Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Misdiagnosis of Leprosy with Severe Reversal Reaction as Psoriatic Arthritis: A Case Report and Literature Review

Hendra Gunawan[1], Risa Miliawati Nurul Hidayah[1], Kartika Ruchiatan[1], Miranti Pangastuti[1], Hermin Aminah Usman[2], Fatimah Amalia[1]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia; [2]Department of Pathological Anatomy, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia

Correspondence: Hendra Gunawan, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Jl. Pasteur 38, Bandung, West Java, 40161, Indonesia, Tel +6281221111215, Email h.gunawan2016@unpad.ac.id

Introduction: Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*. Meanwhile, leprosy reactions are immunologically mediated episodes of acute or subacute inflammation that occur during the chronic course of the disease. Leprosy and leprosy reaction have a wide range of clinical manifestations, including those resembling psoriatic arthritis.

Case Presentation: A 30-year-old male was consulted by a rheumatologist with psoriatic arthritis and psoriasis vulgaris. History of recurrent painfully swollen fingers and multiple erythematous plaques covered with thick scales in the last two years was discovered. A physical examination revealed edema on the eyelids and all fingers of both hands and feet, accompanied by painful interphalangeal joints. There were anesthetic and hypoestetic erythematous plaques covered by thick scales on both upper and lower extremities and epigastric region. Non-tender enlargements with a rubbery consistency were found on the right great auricular nerve and both common peroneal nerves. Slit-skin smear examinations from anesthetic lesions on the left arm showed bacterial index 3+, and skin biopsies from anesthetic lesions on the left thigh revealed a granulomatous reaction with epithelioid cells, Langhans giant cells, and lymphocyte infiltration. The patient was diagnosed as mid-borderline leprosy with severe reversal reaction, then received multidrug therapy–multibacillary and prednisone. The improvement of skin lesions and fingers edema were found on the 40th day of observation.

Conclusion: The varying symptoms of leprosy can lead to misdiagnosis. Proper training for healthcare professionals is crucial to ensure timely and accurate treatment.

Keywords: leprosy, misdiagnosed, psoriatic arthritis, reversal reaction, rheumatic

Introduction

Leprosy is a chronic granulomatous disease caused by the obligate intracellular bacteria, *Mycobacterium leprae (M. leprae)* and *M. lepromatosis*, that primarily affect skin and peripheral nerves.[1,2] Data from the World Health Organization (WHO) shows that leprosy is still a public health problem in Indonesia,[3] as evidenced by the fact that there are still 12,441 new cases in 2022.[4]

Leprosy reactions are immunologically mediated episodes of acute or subacute inflammation that can occur before the start of MDT, during treatment, and even after MDT has been completed. There are two types of leprosy reactions: the type 1 leprosy reaction (reversal reaction) and the type 2 reaction (erythema nodosum leprosum/ENL). Leprosy and leprosy reactions have a wide range of clinical manifestations.[2,5] The various manifestations of leprosy and leprosy reactions can mimic several rheumatic diseases, including psoriatic arthritis.[6]

Early diagnosis is important in leprosy to prevent disabilities.[7] Misdiagnosis is the main factor in health care-related delays in leprosy case detection.[8] Chen et al[9] reported that 44.7% of leprosy cases were misdiagnosed and the results

Received: 28 October 2024
Accepted: 8 January 2025
Published: 16 January 2025

showed that rheumatism, dermatitis, and neuritis were the most common misdiagnosed diseases. Here we present a case of leprosy with a severe reversal reaction. The patient was initially misdiagnosed with psoriatic arthritis by a rheumatologist. The aim of this case report is to describe a case of leprosy with a severe reversal reaction mimicking psoriatic arthritis in a psoriasis patient, emphasizing leprosy's ability to mimic other conditions and the diagnostic challenges it presents.

Case Presentation

A 30-year-old male from a leprosy-endemic area in West Java, Indonesia, was consulted by a rheumatologist with erythematous plaques covered with thick scales on the face, neck, trunk, back, arms, and lower limbs that were neither itchy nor painful for the last month. The complaint was accompanied by swollen eyelids and painfully swollen fingers on both hands and feet. Approximately two years prior to consulting, there was a palm-sized erythematous macule on the left lower leg with decreased sensation. The skin lesion then increased in number and spread to the face, elbow, back, and epigastric region. Six months prior to consulting, there was increased erythema and thickened macules with thick scales. He visited a general practitioner and was diagnosed with an allergic reaction, then received antiallergy medicines. The complaint subsided, and the skin lesions reverted into hyperpigmented macules. The edematous eyelids and fingers, along with the increased erythema and thickened skin lesions exhibited a recurring pattern, particularly when the patient was tired from work. The patient works as a water heater construction worker, occasionally unintentionally encountering hot materials and water, which resulted in injuries. Psoriasis vulgaris and psoriatic arthritis were diagnosed when the patient consulted a rheumatologist. He was then consulted at a dermatology and venereology clinic at Dr. Hasan Sadikin General Hospital for further evaluation regarding psoriasis vulgaris.

The physical examination showed edema on the eyelids and fingers on both hands and feet (Figure 1A–C), accompanied by painful interphalangeal joints of both hands and feet, without madarosis, ear lobe infiltration, or nail changes. There was decreased sensitivity of annular erythematous macules and annular erythematous plaques with clear inner and outer borders that were covered by psoriasiform scales (Figure 2) on almost the entire part of the body (Figure 1D–F). Auspitz sign was negative. The right great auricular nerve and both common peroneal nerves were observed to have non-tender enlargements with a rubbery consistency. Slit-skin smear examinations from anesthetic psoriasiform plaques on the left arm revealed the presence of acid-fast bacilli (AFB) with an average bacterial index (BI) of 3+ and a morphological index (MI) of 34.8%.

The skin biopsies were done on anesthetic erythematous plaques on both thighs. Histopathological examinations revealed a granulomatous reaction with epithelioid cells, Langhans giant cells, and lymphocyte infiltration (Figure 3) that supported the diagnosis of mid-borderline leprosy. The patient was diagnosed with leprosy with a severe reversal reaction and then treated with multidrug therapy (MDT)-multibacillary (MB) regimen consisting of rifampicin 600 mg and clofazimine 300 mg supervised once a month, dapsone 100 mg and clofazimine 50 mg daily, unsupervised given for 12 months. The patient was also given prednisone 40 mg daily, reduced gradually by 5–10 mg every 2 weeks for the treatment of the reversal reaction. The improvement of eyelids edema, fingers edema (Figure 4A–C), and skin lesions was seen on the 40th day of observation (Figure 4D–F).

Discussion and Conclusion

Leprosy is a neglected tropical disease that remains the primary cause of peripheral neuropathy and disability worldwide,[10] occurring in more than 120 countries.[4] Diagnosis of leprosy can be established by finding at least one of the three following cardinal signs: skin lesions accompanied by loss of sensation, enlarged or thickened peripheral nerves accompanied by loss of function, and microscopic detection of AFB in a slit-skin smear.[1,2,5] Leprosy has been classified by the WHO into two categories: paucibacillary (PB) and multibacillary (MB).[1] Ridley and Jopling classified leprosy into five types: tuberculoid leprosy (TT); borderline tuberculoid leprosy (BT), which is categorized as PB, mid-borderline leprosy (BB); borderline lepromatous leprosy (BL); and lepromatous leprosy (LL), which falls under the MB category.[1,2]

Leprosy reactions are periods of acute or subacute inflammation that can cause deformity and disability if not treated promptly and appropriately.[5] The type 1 leprosy reaction is type IV hypersensitivity, while the type 2 reaction is type III hypersensitivity. Clinical signs of a reversal reaction include painful swelling of the peripheral nerve along with increased

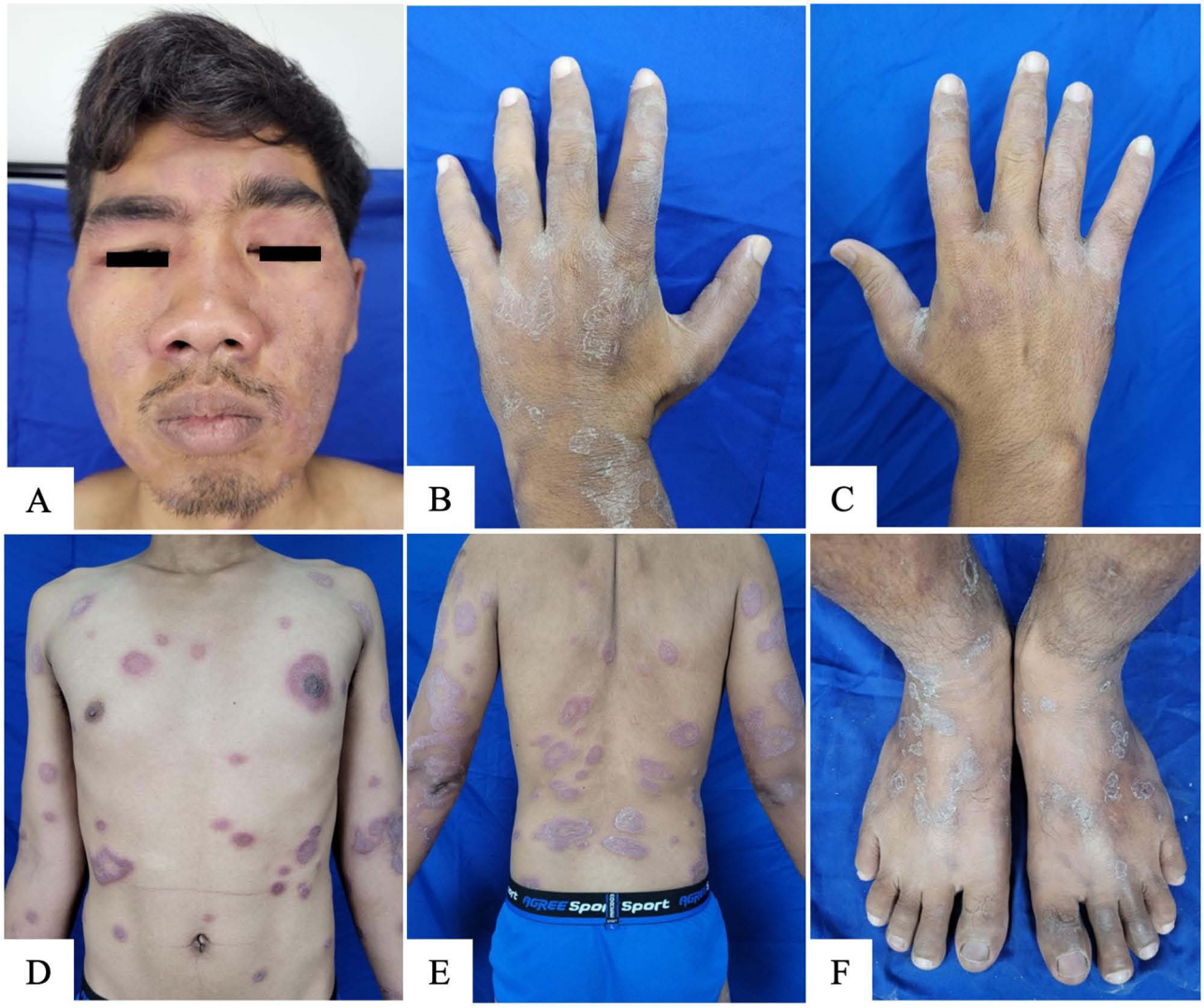

Figure 1 Physical examination at first-day observation showed eyelids (**A**) and fingers edema (**B**) **and** (**C**). Erythematous plaques with thick scales on the trunk (**D**), back (**E**), and feet (**F**).

erythema, edema, and occasionally ulceration of preexisting skin lesions.[2,5] Swelling hands and feet are an unusual presenting symptom in the reversal reaction and have been hypothesized to be caused by synovial inflammation.[1,5] Risk factors of a reversal reaction are the presence of infection, hormonal changes, vaccination, psychological stress,[1,11] and physical stress, which was suspected to be the most precipitating factor.[12] The reaction of skin lesions on the face is one of the severe reversal reaction criteria.[1,5] The patient in this case report was diagnosed with a severe reversal reaction because there was increased erythema and thickened skin lesions, edema on the eyelids and fingers, and painful interphalangeal joints that were precipitated by physical stress.

Rath et al[6] reported a case of a leprosy patient and type 2 leprosy reaction, who presented with gradual onset, progressive joint pain accompanied by multiple nodular swellings and a few erythematous plaques on his back and knee. The patient was misdiagnosed with spondyloarthritis and psoriatic arthritis and was treated with non-steroidal anti-inflammatory drugs (NSAID) and sulfasalazine but had not shown any improvement. He was referred to dermatologist and the diagnosis of leprosy was established based on a slit-skin smear and the finding of a granulomatous reaction on histopathological examination taken from nodular skin lesions.[6] The edematous fingers and interphalangeal joint pain of this patient might be the reason he was misdiagnosed with psoriatic arthritis before.

https://doi.org/10.2147/CCID.S502544

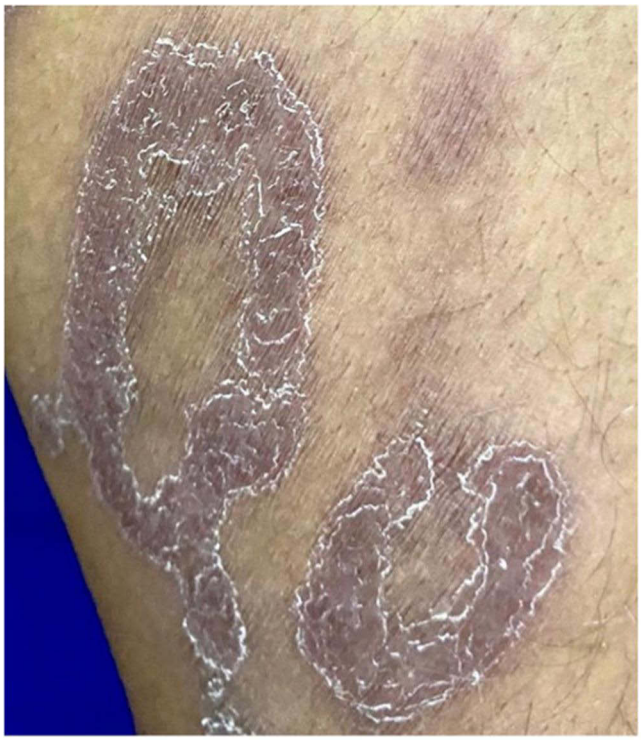

Figure 2 Erythematous plaques covered with psoriasiform scales on the left thigh.

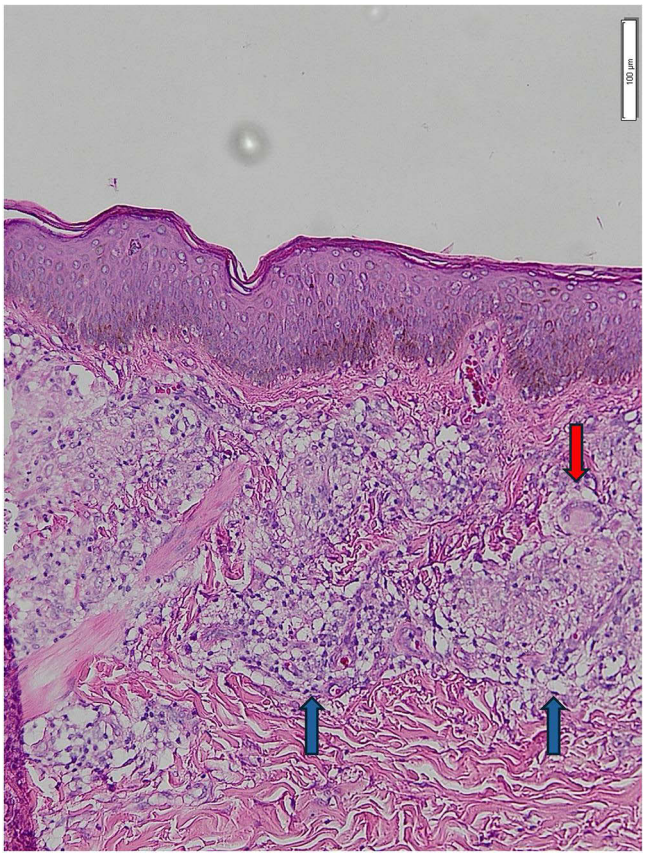

Figure 3 Histopathological findings of the erythematous plaques with psoriasiform scales showed granulomas (blue arrow) composed of a considerable number of histiocytes, Langhans giant cells (red arrow), and lymphocytes. (H and E, x100).

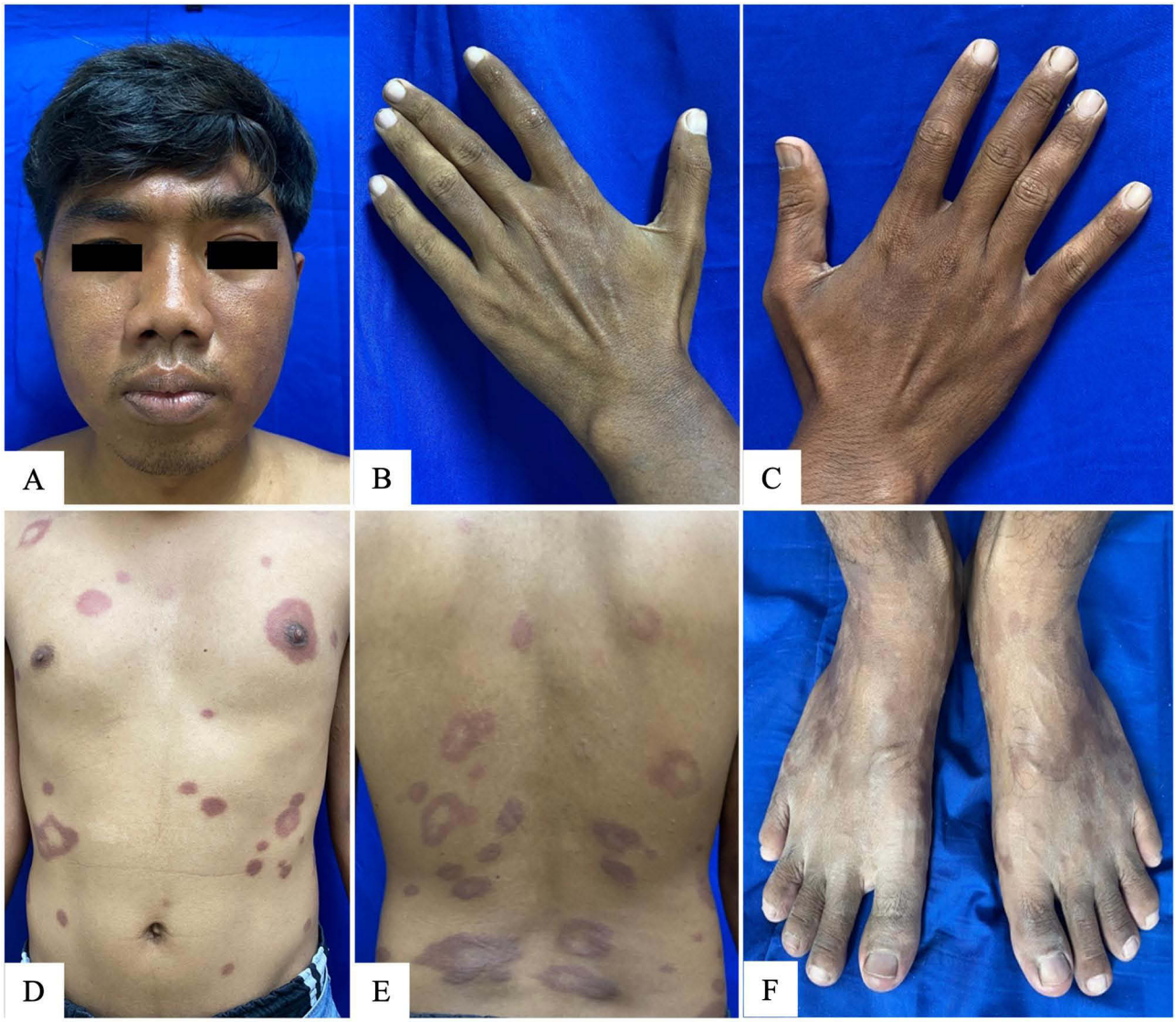

Figure 4 Physical examination at 40th day of observation showed improvement on eyelid (**A**) and fingers edema (**B**) and (**C**). Erythematous plaques with thick scales on the trunk (**D**), back (**E**), and feet (**F**) became erythematous and hyperpigmented macules.

Psoriatic arthritis is an inflammatory arthritis occurring in approximately 20% of psoriasis patients. The condition is typically characterized by recurring, chronic oligoarticular arthritis that affects fewer than five small or big joints asymmetrically.[13] In contrast, arthritis in the leprosy reaction has an early onset and affects only small joints in the hands and feet symmetrically,[14] as our patient had.

It is still unclear what causes articular involvement in leprosy. Theorized pathways include peripheral sensory neuropathy (Charcot's or neuropathic joints), direct synovial infiltration, and reactional states (types 1 and 2 lepra reactions), which result in joint deterioration.[14] Joint dislocations, pathological fractures, and crippling deformities are the hallmarks of Charcot's joints, sometimes referred to as neuropathic arthropathy. These conditions typically affect the weight-bearing joints of the lower limbs, such as the ankles and knees.[15] Even though it can be challenging to locate AFB in the joint, the presence of *M. leprae* in the joint is still the gold standard for diagnosing arthritis caused by direct synovial infiltration.[14] Gunawan et al[16] reported a case of leprosy who presented with joint changes, and AFB was found in the synovial fluid. Arthritis caused by the leprosy reaction is a symmetrical, inflammatory polyarthritis with an early onset that affects the small joints of the hands and feet, usually resembling rheumatoid arthritis.[14] The characteristic of arthritis in our patient suited the manifestation of arthritis caused by the leprosy reaction.

https://doi.org/10.2147/CCID.S502544

Serological testing and histopathological examination of the skin and nerves are investigations that can help establish the diagnosis of leprosy.[2,17] Histopathological examination may help in identifying leprosy cases that are not typical or are still clinically suspected,[17,18] even though it is not a gold standard for diagnosis.[19] Histopathological features of leprosy include the formation of a granuloma that consists primarily of epithelioid cells and macrophages, with lymphocytes scattered around the granuloma.[17] The histopathological examination from the skin lesions of this patient supported the diagnosis of leprosy.

Multidrug therapy, which was initially introduced by the WHO in 1981, is still the recommended treatment and is still widely administered today.[20,21] MDT consists of 600 milligrams (mg) of rifampicin once a month and 100 mg of dapsone daily for PB, and 600 mg of rifampicin with 300 mg of clofazimine once a month, followed by 100 mg of dapsone and 50 mg of clofazimine daily for MB.[20] The drugs were given for a fixed duration, specifically 6 blisters in 6–9 months for PB and 12 blisters in 12–18 months for MB, regardless of the clearance of skin lesions or the presence or absence of AFB in the skin.[22] During the reaction state, MDT remains necessary. The goals of leprosy treatment during the reaction state are to manage the signs and symptoms of acute inflammation and reduce the pain to prevent future nerve impairment.[23] The drug of choice for severe reversal reaction is prednisone 0.5–1 mg per kilogram (kg) of body weight, approximately 30–40 mg daily for most adults. The drugs then gradually tapered off 5–10 mg every two weeks.[24] The patient in this case report was given MDT MB and prednisone starting at 40 mg daily for two weeks then gradually tapered off. Significant improvement was found on the 40th day of observation.

Disability in leprosy can either be caused by direct invasion of bacteria into the skin and mucous membrane that results in nerve damage or secondary due to consequences following peripheral nerve damaged.[1] There are several risk factors for disability in leprosy, including delayed diagnosis, nerve damage, absence of skin lesions, the MB type of leprosy, leprosy reactions, and advanced age.[25] A Study done by Srinivas et al[26] showed that delayed diagnosis is the major reason for the risk of disability among adult leprosy patients. A study conducted in 2021 found that leprosy patients who delayed their diagnosis for longer than two years had a significantly higher risk of developing disabilities when compared to those who delayed their diagnosis for less than two years.[25] Other studies conducted in India found that patients who delayed their diagnosis for more than three months had a 1.6-fold higher risk of disability than those who delayed their diagnosis for less than three months.[26] The patient in this case report was previously misdiagnosed with psoriasis vulgaris and psoriatic arthritis. Fortunately, the patient has not had any disabilities despite being diagnosed two years after the first skin lesions appeared.

In conclusion, leprosy is a disease with diverse clinical manifestations, which increases the risk of misdiagnosis. Providing adequate training for healthcare professionals is essential to prevent diagnostic errors and treatment delays, ultimately improving patient outcomes.

Abbreviations

AFB, acid-fast bacilli; BB, mid-borderline; BT, borderline tuberculoid; BL, borderline lepromatous; BI, bacterial index; ENL, erythema nodosum leprosum; Kg, kilogram; LL, lepromatous leprosy; MB, multibacillary; MDT, multidrug therapy; MI, morphological index; *M. leprae, Mycobacterium leprae*; NSAID, non-steroidal anti-inflammatory drugs; PB, paucibacillary; TT, tuberculoid leprosy; WHO, World Health Organization.

Ethics Approval and Consent to Participate

This study had obtained ethical clearance from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital No. DP.04.03/D.XIV.6.5/415/2024. Written informed consent was obtained from the patient to participate in this case report.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. Approval has been obtained from Dr. Hasan Sadikin General Hospital to publish the case details.

Acknowledgments

The authors would like to thank the staff of Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia.

Funding

The authors received no specific funding for this work. Open access funding provided by University of Padjadjaran.

Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Ramesh V, Kataria JK. Systemic Involvement in Leprosy. In: Kumar B, Kar HK, editors. *IAL Textbook of Leprosy*. 2 ed. New Delhi: Jaypee Brothers; 2017:335.
2. Salgado CG, Brito AC, Salgado UI, Spencer JS. Leprosy. In: Kang S, Amagai M, Bruckner AL, Enk AH, McMichael DLMAJ, Orringer JS, editors. *Fitzpatrick's Dermatology in General Medicine*. 9 ed. New York: McGraw-Hill; 2019:2892–2919.
3. Directorate General for Disease Prevention and Control. Ministry of Health RI. Annual Leprosy Control Program Report 2022. 2023.
4. World Health Organization. *Weekly Epidemiological Record. Downloaded From; Global Leprosy (Hansen Disease) Update, New Paradigm – Control to Elimination (Who.int)*. 2022.
5. Walker SL. Leprosy Reactions. In: Scollard DM, Gillis TP. editors. *International Textbook of Leprosy. American Leprosy Missions*. Greenville, SC. 2020. doi:10.1489/itl.2.2
6. Rath D, Bhargava S, Kundu BK. Leprosy mimicking common rheumatologic entities: a trial for the clinician in the era of Biologics. *Case Rep Rheumatol*. 2014;2014:1–5.
7. Mulugeta SS, Maseresha BM, Wassihun SG, Moyehodie YA. Risk Factors for Disability Upgrading Among Leprosy Patients During Treatment: multilevel Modeling Analysis. *SAGE Open Nurs*. 2022;8:1–10. doi:10.1177/23779608221129936
8. Dharmawan Y, Korfage IJ, Abqari U, Widjanarko B, Richardus JH. Measuring leprosy case detection delay and associated factors in Indonesia: a community-based study. *BMC Infect Dis*. 2023;23(1):555. doi:10.1186/s12879-023-08552-x
9. Chen L, Zheng W, Dong X, Zheng Y, Shi W, Zhang W. Analysis of misdiagnosed or delayed-diagnosed Leprosy bacillus infection from 1990 to 2020 with a prophet time series prediction in Hubei Province, China. *Medicine*. 2023;102(32):e34714. doi:10.1097/MD.0000000000034714
10. Rathod SP, Jagati A, Chowdhary P. Disabilities in leprosy: an open, retrospective analyses of institutional records. *An Bras Dermatol*. 2020;95:52–56.
11. Scollard DM, Martelli CM, Stefani MM, et al. Risk factors for leprosy reactions in three endemic countries. *Am J Trop Med Hyg*. 2015;92 (1):108–114. doi:10.4269/ajtmh.13-0221
12. Gunawan H, Miliawati R, Hanannisa RF. Reversal reaction in leprosy patients: study on prevalence, sociodemographic characteristics, and precipitating factors at a tertiary referral hospital in West Java, Indonesia. *Althea Med J*. 2022;9(1):37–42. doi:10.15850/amj.v9n1.2329
13. Tiwari V, Brent LH. *Psoriatic arthritis*. U.S. National Library of Medicine. StatPearls Publishing; 2024.
14. Chauhan S, Wakhlu A, Agarwal V. Arthritis in leprosy. *Rheumatology*. 2010;49(12):2237–2242. doi:10.1093/rheumatology/keq264
15. Messner RP. Arthritis due to mycobacteria, fungi and parasites. In: Koopman WJ, McCarty DJ, editors. *Arthritis and Allied Conditions*. 13th ed. MD: Williams and Wilkins; 1997:2305–2320.
16. Gunawan H, Wulansari Y, Achdiat PA, Hindritiani R. Leprosy-Related Chronic Arthritis with an Abundance of Mycobacterium Leprae in the Synovial Fluid. *A Rare Case Int Med Case Rep J*. 2021;14:371–376.
17. Porichha D, Natrajan M. Pathological Aspect of Leprosy. In: Kumar B, Kar HK, editors. *IAL Textbook of Leprosy*. 2 ed. New Delhi: Jaypee Brothers; 2017:137–138.
18. Antunes SL, Chimelli L, Jardim MR, Vital RT. Histopathological examination of nerve samples from pure neural leprosy patients: obtaining maximum information to improve diagnostic efficiency. *Mem Inst Oswaldo Cruz*. 2012;107(2):246–253. doi:10.1590/S0074-02762012000200015
19. Moschella SL. An update on the diagnosis and treatment of leprosy. *J Am Acad Dermatol*. 2004;51(3):417–426. doi:10.1016/j.jaad.2003.11.072
20. Chen KH, Lin CY, Su SB, Chen KT. Leprosy: a Review of Epidemiology, Clinical Diagnosis, and Management. *J Trop Med*. 2022;2022:8652062. doi:10.1155/2022/8652062
21. Maymone MBC, Venkatesh S, Laughter M, et al. Leprosy: treatment and management of complications. *J Am Acad Dermatol*. 2020;83(1):17–30. doi:10.1016/j.jaad.2019.10.138
22. World Health Organization. *Guidelines for the Diagnosis, Treatment and Prevention of Leprosy*. New Delhi: World Health Organization, Regional Office for South-East Asia; 2017.
23. Walker S, Lockwood DNJ. Lockwood D. Leprosy type 1 (reversal) reactions and their management. *Lepr Rev*. 2008;1(4):372–386. doi:10.47276/lr.79.4.372
24. World Health Organization. *Leprosy/Hansen Disease: Management of Reactions and Prevention of Disabilities. Technical Guidance*. New Delhi: World Health Organization, Regional Office for South-East Asia; 2017.
25. Chen X, Liu HB, Shui TJ, Zha S. Risk factors for physical disability in patients with leprosy disease in Yunnan, China: evidence from a retrospective observational study. *PLoS Negl Trop Dis*. 2021;15(11):e0009923. doi:10.1371/journal.pntd.0009923
26. Srinivas G, Muthuvel T, Lal V, Vaikundanathan K, Schwienhorst-Stich EM, Kasang C. Risk of disability among adult leprosy cases and determinants of delay in diagnosis in five states of India: a case-control study. *PLoS Negl Trop Dis*. 2019;13(6):e0007495. doi:10.1371/journal.pntd.0007495