leprae* including central Florida. While this region is susceptible to infection spread through travelers and immigrants, around 34% of new cases were locally acquired from 2015-2020 [6]. Even more surprising, "A recent case in a native Missourian that appears to be locally acquired suggests that leprosy may now be endemic in Missouri, possibly due to the expanded range of its zoonotic vector, the nine-banded armadillo" [4]. This article sheds light on the relevance of leprosy as a differential diagnosis even for unsuspecting regions such as the Midwestern United States.

Conclusion

This case report provides a comprehensive overview of a patient

diagnosed with leprosy, encompassing the clinical presentation, diagnostic workup, and management. Leprosy can be a debilitating disease that requires extensive treatment and follow-up. Health care providers, in endemic regions or not, should be aware of how leprosy manifests for evaluation and early institution of appropriate treatment to prevent disease mortality and morbidity for the patient but also for the community.

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