

Clinical Outcomes of Alternative Therapy Rifampicin and Clarithromycin in a Patient with Lucio's Phenomenon Who Declined Standard Multidrug Therapy: A Case Report

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Abstract

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Lucio's phenomenon (LP) is a rare reaction of lepromatous leprosy (LL) characterized by extensive skin necrosis. Standard multidrug therapy (MDT) is the mainstay of treatment, however the patient's refusal of standard MDT may complicate management. This case report describes the management of LP using rifampicin and clarithromycin in a patient refusing standard MDT. A 66-year-old male presented with purpuric patches on the extremities and painful leg ulcers. Examination revealed leonine facies, madarosis, megalobuli, hyperpigmented purpuric macules, and multiple necrotic ulcers. Slit-skin smear showed a bacterial index of +4 and a morphological index of 7%, while histopathology confirmed LP in LL. The patient received rifampicin, clarithromycin, corticosteroids, and wound care. Marked improvement of skin lesions was observed after 3 months. Rifampicin combined with clarithromycin may be an effective alternative regimen for LP in patients who refuse standard MDT, achieving favorable clinical outcomes and improving treatment adherence.

Keywords Lucio's Phenomenon; Leprosy, Lepromatous; Rifampin; Clarithromycin.

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Introduction

Leprosy, also known as Hansen's disease, is a chronic granulomatous infectious disease caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*. It is classified by the World Health Organization (WHO) as one of the 20 neglected tropical diseases (NTDs). Leprosy spans a spectrum from tuberculoid leprosy (TL), characterized by strong cellular immunity and limited lesions, to lepromatous leprosy (LL), marked by weak immunity and widespread disease. Any leprosy patient may experience leprosy reactions that can occur before, during, or after treatment. These reactions can be classified into different variants:

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Type 1 (reversal reaction), Type II (erythema nodosum leprosum), and Lucio's phenomenon (LP).¹⁻³

LP was first described by Lucio and Alvarado in Mexico in 1852. This rare yet potentially fatal reaction manifests as purpuric macules, ulceration, and necrosis and primarily affects the lower limbs. It is typically observed in untreated or inadequately treated diffuse lepromatous leprosy (DLL). LP is most prevalent in Mexico and Costa Rica but is less common in Indonesia, despite Indonesia being an endemic country.^{1,4}

The cornerstone of leprosy management is WHO-recommended multidrug therapy (MDT); however, management becomes particularly challenging when patients refuse standard MDT because of fear of adverse effects, poor treatment adherence, or limited



Figure 1 A-B) Leonine face, madarosis, megalobuli; **C-F)** Skin lesions on all extremities on admission.

access to medication. Evidence regarding alternative antimicrobial regimens for LP remains extremely limited, with most published data consisting of isolated case reports. This case provides additional evidence regarding the potential role of rifampicin–clarithromycin therapy as an alternative option in exceptional circumstances where conventional MDT cannot be administered, while emphasizing that WHO-MDT remains the recommended first-line treatment for leprosy.^{1,5}

Case Report

A 66-year-old male presented with worsening purplish-red patches and sores on both legs over the past month. About 2 years earlier, several reddish patches appeared on both legs without numbness or nerve damage. Around 5 months ago, the lesions changed to a purplish-black coloration and subsequently spread all over the limbs, followed by enlargement of both ears and loss of eyebrows and eyelashes. On both legs, the lesions developed into painful blisters that dried out spontaneously and

formed blackish sores. He also experienced an intermittent itchy and tingling sensation on the limbs. The patient had no prior history of pre-existing evidence of leprosy nor any antimycobacterial treatment. The patient had no history of autoimmune disease, atopy, hypertension, diabetes mellitus, or allergy.

Physical examination revealed normal vital signs; leonine facies, madarosis, and megalobuli (**Figure 1 A-B**). No palpable nerve trunks were detected. Dermatological examination showed multiple purpuric macules with xerotic skin on the limbs (**Figure 1C**), multiple ulcers with irregular shapes and varying sizes accompanied by blackish crusts, slough, and necrotic tissues on both lower extremities (**Figure. 1 D-F**).

Laboratory examination revealed elevated urea (69.7 mg/dL) and creatinine (1.43 mg/dL), yielding an estimated glomerular filtration rate (eGFR) of 54.3 mL/min^{1.73} m². The patient's 24-hour urine output was adequately maintained at >850 ml. Microbiological examination in the form of a slit-skin smear (SSS) taken from the earlobes revealed acid-fast bacilli (AFB) with a bacterial index (BI) of +4 and a morphological index (MI) of 7% (**Figure 2A**). Histopathological analysis of a biopsy specimen taken from the right thigh showed an inflammatory infiltrate composed of neutrophils, lymphocytes, and foamy histiocytes, accompanied by features of vasculitis and luminal thrombosis (**Figure 2B**). Numerous intact AFB were also observed within the foamy histiocytes and the vascular wall (**Figure 2C**).

Based on history, physical examination, and histopathological investigation, the patient was diagnosed with diffuse lepromatous leprosy with Lucio's phenomenon and non-oliguric acute kidney injury. Following the abnormal laboratory results,

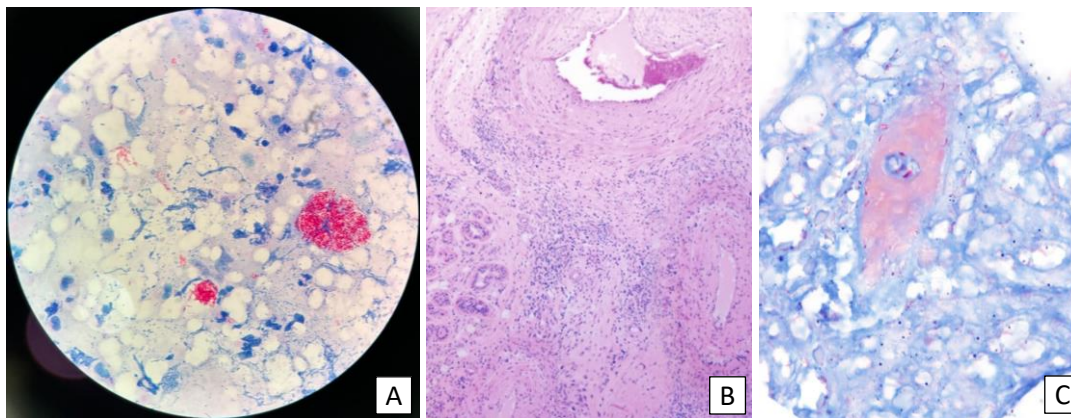


Figure 2 A) Slit-skin smear revealed bacterial index (BI) of +4 and morphological index (MI) of 7%; B) Histopathology section from right thigh showed inflammatory infiltrate composed of neutrophils, lymphocytes, and foamy histiocytes, accompanied by features of vasculitis and luminal thrombosis (Hematoxylin and Eosin stain, 50x) ; C) Many acid-fast bacilli (AFB) were seen within the foamy histiocytes and the vascular wall (Ziehl-Neelsen stain, 1000x)

the patient was referred to the Internal Medicine Department and managed with intravenous crystalloid hydration and strict fluid balance monitoring. The patient was given combination treatment with rifampicin tablet 600 mg/ month, clarithromycin 500 mg/ 24 hours, and oral methylprednisolone 8 mg/ 12 hours. Wound care was carried out with topical treatment in the form of 0.9% NaCl compresses for 10-15 minutes followed by applying 2% fusidic acid cream/ 12 hours on ulcers. Topical cream of 10% urea was applied/ 12 hours to dry skin areas on other parts of his limbs besides the ulcers and 0.25% desoximethasone/ 12 hours was also added specifically on the reddish areas to relieve inflammation.

There was an improvement of the lesions and no new lesions developed within two weeks after initiating treatment. Methylprednisolone was administered at 8 mg/ 12 hours for 7 days, then gradually tapered to 4 mg/ 12 hours for the subsequent 7 days in response to the patient's clinical improvement. The patient was asked to continue the treatment for 6 months with monthly follow-up. After 3 consecutive months of treatment, the purpuric macules on all extremities faded, the ulcers started to heal leaving atrophic scars surrounded by hyperpigmented macules, and the xerotic skin also improved (**Figure 3**).

Discussion

LP is an uncommon leprosy reaction characterized by painful erythematous-violaceous macular and slightly infiltrated plaques on the skin, which subsequently lead to flaky blisters, central necrosis, and ulceration. This condition primarily affects the limbs but may extend to the trunk and face, without significant systemic symptoms initially. LP is typically observed in untreated or inadequately treated patients with the diffuse form of LL and is potentially life-threatening.^{1,2,5,6}

DLL is characterized by diffusely infiltrated skin and a lack of dermal nodules. Initially, it presents as asymptomatic, slightly erythematous, or



Figure 3 Improved skin lesions after 3 months of treatment.

hypopigmented macules that can progress to infiltration and induration if untreated. Other clinical features include madarosis, megalobuli, saddle nose, and impaired extremity sensation. Inflammation and destruction of dermal appendages, sweat glands, and sebaceous glands lead to dry, cracked skin prone to infection and ulceration.^{6,7}

This patient had elevated urea and creatinine levels but a normal urine output, which indicated non-oliguric acute kidney injury. While glomerulonephritis has been documented in both LL and LP, the clinical data in this case strongly suggested a prerenal etiology secondary to dehydration, as the calculated urea-to-creatinine ratio of >40 (approximately 48.7) pointed towards volume depletion. One of the supporting diagnostic examinations of AFB in the form of SSS stained with Ziehl-Nielsen taken from earlobes and skin lesions shows a very positive bacterial and morphological index in LP. In addition to SSS, histopathological examination of a skin lesion was performed, revealing aggregates of AFB within the endothelium, luminal occlusion, and vascular thrombosis. This result aligns with the diagnostic triad that defines LP: skin ulceration, vascular thrombosis, and invasion of the blood vessel wall by Hansen's bacilli. The classic clinical features and results of diagnostic investigations in this patient support the diagnosis of DLL with LP.⁵⁻⁸

While the treatment protocol for LP remains unstandardized, WHO-MDT consisting of rifampicin, dapsone, and clofazimine is commonly used to combat the underlying mycobacterial infection. However, management becomes challenging when standard MDT cannot be administered because of contraindications, drug intolerance, or patient refusal. In such situations, evidence supporting alternative antimicrobial regimens remains limited and is largely derived from isolated case reports. Clarithromycin is one of the newest leprosy drugs, known to be effective against *Mycobacterium leprae* infection. Furthermore, it has good tolerance, rarely causes side effects, and can shorten the duration of treatment. Previous research

in Indonesia reported that a combination of rifampicin 600 mg/ month and clarithromycin 500 mg/ day led to a significant improvement in general condition and skin lesions healing in an LP patient within 30 days. A comprehensive systematic review of LP cases, alongside a recent report from a non-endemic region, has similarly highlighted clarithromycin-based regimens as effective rescue therapies when standard MDT is contraindicated, poorly tolerated, or declined. Corticosteroid use is controversial. In severe and treatment-refractory cases, plasmapheresis has been considered as a therapeutic alternative due to the presence of circulating immune complexes, although further studies are required to validate this strategy.^{1,3,9,10}

In the present case, the patient declined standard WHO-MDT despite repeated counseling, primarily because of concerns about treatment-related hyperpigmentation, particularly the cosmetic impact of clofazimine, and the lack of continuous availability of MDT medication. Therefore, rifampicin 600 mg once monthly and clarithromycin 500 mg once daily were administered as an alternative antimicrobial regimen. Regarding the renal safety profile, pharmacological guidelines mandate a reduction in the clarithromycin dose only in cases of severe renal impairment, specifically when the creatinine clearance falls below 30 mL/min. As the patient's estimated creatinine clearance (calculated via the Cockcroft-Gault equation) was 50.3 mL/min, the standard therapeutic dose was safely administered without exacerbating the existing renal condition. Topical antibiotics were delivered to prevent secondary infection. Additionally, topical urea was applied to treat dry skin, while targeted corticosteroid cream was applied to relieve the inflamed area. During the three-month follow-up, the patient demonstrated substantial clinical improvement, with resolution of most necrotic and ulcerative lesions, absence of new lesions, and progressive wound healing, although residual atrophic scars and post-inflammatory hyperpigmentation persisted. These findings are consistent with previous reports suggesting that the combination of rifampicin and clarithromycin

therapy may provide clinical benefit in carefully selected patients who cannot receive standard MDT.^{2,8-10}

Conclusion

The inability to administer standard Multidrug Therapy (MDT) in Lucio's Phenomenon requires an urgent and effective alternative approach. This case demonstrates that the alternative combination of rifampicin and clarithromycin is clinically effective and well-tolerated. It effectively halted the severe necrotizing reactions and improved the patient's overall clinical condition, highlighting its utility as a successful alternative treatment when standard MDT is declined.

Declaration of patient consent Author certify that they had obtained all appropriate patient consent.

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Author's contribution

ISP: Identification, diagnosis & management of the case and manuscript writing.

RH,E: Identification, diagnosis & management of the case, critical review of the manuscript.

All authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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