

A Rheumatoid Arthritis-Like Presentation in Multibacillary Leprosy with Concurrent Erythema Nodosum Leprosum

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ABSTRACT:

Leprosy is a chronic infectious disease caused by a *Mycobacterium leprae* (*M.leprae*), continues to be a diagnostic challenges because of its rarity and diverse clinical manifestations. Classic erythema nodosum leprosum (ENL) typically presents in patients with preexisting borderline lepromatous or lepromatous leprosy. This case report discusses the atypical presentation of ENL in a 69-year-old woman who experienced intermittent crops of red nodules with fever, accompanied by glove and stocking anesthesia, joint deformities without clinical evidence of classic multiple symmetrical papulonodular lesions of lepromatous leprosy. The initial diagnosis of rheumatoid arthritis, followed by treatment with Disease-modifying antirheumatic drugs, failed to provide symptom relief, leading to further investigation. Biopsy results and slit skin smears confirmed multibacillary leprosy with necrotizing suppurative vasculitis, and special stains confirmed the presence of *M. leprae*. Multidrug therapy was initiated, resulting in an initial improvement in symptoms. This case report emphasizes the importance of considering leprosy with erythema nodosum leprosum in the differential diagnosis for patients presenting with rheumatoid arthritis-like symptoms, particularly in atypical clinical manifestations and when there is no response to standard treatments.

Key words: Erythema Nodosum Leprosum, Multibacillary Leprosy

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Introduction

Leprosy is a chronic infectious disease caused by a *Mycobacterium leprae* (*M.leprae*). The transmission of *M. leprae* is not fully understood, but it is generally believed to occur through respiratory droplets from infected individuals. The incubation period between exposure and the appearance of cutaneous symptoms in leprosy can range from months to 30 years¹. The clinical and histopathologic manifestations of leprosy are diverse and continue to present diagnostic challenges. They can be categorized into two primary forms- tuberculoid and lepromatous leprosy- depending on the immunologic response of the host². Furthermore, immunologic reactions are common in leprosy, affecting 30%-50% of all patients². There are two types of leprosy reactions: type 1 (reversal reaction), which occurs in patients with tuberculoid or borderline leprosy, and type 2 (erythema nodosum leprosum (ENL)), which usually occurs in patients with lepromatous leprosy. We describe a patient with multibacillary leprosy concurrent with ENL, presenting as rheumatoid-like joint deformities and recurrent painful red nodules over the past two years, making it difficult to diagnose leprosy due to the absence of classical multiple symmetrical papulonodular skin lesions typically associated with the lepromatous leprosy. However, infiltrating skin lesions on both earlobes were observed later. Our aim in reporting this case is to remind healthcare professionals that leprosy can mimic various diseases and requires careful attention to avoid delayed or incorrect diagnoses.

Case report

A 69-year-old woman was referred for recurrent painful raised red nodules on her arms,

legs, and trunk over the past 2 years (Figure 1). Her underlying diseases are dyslipidemia, and homozygous E thalassemia. She was born in Phetchabun but moved to Pathum Thani 20 years ago. She denied any familial members or neighbors with history of leprosy.



Figure 1 Multiple erythematous subcutaneous nodules on both forearms(A,B)



Figure 2 Contracture deformity with claw hands on ulnar sides

She began experiencing glove and stocking anesthesia 15 years ago, leading to limited finger motion of third, fourth, and fifth fingers of both hands and bilateral contracture

deformity (Figure 2). Initially diagnosed by previous community hospital with seronegative rheumatoid arthritis by the ACR/EULAR 2010 classification criteria with score of 7 (5 for more than 10 small joints involvement; 1 for more than 6 weeks symptoms duration and 1 for abnormal C-reactive protein)^{3,4}. She received treatment with oral methotrexate 10 mg/week, sulfasalazine 1000 mg daily, and prednisolone 10 mg daily. In the last 2 years, she had intermittent crops of painful red nodules accompanied by fever, joint pain and fatigue every 1 to 2 weeks. These symptoms subsided within 7 days upon the treatment with paracetamol and prednisolone.



Figure 3 Skin-colored infiltrative skin lesions on both earlobes (A,C)

Note the erythematous patch on both earlobes were resulted from slit skin smears (A,C)

Multiple erythematous subcutaneous nodules on both arms and thighs were erythema nodosum leprosum (D-E)

There are no typical papulonodular lesion on trunk (F)

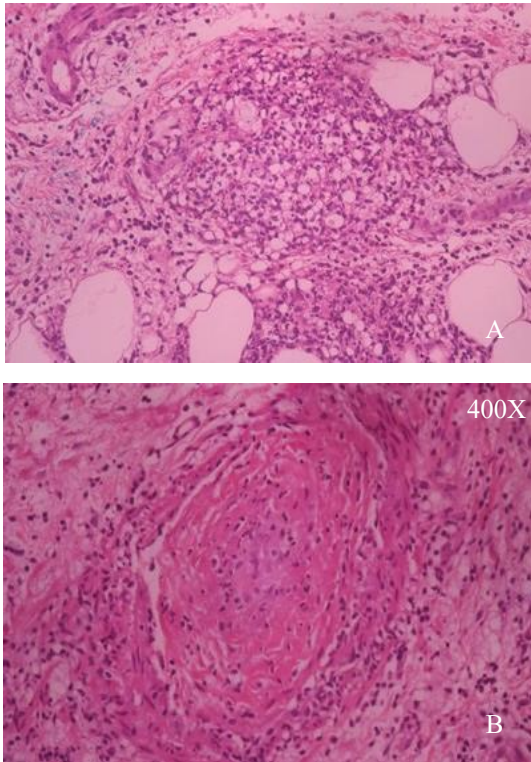


Figure 4 Multiple aggregations of intracellular organism (globi) (A) necrotizing suppurative vasculitis of medium-sized vessels with focally organized thrombosis (B)

On physical examination, she had multiple tender erythematous subcutaneous nodules on both upper and lower extremities, with postinflammatory hyperpigmentation on both legs. No other patches, plaques, nodules were seen. Her eyebrows, eyelashes, and hair on the whole body were normal. Nevertheless, after a careful physical examination, mild skin-colored infiltration on both ear lobules were observed (Figure 3). She exhibited bilateral loss of pain, touch and temperature sensation on both palms and soles, with traumatic hematoma on the tip of right index finger with bilateral median and ulnar claw-hand deformities. Bilateral ulnar and right radial nerves can be palpated with

tenderness next to the medial epicondyle and distal radial portion at wrist area respectively.

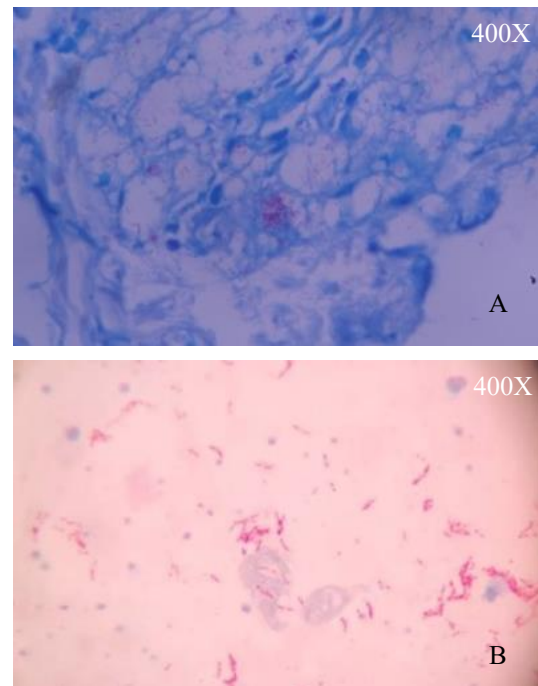


Figure 5 Numerous acid-fast bacilli from tissue biopsy were seen in Wade-Fite stain (A) and Acid-fast bacilli (AFB) stain from slit skin smear from right earlobe with BI = 4+ (10-100 bacilli/HPF)(B)

Blood investigations, including liver function, renal function, rheumatoid factor, anti-HIV and urine protein were normal, except for hypochromic microcytic anemia and a high C-reactive protein of 38.90 mg/L. Computed tomography scan of the chest and whole abdomen showed right axillary lymph node enlargement, with normal size of liver and spleen. Right axillary lymph node biopsy revealed reactive lymphoid hyperplasia.

The incisional biopsy at the subcutaneous nodule on the left forearm showed superficial and deep perivascular dermatitis with

panniculitis, a severe degree of neutrophils, and foamy histiocytes with aggregation of intracellular organism (globi) seen with necrotizing suppurative vasculitis in the deep dermis and subcutis. Medium-sized vessels were focally occluded by organized thrombi (Figure 4). Additional special stains tissue for acid-fast bacilli (AFB) stain and Wade-Fite stain were positive with solid and granular bacilli with a BI of 4+ (10-100 bacilli/HPF) (Figure 5A). The slit skin smears from both earlobes also showed positive results on AFB with a BI 4+ on the right ear (solid 75%, fragmented 25%) and a BI of 2+ on the left ear (Figure 5B).

She was diagnosed with lepromatous leprosy with concurrent erythema nodosum leprosum (ENL), and her Disease-modifying antirheumatic drugs (DMARDs) were discontinued. She was initiated on a multidrug-therapy regimen (MDT) for multibacillary leprosy (MB) (rifampicin 600 mg monthly, clofazimine 300 mg monthly together with dapsone 100 mg daily). She also received clofazimine 200 mg daily and prednisolone 5 mg daily for ENL. At the 1-week follow-up, patient developed fever with more nodules erupted on both forearms. The dose of clofazimine was increased to 300 mg/day, and prednisolone was raised to 40 mg/day. In the next 2 weeks, subcutaneous nodules improved, and generalized dark orange to red skin, hyperpigmentation was seen due to clofazimine side effects. After completing 1 month of treatment, she experienced fatigue, dyspnea, and near syncope. Her blood test showed marked anemia from hemolysis. Dapsone was discontinued from the MDT regimen for MB, with the continuation of rifampicin 600 mg monthly, and clofazimine 300 mg daily.

Discussion

This patient initially presented with polyarthrititis and neuritis resulted in the diagnosis of rheumatoid arthritis. However, she was later detected to have recurrent painful nodules and skin-colored infiltrative skin lesion on both ear lobules, which led to the final diagnosis of multibacillary leprosy with concurrent ENL from the skin histopathology and slit skin smear.

Erythema nodosum leprosum (ENL) or type 2 leprosy reaction is an acute to subacute immune-mediated reaction that can causes severe nerve damage and illness. ENL affects approximately 50% of patients with lepromatous leprosy and 10% of borderline leprosy and associates with multiple systemic involvements such as neuritis, arthritis, dactylitis, lymphadenitis, iridocyclitis, orchitis, and nephritis⁵. Leprosy reaction of both type 1 (reversal reaction) and type 2 (ENL) are known to be able to occur any time eg. before, during, and after the treatment with MDT^{6,7}. Few cases of patients with ENL lacking leprosy skin lesions have been reported. Some authors have postulated that the absence of leprosy skin lesions is due to the complete depletion of a Th1 immune response, causing a high intracellular bacillary load in macrophage and a Th2-mediated excessive production of specific antibodies. Any events that shift from Th2 to a Th1 response will cause numerous extracellular release of mycobacterial antigens, leading to severe immune complex-mediated reactions that produce neuritis and ENL skin lesions, consequently⁸. Even many atypical patterns of ENL have been described such as bullous, ulcerative-necrotic lesions, erythema multiforme-like, Sweet's syndrome-like, fever

and constitutional are the shared presentations among variations⁹.

In conclusion, regardless of whether the demonstration of typically papulonodular lesion of leprosy is present, ENL should be suspected in any patients presenting with neuropathy involving hands and feet, tender erythematous nodules, especially in an endemic area. Lastly, in the undiagnosed case of leprosy, careful holistic physical examination especially neurological examination and palpating skin infiltration on ear lobules together with slit skin smear and skin biopsy should be done to confirm the diagnosis of leprosy.

References

1. Park L, Wallace CE, Vasile G, Buckley C. A Case of Lepromatous Leprosy With Erythema Nodosum Leprosum. *Cureus* 2023;15:e33846.
2. Scollard DM. Time and change: new dimensions in the immunopathologic spectrum of leprosy. *Ann Soc Belg Med Trop* 1993;73:5-11.
3. Mjaavatten MD, Bykerk VP. Early rheumatoid arthritis: the performance of the 2010 ACR/EULAR criteria for diagnosing RA. *Best Pract Res Clin Rheumatol* 2013;27:451-66.
4. Andrade TCPC, Martins TY, Vieira BC, Santiago TM, Soares CT, Barreto JA. Lepromatous leprosy simulating rheumatoid arthritis - Report of a neglected disease. *An Bras Dermatol* 2017;92:389-91.
5. Negera E, Walker SL, Girma S, et al. Clinico-pathological features of erythema nodosum leprosum: A case-control study at ALERT hospital, Ethiopia. *PLoS Negl Trop Dis* 2017;11:e0006011.
6. Prabhu S, Shenoi SD, Pai SB, Sripathi H. Erythema nodosum leprosum as the presenting feature in multibacillary leprosy. *Dermatol Online J* 2009;15:15.
7. Tournalaki A, Marzano AV, Gianotti R, Fiallo P, Nunzi E, Alessi E. Necrotic erythema nodosum leprosum as the first manifestation of borderline lepromatous leprosy. *Arch Dermatol*. 2008;144:818-20.
8. Andreoli A, Brett SJ, Draper P, Payne SN, Rook GA. Changes in circulating antibody levels to the major phenolic glycolipid during erythema nodosum leprosum in leprosy patients. *Int J Lepr Other Mycobact Dis* 1985;53:211-7.
9. Alakad R, Nofal A, Assaf M. Atypical presentations of erythema nodosum leprosum: Diagnostic and therapeutic aspects. *J Dtsch Dermatol Ges* 2021;19:1133-1143.