Borderline Tuberculoid Leprosy Mimicking Kaposi Sarcoma in an HIV-positive Patient: A Case Report and Review

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ABSTRACT:

Leprosy, or Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae*. It affects the skin, peripheral nerves, and eyes[1]. Although curable with multidrug therapy (MDT), nearly 200,000 new cases are reported globally each year[3]. Early diagnosis and efforts to reduce social stigma are essential for disease control and prevention[2].

Leprosy and human immunodeficiency virus (HIV) infection frequently coexist in endemic regions, yet their immunologic interaction remains complex and paradoxical. Although HIV-induced immunosuppression could theoretically increase susceptibility to *Mycobacterium leprae*, the clinical spectrum of leprosy is not markedly altered in most co-infected patients[12,13].

We present the case of a male patient with a known history of HIV, who presented with erythematous and violaceous lesions suggestive of Kaposi sarcoma. The lesions, characterized by both plaques and nodules, were widely distributed across the face, trunk, back, and extremities. A slit-skin smear yielded negative results, while a biopsy from the left arm revealed elongated sausage-like tuberculoid granulomas in the superficial perivascular plexus and along the neurovascular bundle. The Fite stain failed to reveal the organisms. Further examination using fluorescent staining with auramine O showed a positive result in the left ear. In addition, molecular analysis via Nested PCR targeting the M. leprae-specific repetitive element (RLEP) confirmed a diagnosis of leprosy. The patient underwent multidrug therapy, after which the skin lesions showed improvement. Fluorescent staining and nested PCR testing may aid in diagnosing cases of paucibacillary leprosy, where slit-skin smear examination is often inconclusive. These methods may serve as supplementary diagnostic tools, particularly in cases presenting with atypical skin lesions.

Key words: Borderline Tuberculoid leprosy, Paucibacillary leprosy, Nested PCR

Case report

A 34-year-old male patient with a known history of HIV infection diagnosed two years ago, with a most recent CD4 count of 220 cells/mm³ in May 2024. Approximately one month after initiating antiretroviral therapy (ART) two years ago, he developed erythematous, raised skin lesions on his extremities and trunk. He first sought treatment at a private hospital, where a skin biopsy revealed granulomatous dermatitis. The initial PCR testing for non-tuberculous mycobacteria (NTM) was positive, but tissue culture showed no growth. He was treated empirically with clarithromycin, levofloxacin, and rifampicin for about one year, with no clinical improvement of the skin lesions. Subsequently, the patient was suspected to have an allergic

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reaction to rifampicin, and rifampicin was discontinued. The patient continued the remaining two medications for a total duration of one year; however, there was no clinical improvement. The medications were then discontinued.

One year before his presentation at our hospital, he transferred to another private Hospital, where the prior antibiotic regimen was discontinued due to a lack of response. A repeat biopsy performed in December 2024 showed chronic granulomatous inflammation. Tissue culture again yielded no growth, and PCR for NTM was negative.

A third skin biopsy in May 2025 revealed focal granulomatous formation and superficial perivascular infiltration with lymphohistiocytes. Tissue culture remained negative. Chest X-ray showed no evidence of pulmonary tuberculosis, and VDRL testing was negative.

The patient was subsequently referred to the Institute of Dermatology for further evaluation.

On physical examination (**Figure 1**), he presented with multiple discrete, well-defined erythematous to violaceous patches and plaques on the face, trunk, back, and extremities, with sensory loss over the lesions and no oral mucosal involvement. No nerve enlargement.



Figure 1 Multiple erythematous to violaceous plaques and nodules on trunk, back, and extremities

Slit skin smear from the posterior neck, abdomen, and post-auricular areas of both ears was negative.

A Skin biopsy from the abdomen, performed at the Institute of Dermatology in August 2024, is shown in **Figure 2** and revealed elongate, sausage-like tuberculoid granulomas in the superficial dermis and along the neurovascular plexus, without caseating necrosis. The inflammatory cell infiltrate consists of histiocytes, multinucleated giant cells (MNGs), and surrounding lymphocytes. No organisms were identified. The Fite stain yields a negative result. No leprosy reaction was observed. The histopathological findings suggest borderline tuberculoid leprosy.

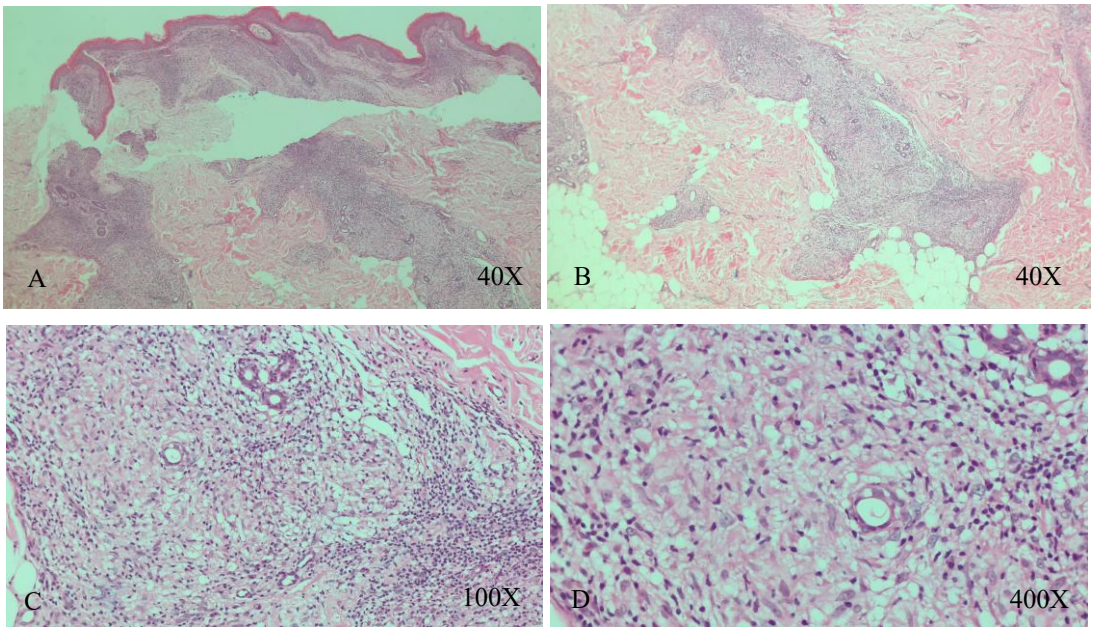


Figure 2 Aggregation of histiocytes and multinucleated giant cells that were surrounded by lymphocytes in the upper and mid-dermis (H&E; original magnification: A. 40X, B. 40X, C. 100X, D. 400X)

PCR testing for mycobacteria and fungi was negative in all samples. All mycobacterial and fungal cultures were negative.

Although the slit-skin smear was negative, the histopathological findings were consistent with borderline tuberculoid leprosy. Because of the extensive distribution and number of skin lesions, the patient was initiated on multidrug therapy (MDT). However, due to a known allergy to rifampicin, the treatment regimen consisted of Clofazimine 50 mg/day, Ofloxacin 400 mg/day, and Clarithromycin 500 mg/day. Following six months of therapy, the cutaneous lesions showed no significant clinical improvement. Consequently, a repeat skin biopsy was undertaken to reaffirm the diagnosis.

In the second skin biopsy from the left forearm, histopathological examination revealed dense diffuse histiocytic aggregates in the upper and mid-dermis. These aggregates predominantly consist of histiocytes, with occasional multinucleated giant cells, and are surrounded by lymphocytic infiltrates. A distinct Grenz zone is observed. There is no evidence of neutrophilic infiltration or vasculitis. The fite stain is negative. The

histopathological findings are still consistent with borderline tuberculoid leprosy.

Further examination using fluorescent staining with auramine O showed a positive result in the left ear (**Figure 3**). In addition, molecular analysis via Nested PCR targeting the M. leprae-specific repetitive element (RLEP) confirmed a diagnosis of leprosy (**Figure 4**).

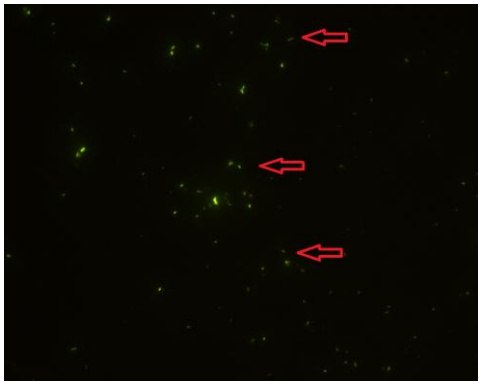


Figure 3 Numerous small greenish bacilli were seen in Auramine O fluorescent staining from the left ear lobe.

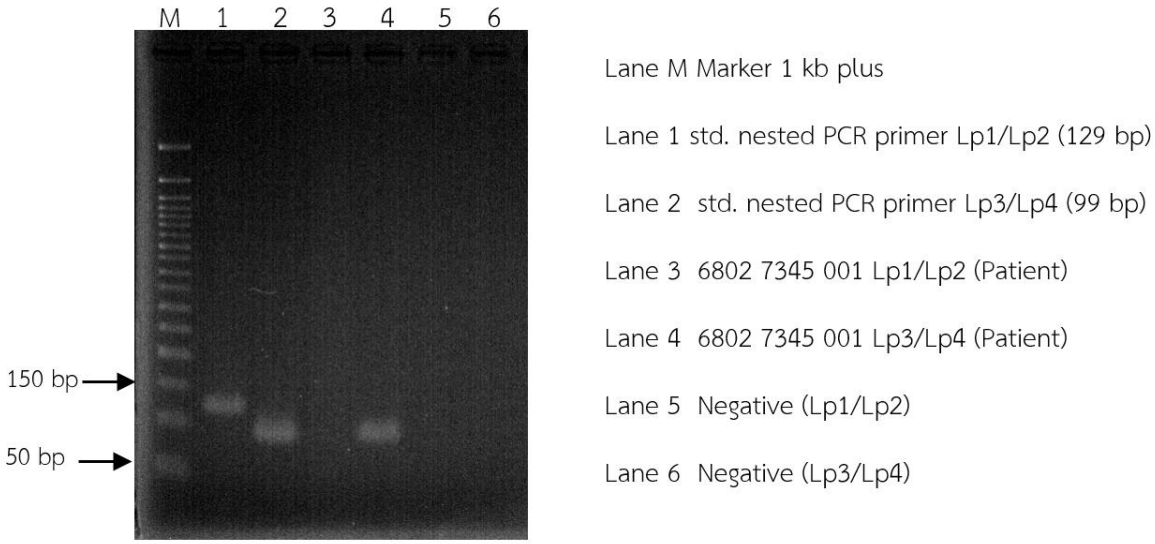


Figure 4 Lane 1 showed a positive result from the first PCR, and Lane 2 showed a positive result from the prior PCR products. Lane 4 showed a positive result in Nested PCR from this patient, targeting the *Mycobacterium leprae*-specific repetitive element (RLEP)

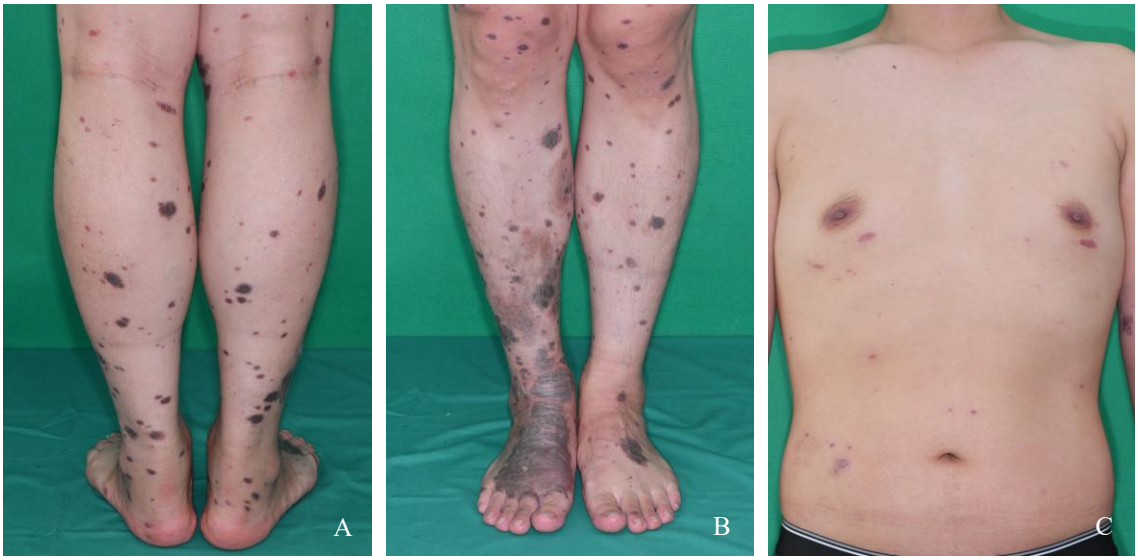


Figure 5 After one year of treatment, the lesions decreased in size, and their color changed from violaceous-red to hyperpigmented patches.

Based on the overall findings, the definitive diagnosis for this patient was Borderline Tuberculoid leprosy. The patient remained on clofazimine, ofloxacin, and clarithromycin therapy, following which the skin lesions gradually improved (**Figure 5**).

Discussion

Leprosy, or Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae*. It primarily affects the skin and peripheral nerves, leading to a wide spectrum of clinical manifestations. If left untreated, it can result in significant deformities and disabilities[1,2,3]. Despite global efforts to eliminate the disease, new cases continue to be reported, which still require treatment and control measures to prevent further infections.

Leprosy can be classified into two primary polar forms: tuberculoid and lepromatous. Tuberculoid leprosy is characterized by a strong immune response, presenting with few, well-defined skin lesions and nerve involvement, often leading to sensory loss[3]. In contrast, lepromatous leprosy involves a weak immune response, leading to widespread, symmetric skin lesions, nasal congestion, and severe nerve damage, often with deformities and limb weakness[2]. Clinical manifestations of tuberculoid leprosy include hypopigmented or erythematous patches, while lepromatous leprosy presents with multiple macules, nodules, and plaques[1]. The differentiation between these two forms is crucial for appropriate treatment and prognosis.

According to the World Health Organization[1], leprosy is diagnosed based on three cardinal signs: (1) skin lesions with definite loss of sensation, (2) thickened peripheral nerves with sensory or motor loss, and (3) the presence of acid-fast bacilli in skin smears. Clinical examination remains the primary method for diagnosis. Early detection and treatment are essential to prevent disability. Laboratory tests, including slit-skin smears or biopsies, help confirm the diagnosis and determine disease classification.

While clinical examination and slit-skin smear microscopy remain the standard diagnostic tools, several alternative methods have been developed to enhance diagnostic accuracy, especially in early or paucibacillary

cases. These include skin pathology[1], fluorescent staining with auramine O[4], polymerase chain reaction (PCR)[5], and nested PCR[6,7].

Histopathological examination of a skin biopsy is a valuable tool for diagnosing leprosy. It allows for identifying characteristic features such as granulomatous inflammation and nerve involvement. In multibacillary cases, numerous acid-fast bacilli can be observed with Fite-Faraco staining. Skin pathology not only helps confirm diagnosis but also aids in disease classification[8].

Auramine O staining is a fluorochrome technique to detect acid-fast bacilli under a fluorescence microscope. Compared to the Ziehl-Neelsen method, auramine O offers improved sensitivity and quicker screening of large sample volumes. A study from Ethiopia demonstrated that auramine O staining on tissue sections had a sensitivity of 77.9%, which was higher than conventional methods like Fite-Faraco staining (77%) and Ziehl-Neelsen staining (59.3%)[4].

PCR is a molecular method that detects *M. leprae* DNA in clinical specimens, providing high sensitivity and specificity. PCR is especially useful for diagnosing early-stage leprosy or in cases with atypical presentations where bacilli are difficult to detect by conventional methods. It can be performed on skin biopsies, nasal swabs, or slit-skin smears. A study involving 126 skin biopsies and 25 slit-skin smears found that quantitative PCR (qPCR) had a sensitivity of 84.9% and a specificity of 100% when using the RLEP primers[5].

Nested PCR is a two-step amplification technique that increases the sensitivity of conventional PCR. It is beneficial for detecting low bacterial loads, making it suitable for diagnosing paucibacillary leprosy. This method enhances diagnostic precision and reduces the risk of false negatives, especially in complex or borderline cases. Research indicates that nested PCR has higher sensitivity than conventional PCR, with detection rates exceeding 80% in multibacillary cases and 30–40% in paucibacillary cases[6,7].

In this case, the patient, diagnosed with HIV, presented with numerous erythematous to violaceous, raised plaques and nodules distributed across the body, including the face, trunk, and extremities. There were signs of sensory loss on skin lesions. Upon examination, several differential diagnoses were considered, including Kaposi's sarcoma, chronic infection, cutaneous tuberculosis, and leprosy. Consequently, a slit-skin smear and skin biopsy were performed. The slit-skin smear results were negative at all sites. However, the skin biopsy showed findings consistent with tuberculoid granuloma in the dermis, along the neurovascular bundles with a grenz zone, which suggests a possible diagnosis of borderline tuberculoid leprosy. Nevertheless, there is some uncertainty due to the widespread distribution and appearance of the rash, which is erythematous to violaceous, raised, and numb, more closely resembling the rash seen in lepromatous leprosy.

Atypical presentation of tuberculoid leprosy can pose diagnostic challenges due to its variable clinical features unlike the classic form, which is characterized by hypopigmented, well-defined, and asymmetrical skin lesions, the atypical form may present with subtle signs such as nodular lesions, widespread erythema, or a more diffuse involvement of the skin and peripheral nerves, Sweet syndrome-like lesions or exhibit features resembling granuloma annulare or urticarial vasculitis[9]. In addition, features such as psoriatic plaques, verrucous plaques, or hypertrophic scars have been reported[10].

Leprosy associated with immune reconstitution inflammatory syndrome (IRIS) has been increasingly recognized among HIV-infected individuals following the initiation of highly active antiretroviral therapy (HAART).

In most cases, leprosy emerges as a paradoxical inflammatory response unmasking a previously subclinical infection.

According to the systematic review by Mouchard et al. (2022)[11], a total of 73 HIV-positive patients worldwide were reported over a 20-year period to have developed IRIS presenting as leprosy after starting HAART. The majority of these patients exhibited the borderline tuberculoid (BT) form (56.2%), followed by tuberculoid (TT) (10.9%) and borderline lepromatous (BL) (13.7%) forms. Notably, 74% of the patients experienced a type 1 lepra reaction, and 68% of these occurred concurrently with the diagnosis of IRIS, while others developed reactions subsequently after initiating multidrug therapy (MDT). On average, IRIS onset occurred approximately 2.5 months after HAART initiation.

In this review[11], it was noted that among patients classified as BT and TT, nearly two-thirds presented with type 1 lepra reactions, suggesting a relatively preserved cell-mediated immune response. This observation aligns with the immunologic changes typically seen in IRIS, characterized by an increase in CD4+ T-cell counts and a decline in HIV viral load following HAART initiation. It has been suggested that HAART may act as a trigger, unmasking subclinical Mycobacterium leprae infection in the incubation phase by enhancing both innate and cellular immune responses. The type 1 reaction in this context is thought to result from an exaggerated pro-inflammatory response during immune reconstitution[12].

In this patient, a history of generalized skin eruptions was noted shortly after initiating HAART. At that time, a skin biopsy revealed granulomatous dermatitis, but the findings were inconclusive for leprosy or a leprosy reaction. Additionally, there were no available data on CD4+ count or viral load changes, making it impossible to determine whether the episode represented true immune reconstitution inflammatory syndrome (IRIS). Two years later, the patient continued to have violaceous skin lesions that were non-tender, with sensory loss. The two most recent histopathologic examinations demonstrated findings consistent with borderline tuberculoid (BT) leprosy, without evidence of a leprosy reaction. Taken together, these findings suggest that the likelihood of IRIS or a leprosy reaction at this stage is low and not definite.

In this case, the patient initially received multidrug therapy (MB regimen) due to extensive cutaneous lesions. However, owing to a documented allergy to rifampicin, an alternative treatment regimen comprising clofazimine, ofloxacin, and clarithromycin was administered. According to the World Health Organization (WHO) guidelines[1] published in 2018, when rifampicin cannot be used for patient treatment, an alternative regimen should be considered. The WHO recommends treatment with at least two of clarithromycin, minocycline, and quinolone, in addition to clofazimine, daily for 6 months, followed by clofazimine and 1 of the above drugs for an additional 18 months. This rifampicin-sparing regimen[1] is conditionally recommended based on low-certainty evidence; small clinical series have demonstrated favorable bacteriologic and clinical outcomes, suggesting that this regimen is effective in achieving good therapeutic results, although long-term relapse data remain limited. In the study by Narang et al[14], after completion of the alternative regimen, the mean bacterial index (BI) decreased from 5.3 ± 0.6 to 1.7 ± 0.7, and the morphological index (MI) from 14 ± 6.8% to 0% ($P < 0.0001$), with complete resolution of infiltrated plaques and nodules in all patients.

After six months of therapy, the skin lesions had minimal clinical improvement, warranting a repeat skin biopsy. Histopathological examination again demonstrated tuberculoid granulomatous inflammation involving the dermis and nerve bundles, consistent with the

initial findings. The biopsy specimen was subjected to fluorescent staining using Auramine O to investigate the persistent lesions further, which yielded a positive result for acid-fast bacilli. Moreover, Nested polymerase chain reaction (PCR) targeting the *Mycobacterium leprae*-specific repetitive element (RLEP) was performed on lesional tissue to confirm the presence of *M. leprae* DNA.

As previously described, Auramine O fluorescent staining[4] demonstrates superior sensitivity compared to conventional slit skin smear techniques, while Nested PCR provides enhanced diagnostic accuracy over standard PCR and traditional methods. [5,6,7] These modalities are particularly valuable in patients with atypical clinical features or paucibacillary cases. Based on these findings, the patient continued treatment with the alternative regimen, resulting in gradual and sustained clinical improvement.

Conclusion

We present a case of an HIV-positive patient who exhibited multiple cutaneous lesions initially mimicking Kaposi sarcoma. The diagnosis of tuberculoid leprosy was established based on histopathological findings from a skin biopsy, supported by positive results from Auramine O fluorescent staining and nested PCR targeting the *Mycobacterium leprae*-specific repetitive element (RLEP). The patient was managed with an alternative multidrug regimen comprising clofazimine, ofloxacin, and clarithromycin, leading to gradual clinical improvement. Incorporating these advanced diagnostic techniques, such as skin pathology, auramine O staining, PCR, and nested PCR, can significantly improve the accuracy and early detection of leprosy.

Clinicians should maintain a high index of suspicion for leprosy in HIV patients presenting with violaceous nodules, even when the slit-skin smear is negative. Advanced diagnostics, such as Auramine O staining and Nested PCR, can be crucial for confirmation.

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