



Advances in Dermatology

Article History :

Received date : 2026/07/14
Revised date : 2026/08/23
Accepted date : 2026/09/05
Published date : 2026/10/16



Copyright: © by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

RELAPSE OR REACTION: POST-MDT ERYTHEMA NODOSUM LEPROSUM AS AN INITIAL DIAGNOSTIC DILEMMA IN PRIMARY CARE

Aletha Ayu¹, Andita Rizky Cinanthia ², Dhia Ulfajri Handayani ³

¹ Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta,
Indonesia

^{2,3} Faculty of Medicine, Universitas Tarumanagara, Indonesia

Corresponding email: alethaayu@gmail.com

ABSTRACT

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that remains a health problem in endemic countries such as Indonesia. The challenge lies not only in early diagnosis but also in the identification of post-treatment immunological complications. Although *multidrug therapy* (MDT) is effective in reducing case numbers and preventing disability, leprosy reactions may still occur and give rise to diagnostic difficulties. Type 2 leprosy reaction, or *Erythema Nodosum Leprosum* (ENL) is a complex immune response that may mimic leprosy relapse or recurrence, defined as the reappearance of signs and symptoms of leprosy after the patient has adequately completed *Multidrug Therapy* (MDT), particularly when accompanied by new skin lesions, systemic symptoms, and persistently positive bacteriological findings. We report a 30-year-old man with a history of multibacillary (MB) leprosy who had completed MDT and, eight months after therapy, presented with fever, new skin lesions, and extremity edema. The *slit skin smear* showed an increase in the bacteriological index (BI) from +1 to +2, which initially raised suspicion of *relapse*; however, further evaluation established the diagnosis of ENL. This case highlights that the presence of bacilli and new lesions after MDT does not always reflect recurrence, but may instead represent a manifestation of an immunological reaction; hence, the ability to distinguish *relapse* from ENL in primary care is crucial to prevent misdiagnosis and to ensure appropriate management.

Keywords: Erythema Nodosum Leprosum, Leprosy Relapse, *Multidrug Therapy*, Leprosy

INTRODUCTION

Indonesia still ranks third worldwide in the number of new leprosy cases.¹ In 2024, the prevalence of leprosy was 0.63 cases per 10,000 population and the new case detection rate was

5.3 per 100,000 population, with 14,698 new cases, nearly 90% of which were of the multibacillary (MB) type.^{2,3} MDT has been proven effective in reducing case numbers and preventing disability; however, patients, particularly those with the MB type, remain at risk of developing leprosy reactions, which may cause significant morbidity and permanent nerve damage. A leprosy reaction is an acute episode arising during the chronic course of leprosy and comprises two types, namely type I or reversal reaction and type II or Erythema Nodosum Leprosum (ENL).^{4,5} Type II leprosy reaction or ENL occurs in patients with a very high bacterial load, namely in the LL and BL types.⁴ Type II reaction is characterized by painful erythematous subcutaneous nodules, which more frequently appear on the face and the extensor aspects of the upper and lower limbs. Accompanying systemic symptoms may include fever and malaise, as well as involvement of the inner eye (iritis or iridocyclitis). Factors presumed to trigger ENL reactions include skin infiltration in leprosy patients, $BI \geq 4$, age < 40 years, primary infections caused by bacteria, viruses, or other parasites, recurrent infections, surgical procedures, physical stress, immunization, pregnancy, and the postpartum period.⁶ ENL is an immune-mediated inflammatory complication that may appear both during and after *completion* of MDT, and it clinically often mimics relapse owing to the presence of new skin lesions, fever, and other systemic symptoms. Furthermore, acid-fast bacilli may remain detectable on *slit skin smear* even though they do not always reflect active infection, thereby causing confusion in clinical practice at the primary care level. Relapse or recurrence is defined as a patient who has adequately completed MDT but subsequently develops signs and symptoms of leprosy again during the surveillance period or thereafter. The surveillance period is defined as two years for PB leprosy and five years for MB leprosy.⁷ This case report aims to

describe a manifestation of ENL *post*-MDT that mimics relapse, and to highlight the diagnostic challenges and the role of primary care physicians in distinguishing between the two.

CASE REPORT

A 30-year-old man presented to the primary health center (Puskesmas) with a complaint of sudden-onset fever for one week, followed by the appearance of spots on the body, predominantly on the ears and face, as well as swelling of the legs, accompanied by joint pain. The nodules first appeared on the left ear, then on the right ear, and subsequently on the face. The patient felt that his ears had become thickened and numb. He had received treatment at a clinic, where he was given analgesics and vitamins, without improvement. The patient had a history of MB leprosy diagnosed in 2024, underwent MDT in accordance with the guidelines, and was declared to have completed treatment in May 2025, with no history of leprosy reactions or disability during the treatment period. A similar illness had been experienced by the patient's mother, who is now deceased. The patient lives with his wife and works as a field worker.

On physical examination, the patient was *compos mentis*, with a blood pressure of 118/62 mmHg, pulse rate of 87 beats per minute, respiratory rate of 20 breaths per minute, and temperature of 36.3°C. The patient had a normal nutritional status, with a body mass index (BMI) of 20.57 kg/m².

No anesthetic macules or *patches* were found. Infiltrates were found on both auricles (Figure 1a, 1b), along with diffuse edema with hyperpigmented discoloration of both feet (Figure 2). On dermatological examination, there were multiple skin-colored nodules and papules on the face. Neurological examination revealed thickening of the great auricular nerve on palpation and

tenderness of both ulnar nerves. Motor function of the upper and lower limbs was within normal limits. Sensory examination revealed numbness of both ears.



Figure 2(a) and (b) Bilateral auricular infiltrates; nodules in the frontal region



Figure 1. Bilateral dorsum pedis showing edema with hyperpigmentation

Skin acid-fast bacilli (AFB) smear examination at the Puskesmas revealed acid-fast bacilli with a BI of +2, an increase compared with the initial BI of +1 when the patient was first diagnosed with leprosy. Based on the history, physical examination, and limited supporting investigations, the patient was suspected of having MB leprosy relapse, with leprosy reaction as the differential diagnosis. The patient was referred to the hospital for further evaluation.

On follow-up, the patient underwent a skin biopsy at the hospital; while awaiting the results, he was given vitamin B complex and vitamin D by the hospital. The biopsy results subsequently showed histological features supporting a granulomatous inflammation that can be found in *Morbus Hansen* of the *Borderline leprosy* type, DD/ *Erythema Nodosum Leprosum* Reaction. The patient was given Methylprednisolone 16mg, 2 tablets once daily (for 2 weeks), Omeprazole 20mg

twice daily, Vitamin B complex 2 mg once daily, Vitamin Calcium Carbonate 500mg once daily, and Vitamin D3 1000 IU once daily. The pain resolved and the skin lesions improved. Based on the response to corticosteroid therapy and the skin biopsy findings, a diagnosis of type 2 leprosy reaction (ENL) was established.

DISCUSSION

Leprosy is a chronic infectious disease that primarily affects the skin and peripheral nerves and may lead to neuropathy, deformity, and disability. The diagnosis of leprosy is established when at least one of three cardinal signs is present, namely loss of sensation in a hypopigmented/erythematous skin lesion, thickened peripheral nerve with functional impairment, or the presence of acid-fast bacilli in a skin smear.⁸

In MB leprosy, particularly borderline lepromatous (BL) and lepromatous (LL) leprosy, leprosy reactions occur frequently. One of these is the type 2 reaction or ENL, an immune-mediated inflammatory complication (type II hypersensitivity). ENL manifests as fever, multiple painful erythematous nodules, malaise, headache, myalgia, arthralgia, and bone pain, with lesions predominantly on the extensor surfaces or the face. ENL may arise during therapy as well as after *completion* of MDT and may cause permanent nerve damage if not adequately managed.⁸ In this case, the patient had completed 12 months of treatment for MB leprosy 8 months prior to admission and presented with complaints of fever, generalized body aches, swelling of both legs, swelling and redness of both ears, and the appearance of nodules around the face, consistent with the manifestations of ENL.

Conversely, leprosy relapse reflects the return of infectious activity due to viable bacilli after the patient has completed adequate MDT. Clinical criteria for relapse include an increase in

the extent of lesions, infiltration and erythema, new skin and nerve lesions, a skin smear that becomes positive again in previously negative cases, or an increase in BI of 2+ at any site compared with the previous value in two consecutive examinations. Relapse is characterized more by the progression of chronic lesions and a persistent increase in bacillary load, whereas prominent acute systemic symptoms are not a principal feature. Relapse and reaction share similar granulomatous features on histopathological examination. The difference is that the increase in BI seen in relapse is not found in reaction.⁹ In this case, three initial findings did support the suspicion of *relapse* in primary care, namely an MB patient after MDT, the presence of new lesions and infiltration at predilection sites, and an increase in BI from +1 to +2 on *slit skin smear*. However, a more detailed clinical evaluation revealed a pattern more consistent with an ENL reaction than with relapse, for several reasons, namely the predominance of acute systemic symptoms such as acute fever, multiple painful nodules, joint pain, and extremity edema, consistent with the characteristic features of ENL. Manifestations in the form of new skin lesions accompanied by systemic symptoms such as fever and edema are, in fact, described as characteristic of ENL, which frequently mimics relapse. The timing of onset is consistent with the spectrum of post-MDT ENL, as ENL reactions may occur in patients who have completed MDT, not only during ongoing therapy. The onset of symptoms eight months after *completion* of MDT still falls within the reported time frame for ENL. There is a rather confounding role in primary care, given the limitations of BI results in distinguishing relapse from ENL pathophysiologically. Relapse is characterized by the return of infectious activity, whereas ENL is an immunological process without increased bacterial replication. In this patient, a BI of 2+ was found, compared with only +1 previously. However, in MB patients, acid-fast bacilli may remain detectable on slit skin smear

even though they do not reflect active disease. Therefore, the increase in BI from +1 to +2 in this case cannot serve as the sole evidence of relapse and must be interpreted together with the systemic clinical features, which are more typical of ENL. Furthermore, after further evaluation at an Advanced Referral Health Facility, the patient showed a response to short-term steroid therapy. Management of reactions with corticosteroids is a safe and effective option. Prednisolone is recommended by the WHO for ENL reactions at an initial dose of 0.5-1 mg/kg body weight/day, or 40-60mg per day, administered until clinical improvement is achieved and then gradually tapered by 5-10 mg every week over 6-8 weeks.⁶ The principles of leprosy reaction management include the administration of anti-reaction drugs, immobilization, analgesics and sedatives, and continuation of antileprosy drugs. The goals of treatment are to control inflammation, relieve pain, and treat neuritis in order to prevent further damage and disability, as well as to prevent recurrence of ENL.⁶

In practical terms, one suggested approach is to administer steroids for approximately four weeks; if the inflammation does not improve significantly, the diagnosis points toward leprosy relapse. In this case, the pain and skin lesions improved markedly after methylprednisolone administration, and the biopsy findings supported an ENL reaction, further reinforcing that the principal process underlying the patient's complaints was a leprosy reaction (ENL) rather than bacteriological *relapse*.

The combination of acute systemic symptoms characteristic of ENL, a post-MDT onset still within the time frame for reactions, the limited interpretability of BI in MB patients, and a good response to corticosteroids supports that this case is more appropriately classified as post-MDT ENL rather than leprosy *relapse*. This underscores that, in primary care, new lesions with a

positive BI in MB patients after MDT must always be evaluated together with systemic symptoms and clinical patterns, rather than being immediately concluded to represent *relapse*.

CONCLUSION

Type 2 leprosy reaction (ENL) may arise after completion of MDT and clinically closely mimics relapse, particularly when accompanied by new skin lesions, fever, edema, and a still-positive *slit skin smear* result. However, this case demonstrates that an increase in the bacteriological index and the emergence of new lesions after MDT in patients with multibacillary leprosy do not always reflect disease relapse, as acid-fast bacilli may persist without active infectious activity and form part of the immunological process of ENL

The predominance of acute systemic symptoms (fever, painful erythematous nodules, edema, joint pain), onset eight months after *completion* of MDT, rapid and favorable clinical improvement with corticosteroids, and histopathological confirmation collectively support that this condition is more appropriately diagnosed as post-MDT ENL rather than leprosy relapse; hence, distinguishing between the two is crucial to prevent misdiagnosis and inappropriate management.

REFERENCES

1. Samosir PM, Axelia PG, Alkaff FF, Salamah S, Alinda MD. Prevalence and risk factors for disability in leprosy patients in Indonesia during the post-elimination era. *Dermatology Reports*. 2013;15(4):9777. Available from: <https://doi.org/10.4081/dr.2023.9777>
2. Dinas Kesehatan Provinsi DKI Jakarta. Profil kesehatan DKI Jakarta 2024 [Health profile of DKI Jakarta 2024]. Jakarta: Unit Pelaksana Pusat Data dan Teknologi Informasi Kesehatan Daerah, Dinas Kesehatan Provinsi DKI Jakarta; 2024. Indonesian.

3. Kementerian Kesehatan Republik Indonesia. Profil Kesehatan Indonesia 2023 [Indonesia health profile 2023]. Jakarta: Sekretariat Jenderal Kementrian Kesehatan RI: 2024. Indonesian.
4. Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, et al. Fitzpatrick's dermatology. 9th ed. New York: McGraw-Hill Education; 2019.
5. Ruslan LA, Devina W, Pemayun TD. Morbus Hansen dengan reaksi eritema nodosum leprosum pada kasus putus obat: laporan kasus [Morbus Hansen with erythema nodosum leprosum reaction in a treatment default case: a case report]. Syntac Lit JII. 2025;10(1). Indonesian. Available from: <https://jurnal.syntaxliterate.co.id/index.php/syntax-literate/article/view/56044>
6. Pratama N, Rusyati LMM, Sudarsa PSS, Karmila IGAA D, Karna NLP RV. Borderline lepromatous leprosy with severe erythema nodosum leprosum: a case report. Berkala Ilmu Kesehatan Kulit Kelamin. 2022;34(3): 210-216. Available from: doi:10.20473/bikk.v34.3.2022.210-216
7. Oktarina C, Marissa M, Indriatmi W, Menaldi SL. Diagnosis dan tata laksana kekambuhan kusta [Diagnosis and management of leprosy relapse]. Med Derm Venereol Indonesia. 2022; 49(2)110-116. Indonesian.
8. Chelsea E, Yolanda L, Irawan Y. Kusta multibasiler dengan reaksi eritema nodosum leprosum: sebuah kasus terabaikan dari daerah terpencil [Multibacillary leprosy with erythema nodosum leprosum: a neglected case from a remote area]. eJKI.2024;12 (3). Indonesian. Available from: <https://ejki.fk.ui.ac.id/index.php/journal/article/view/482>

9. Kaimal S, Thappa DM. Relapse in leprosy. Indian J Dermatol Venereol Leprol. 2009; 75(2):126-133. Available from: <https://doi.org/10.4103/0378-6323.48656>



Advances in Dermatology