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Case Report **OPEN ACCESS**

Hidden in plain sight: A case of misdiagnosed leprosy mimicking rheumatoid arthritis

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ABSTRACT

Mycobacterium leprae is a causative agent of leprosy, a chronic granulomatous infection that primarily affects the skin and the peripheral nerves. Musculoskeletal involvement, including inflammatory arthritis, is quite common despite being under recognized. Leprosy presents protean manifestations, making it a great mimicker. Herein, we report a case of a 41-year-old Indonesian who resided in Malaysia for the past 20 years and presented with chronic joint pain and swelling of hands for a year, along with gradual facial swelling and numbness in the toes. Retrospectively, the patient noticed an erythematous skin lesion over the trunk and lower limbs 6 months before these symptoms, which did not improve with standard treatment for allergic reactions. These spectral manifestations and the subtle signs of leprosy led to a diagnostic delay of more than a year. In this study, we aim to enhance clinical awareness among primary care providers about recognizing, classifying, and appropriately treating the disease to prevent life-long deformity and disability.

Keywords: leprosy, *mycobacterium leprae*, joint pain, numbness, allergic reactions

INTRODUCTION

The global prevalence of leprosy has significantly declined since the introduction of multidrug therapy (MDT) in the 1980s. According to the World Health Organization (WHO) data for 2022, 174,087 new cases were reported globally, with Brazil, India, and Indonesia as the top three countries with the highest leprosy burden [1]. The international migration and importation of workers from endemic areas can spread leprosy to regions where it is uncommon. In 2017, 35% of the reported leprosy cases in Malaysia were from non-citizens and were primarily from Indonesia, Philippines, and Nepal [2]. These cases accounted for approximately 91% of new cases for the following year, grade 2 deformity and multibacillary (MB) leprosy cases were also documented, and these cases accommodate higher bacterial loads that are comparable with paucibacillary leprosy [2]. Diagnosing leprosy in a primary care setting can be challenging, especially in non-endemic regions. The low recorded incidence of leprosy in Malaysia conditions insufficient experience in recognizing the signs and symptoms of the disease [3]. Articular involvement in leprosy is regarded as the third most frequent manifestation, following dermatological and neurological involvement [4]. As reported, 75% of leprosy cases have joint involvement and might occasionally present arthritis as the only noticeable symptom [4]. Leprosy is a highly curable disease; hence, it is essential to highlight the aggravating circumstances through comprehensive history-taking and a meticulous physical examination, as establishing a diagnosis is crucial in prompt treatment and preventing interhuman transmission.

CASE REPORT

A 41-year-old Indonesian man from Kalimantan, who has been living in Malaysia for 20 years, presented with symmetrical small joint swellings and hand pain for the past year. The onset was insidious and persistent, with a dull, aching character. The patient denied morning stiffness or any exacerbating factors throughout the duration. These symptoms were accompanied by fatigue, gradual onset of facial swelling, and paresthesia in both toes. Six months earlier, the patient had extensive erythematous rashes on the back and calves with a burning and occasional numbness, which did not improve with the topical steroids or oral antihistamines prescribed by the primary care clinician, but gradually disappeared within a few months.

The patient sought treatment at another primary care clinic because of chronic joint pain and swelling that were affecting his daily work routines. The laboratory investigations showed positive inflammatory markers with a high erythrocyte sedimentation rate of 110 mm/h and a positive rheumatoid factor (RF) of 24 U/ml.

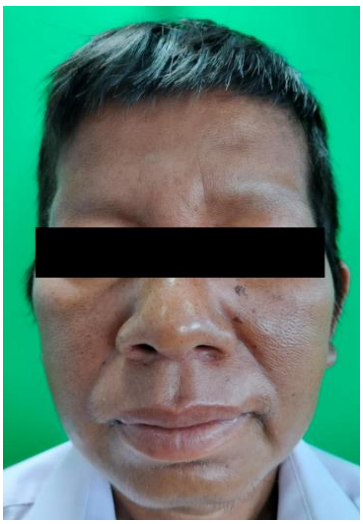

Figure 1. Diffuse infiltration with loss of facial hair and madarosis (reprinted with permission of the patient)

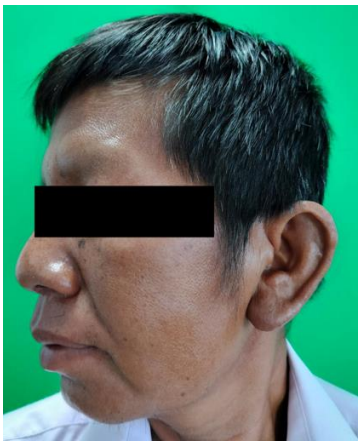

Figure 2. Lateral view showing sparse facial hair and thickened earlobe (reprinted with permission of the patient)

The routine blood investigations, full blood count, and other connective tissue disease parameters, including anti-nuclear antibody (ANA), complement components 3, and complement components 4, were negative. The radiographic findings of bilateral hands were unremarkable; spot sputum acid-fast bacilli (AFB) was negative; and the Mantoux test was 0 mm. Consequently, the patient was diagnosed with rheumatoid arthritis (RA) with an ACR/EULAR score of 7. The patient was treated with oral ibuprofen 200 mg twice daily and referred to a rheumatology specialist at the tertiary center. While awaiting the rheumatology appointment, the patient was referred to a family physician because of persistent joint pain despite regular analgesic use. A skin slit smear (SSS) test was performed considering the high index of suspicion for leprosy. The SSS confirmed this, showing a bacteriological index of 4.2. The vision and G6PD tests were conducted before referring the patient to the dermatology specialist clinic. All results returned normal.

Upon physical examination, the patient has facial puffiness and diffuse skin infiltration, eyebrow loss (**Figure 1**), and thickened and elongated earlobes (**Figure 2**). The skin of both hands was dry, with attenuation of skin creases, hair loss, and swelling of the whole fingers, but no deformities or rashes (**Figure 3**). Extensive hyperpigmented patches were noted on the back (**Figure 4**), with sensation sparing. Erythematous patches were also present on both lower legs. All toes showed

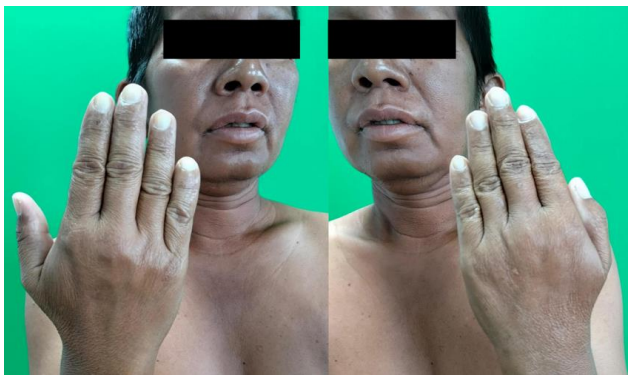

Figure 3. Dorsal view of bilateral hands showing swollen of the whole fingers, dry skin with attenuation of skin creases and loss of hair (reprinted with permission of the patient)

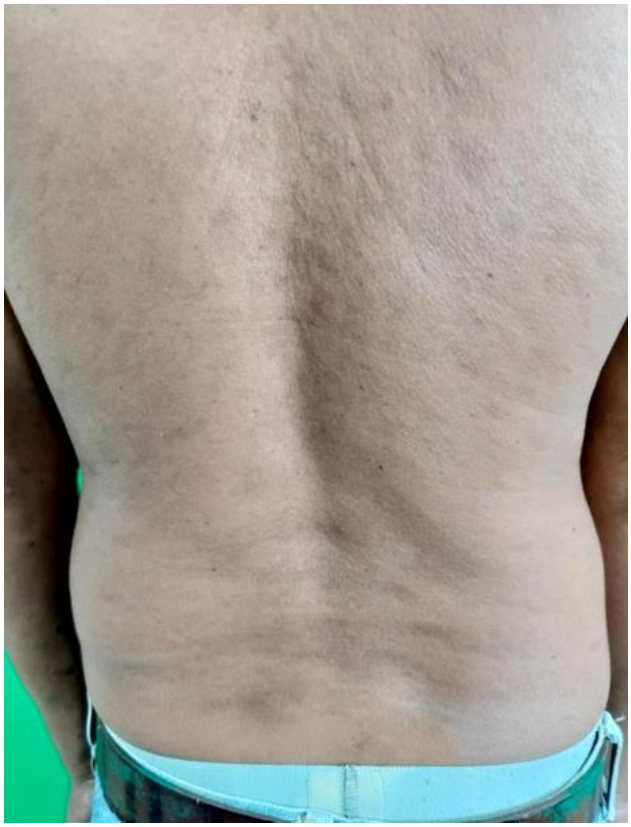

Figure 4. Dorsal view of the back of the patient showing diffuse hyperpigmented patches with poorly defined borders (reprinted with permission of the patient)

signs of dactylitis (**Figure 5**). A peripheral neurological examination revealed peripheral neuropathy, with monofilament test scores of 5/10 on the toes and 8/10 on the forearms. No palpable peripheral nerve enlargements were noted, including the greater auricular, ulnar, common peroneal, and sural nerves.

A skin biopsy (left knee) revealed aggregates of foamy and occasional epithelioid histiocytes forming granulomas around the blood vessels, skin appendages, and nerve bundles. Positive Ziehl-Neelsen and Wade-Fite stains for AFB confirmed the diagnosis. These histopathological findings indicate a granulomatous inflammation consistent with lepromatous leprosy (**Figure 6**). According to the WHO classification system, the patient was diagnosed with MB leprosy with grade 1 deformity, indicating a nerve function impairment in the feet.

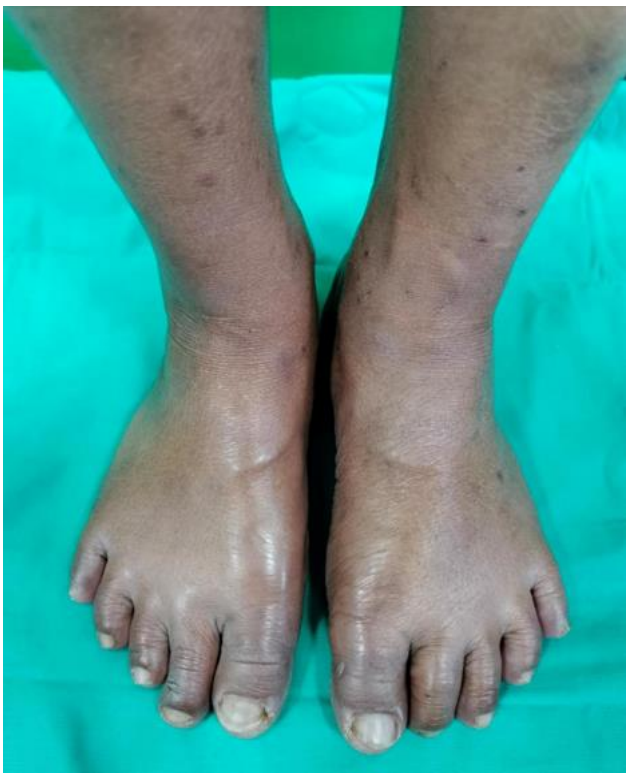

Figure 5. Dactylitis of all toes with shiny skin (reprinted with permission of the patient)

Treatment was started with an MDT regimen, including oral rifampicin 600 mg and clofazimine 300 mg once a month, along with dapsone 100 mg and clofazimine 50 mg daily for 1 year. At the 2-week follow-up, the joint pain and the facial swelling had improved, and the numbness had decreased. A monthly follow-up was planned for the next 3 months, followed by visits every 3 months to assess the patient's clinical response, monitor the side effects of the MDT, and conduct routine blood tests. Additionally, annual follow-ups will be scheduled for up to 10 years to ensure optimal clinical outcomes.

DISCUSSION

Leprosy is a bacteriologic and immunologic disease [5] leading to various clinical expressions depending on the strength of individual cellular immune responses toward *mycobacterium leprae* [5]. Leprosy diagnosis can be challenging when rheumatological features are predominant over the skin or nerve involvement. Even though the underlying mechanism is not yet fully understood, articular involvement is described by the deposition of immune complexes within the joints, complement activation, direct infiltration of the synovium by bacilli, or reactive arthritis triggered by mycobacterium antigens [6]. Inflammatory arthritis is frequently observed in lepromatous leprosy with or without lepra reactions [6, 7]. Arthritis associated with the lepra reaction typically manifests as acute, symmetrical, inflammatory polyarthritis affecting the small joints of the hands and the feet, like RA [4, 6]. Chronic arthritis without the association of a lepra reaction is also identified in leprosy patients [4]. This is characterized by relapse and remission periods resembling the joint distribution of RA, which affects symmetrical inflammatory polyarthritis primarily in the wrists, metacarpal joints, and proximal interphalangeal joints of the hands [4].

Autoantibodies may be present in leprosy patients, but the prevalence data remain controversial [6]. The most frequent autoantibodies in leprosy are RF, ANA, anti-SS-B, antimitochondrial, and antithyroglobulin [6]. Studies showed that 26.6% were seropositive for RF and 37.5% for ANA among patients with inflammatory arthritis and leprosy. Other extracutaneous manifestations in leprosy include peripheral edema at 52.4%, dactylitis at 13.7%, and lymphadenitis at 14.7% [6]. This patient's rheumatic-like features and facial swelling misled primary care doctors to suspect an autoimmune disease instead of leprosy.

Despite the similarities between these two entities, they can be clinically differentiated through a thorough evaluation

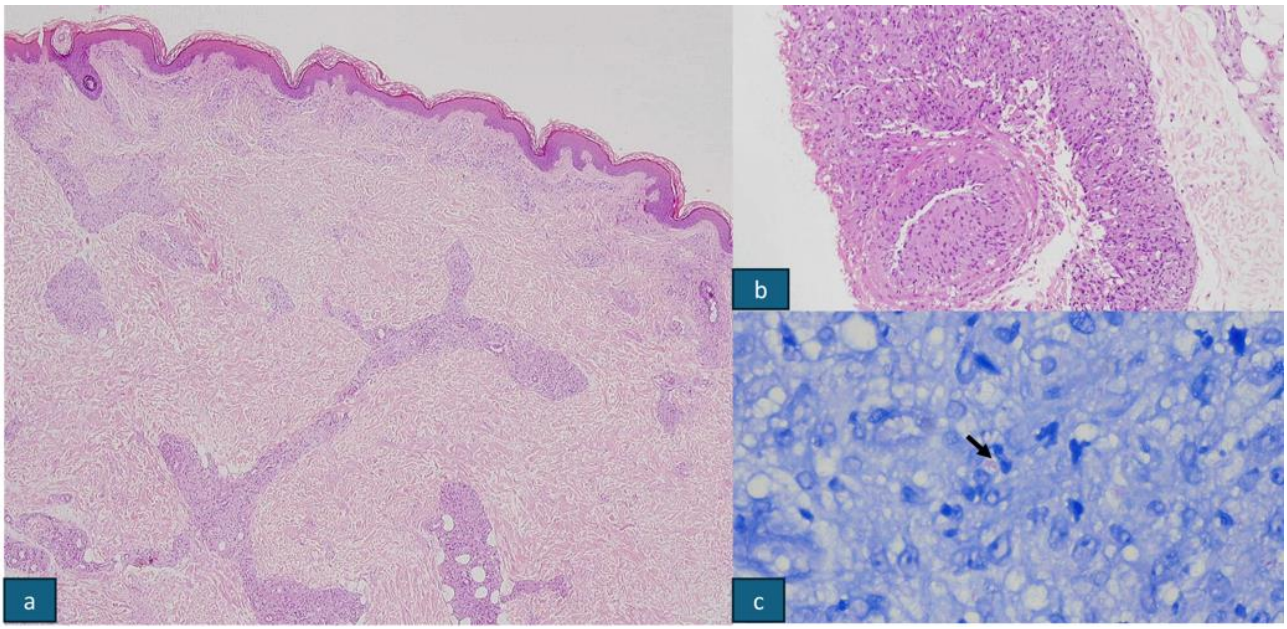

Figure 6. A skin biopsy showed (a) numerous granulomas seen around blood vessels, skin appendages, and nerve bundles (H&E 40× magnification), (b) granuloma around the blood vessels (H&E 100× magnification), and (c) wade fite stain showing acid fast bacilli (arrow) under 600× magnification (reprinted with permission of the patient)

of the skin lesions, including hypo/anesthetic macules or patches or erythematous macules and nodules, obtaining a history of paresthesia, assessing for thickened and tender peripheral nerves, and identifying sensory and motor neuropathy. These indicators should be considered when examining unexplained rheumatological symptoms, particularly in at-risk individuals from endemic areas. In this case, we suspect that arthritis is associated with leprosy due to the erythematous patches over the lower legs with signs and symptoms of sensory peripheral neuropathy. The patient displayed other common features of leprosy, such as madarosis, skin dryness, and diminished skin creases on the hands, resulting from the inflammation and destruction of dermal appendages [5, 8].

Early symptoms of leprosy are often non-specific and can resemble those of more common dermatological and neurological conditions. Cutaneous lesions may present in all clinical forms–macular, papulonodular, or plaque-type lepromatous lesions–depending on the host's immune status [5, 8]. Given this situation, the previous rashes over the trunk and the lower limbs might resemble allergic reactions, eczema, psoriasis, or other skin diseases. However, leprosy should be considered in chronic skin lesions that do not respond to standard treatments, particularly when hyperesthesia or hypesthesia indicates peripheral neuropathy. Furthermore, the patient's skin manifestation region is correlated with common lepromatous lesions that occur on cooler body parts, sparing warmer areas, also known as the immune zones, such as the intertriginous region and the scalp [5, 8].

The Ridley–Jopling classification describes leprosy as a spectrum disease from the clinical, immunological, and histopathological viewpoints [8]. WHO's simplified version, which is based on the number of skin lesions or AFB detection in an SSS [9], is useful in resource-limited settings. Although the patient does not have typical skin lesions or peripheral nerve involvement, the presence of suspicious signs of leprosy, such as facial swelling, thickened earlobes, and foot numbness, prompts an SSS test. He was diagnosed with MB leprosy, and a skin biopsy confirmed lepromatous leprosy consistent with the Ridley–Jopling classification.

The WHO recommends MDT (a combination of rifampicin, dapsone, and clofazimine) for all leprosy patients to prevent the development of resistance to any single anti-leprosy medication [9]. Aside from chemotherapy and monitoring, doctors should educate patients about the prognosis, address the stigma, and identify any psychological issues that may arise throughout the long-term course of treatment. In conclusion, diagnosing leprosy requires skilled healthcare professionals to recognize its broad symptoms, particularly in low-endemic regions. We emphasize herein the importance of considering leprosy as a differential diagnosis for any cutaneous or nervous lesions, including arthritis and other autoimmune-like manifestations, especially in at-risk individuals from endemic regions. A thorough approach is vital for early diagnosis, effective treatment, and prevention of disability and transmission.

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Ethical statement: The authors have removed any possible clues of identifying the patient. Informed consent was obtained from the patient, and no identifying details will be disclosed. The information provided is strictly for educational purposes. The authors stated that this study does not require any ethical approval.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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