IeJSME 2025 Vol 19 (1): 67-70

Isolated Bone Marrow Involvement of Lepromatous Leprosy in an HIV-infected Patient with No Apparent Skin Lesions: A Case Report

Joshua Shadrach Daniel[1], Kwee Choy Koh[2], Thin Thin Win[3]

Leprosy caused by *Mycobacterium leprae*, primarily manifests with cutaneous and neurological symptoms. Bone marrow (BM) involvement without skin lesions is exceedingly rare, particularly in immunocompromised patients. Here is a case of a 40-year-old HIV-infected man with a nadir CD4 count of 29 cells/mm³ who presented with recurrent anaemia, massive hepatosplenomegaly, and no apparent skin lesions. BM analysis revealed epithelioid granulomas with foamy histiocytes containing acid-fast bacilli, confirmed by Wade-Fite staining. This case highlights the rare presentation of lepromatous leprosy, emphasising the diagnostic challenges posed by the absence of typical cutaneous features.

Keywords: *Leprosy, HIV, Bone marrow involvement*

INTRODUCTION

Leprosy, or Hansen's disease, is a chronic infection caused by *Mycobacterium leprae*. Identified by Armauer Hansen in 1873, leprosy has been linked to social stigma, driven by illiteracy and poverty. While global efforts led by the World Health Organization (WHO) have reduced its prevalence by 90%, it remains a public health issue in Malaysia. Though officially eliminated there in 1994, recent incidence increases are linked to migrant workers from endemic regions.[1] Leprosy-HIV co-infection, though less common than Tuberculosis-HIV (TB-HIV) co-infection, still presents as a significant challenge. Bone marrow granulomas in lepromatous leprosy are rare and require thorough diagnosis, especially in regions where tuberculosis and atypical mycobacteria are prevalent.[2]

CASE REPORT

A 40-year-old man was diagnosed with HIV infection in September 2014 after presenting with extensive oral thrush. His nadir CD4 count at diagnosis was 29 cells/mm^3 (normal range: 500-1500 cells/mm^3), but baseline viral load (VL) was not measured. He was started on anti-retroviral therapy (ART) consisting of tenofovir-emtricitabine (Ten-Em) and efavirenz. Trimethoprim-sulfamethoxazole (TMP-SMX) was added to the ART regimen for *Pneumocystis jiroveci* prophylaxis. However, he defaulted on the proposed treatment and only returned for follow-up after three months.

On the follow-up, the patient presented with symptomatic anaemia (Hb 6.7 g/dL) and altered bowel habits. Physical examination revealed pallor and hepatomegaly without lymphadenopathy or skin lesions. Endoscopic and colonoscopic evaluations were unremarkable. He received two units of red blood cells. After eight weeks, his CD4 count improved to 43 cells/mm^3, although viral load was not measured. Over the following months, the patient had recurrent hospitalisations for anaemia (haemoglobin 7.5-8.0 g/dL) requiring transfusion. Examination consistently noted hepatosplenomegaly without lymphadenopathy or skin lesions. Despite improved adherence, his CD4 count remained low (86 cells/mm^3). Chronic infection or ART-associated anaemia was suspected, but further evaluation was not pursued.

Three weeks before his final admission, he presented with lethargy and abdominal pain. Examination revealed massive hepatosplenomegaly (liver 8 cm below the costal margin, spleen 18 cm). The complete blood count consistently showed hypochromic

[1] Medical Graduate, IMU University, Seremban, Negeri Sembilan, Malaysia
[2] Deputy Dean, Clinical Science, Development & Community Engagement, Infectious Diseases Consultant, IMU University, Seremban, Negeri Sembilan, Malaysia
[3] Department of Pathology and Pharmacology, School of Medicine, IMU University, Bukit Jalil, Kuala Lumpur, Malaysia

Corresponding author:
Dr Joshua Shadrach Daniel
Tel: +6016-2032528 Email: joshua.shadrach@gmail.com

microcytic anaemia, with peripheral blood smear revealing neutrophil dysplasia and microcytic red blood cells. These were all suggestive findings of a bone marrow pathology Differential diagnoses included chronic myeloid leukaemia and myelofibrosis. Bone marrow aspiration and trephine (BMAT) analysis were performed, but the patient succumbed to cardiogenic shock before the results could guide management.

BMAT analysis showed mildly hypocellular marrow with epithelioid granulomas with numerous foamy histiocytes. (Figure I). Ziehl-Neelsen (ZN) staining demonstrated acid-fast bacilli (Figure II). Periodic acid- Schiff (PAS) and Grocott–Gömöri's methenamine silver (GMS) stains were negative for fungi. However, the Wade-Fite stain was strongly positive, indicating numerous globi within the cytoplasm of the histiocytes (Figure III). All the above findings were consistent with the diagnosis of lepromatous leprosy infection.

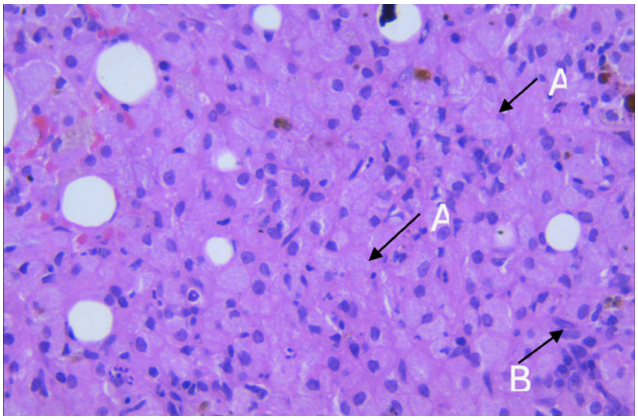

Figure I: Bone Marrow Trephine Biopsy. Low-power view (40x magnification) showing multiple foamy histiocytes (A), and presence of epithelioid granuloma formation (B).

DISCUSSION

This case highlights the diagnostic challenge of leprosy in the context of an atypical presentation. The patient presented with persistent anaemia and hepatosplenomegaly without apparent skin findings, which led to an extensive workup before leprosy was ultimately diagnosed. While leprosy is typically

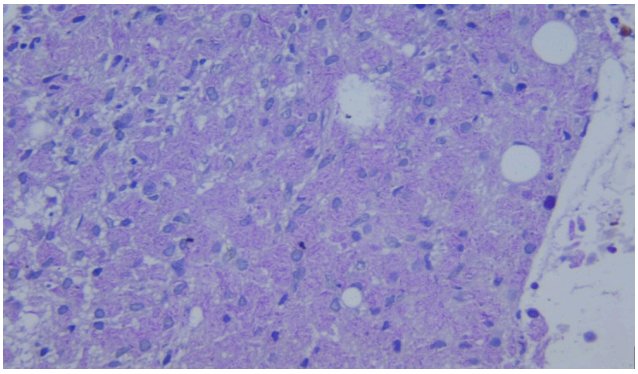

Figure II: Bone Marrow Trephine Biopsy with Ziehl-Neelsen (ZN). High-power view (100x magnification) showing numerous acid-fast bacilli.

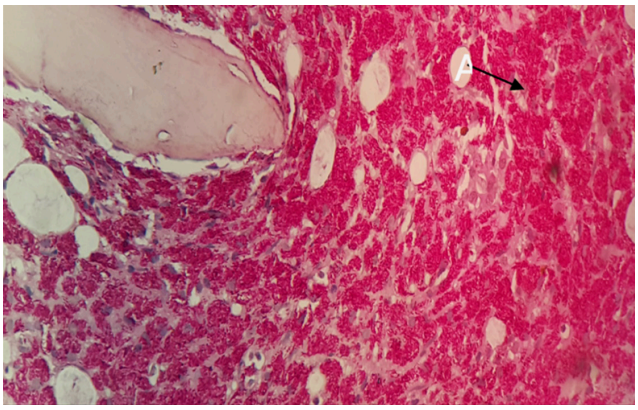

Figure III: Bone Marrow Trephine Biopsy. Wade-Fite stain showing numerous acid-fast bacilli (globi) within the cytoplasm of histiocytes.

identified by its cardinal signs, (i) loss of sensation with a pale (hypopigmented) or reddish skin patch, (ii) thickened or enlarged peripheral nerves with sensory or muscle loss, and (iii) the presence of acid-fast bacilli in a slit-skin smear[3], diagnosis was finally made through BMAT analysis. Thus, this case reinforces the complexity of diagnosing atypical presentations.

In addition to the atypical presentation in this patient, local burden of *M. leprae* infections in Malaysia is relatively low. Since 1994, the incidence of leprosy in Malaysia is < 1 per 10000 population. Although leprosy is primarily observed in East Malaysia and Kuala Lumpur, it is increasingly seen among foreign workers, as opposed to local individuals.[4] This low

incidence, coupled with the atypical presentation in this patient, have likely contributed to the reduced clinical suspicion for *M. leprae* infection.

In reviewing further literature regarding its pathogenesis, *M. leprae* infections have been shown to exhibit a broad clinical spectrum. The Ridley-Jopling classification system categorises leprosy into two poles – lepromatous and tuberculoid – with an intermediate form referred to as borderline leprosy. Tuberculoid leprosy, characterised by high cell-mediated immunity, involves a Th1-type immune response and localised paucibacillary (PB) forms. In contrast, lepromatous leprosy, associated with a Th2 humoral response due to low cell-mediated immunity, is characterised by anergic, disseminated multibacillary (MB) forms.[5]

Given the patient's HIV infection, which compromises cell-mediated immunity, it is highly likely that his leprosy presentation aligns with lepromatous leprosy. This form is characterised by a Th2 humoral response and disseminated multibacillary forms due to diminished cell-mediated immunity. In immunocompromised individuals, lepromatous leprosy can present atypically, as seen in this patient who lacked typical skin and neurological findings.[6] A similar case was reported where lepromatous leprosy was a feature in an HIV-positive patient, highlighting the diagnostic challenges of such co-infections.[7]

Another possible reason for the atypical presentation in this patient is the dissemination of *M. leprae* to the bone marrow. This dissemination creates localised granulomas within the bone marrow and suppresses lymphocyte sensitivity towards mycobacterial antigens.[8] In this case, the suppression, combined with the HIV co-infection, may have significantly reduced the overall immune response in peripheral tissues, allowing *M. leprae* to reactivate and spread without skin manifestion.[7] The bone marrow infiltration by leprae cells in this case is particularly noteworthy given the absence of clinical suspicion of leprosy before the bone marrow assessment. Although there is a case report documenting bone marrow involvement and pancytopenia in leprosy, it presented with typical skin lesions, unlike this patient. This further highlights the challenge of diagnosing leprosy in immunocompromised individuals, where clinical signs may be less apparent.[9]

However, a pertinent question arises regarding why the patient developed active leprosy after initiating ART therapy. A recent systemic review highlighted that individuals with HIV may develop immune reconstitution inflammatory syndrome (IRIS) following the initiation of highly active antiretroviral therapy (HAART).[10] IRIS is characterised by an exaggerated inflammatory response to previously latent or subclinical infections, such as *M. leprae*, due to partial restoration of immune function. It is plausible that the initiation of ART in this patient led to IRIS, reactivating previously undiagnosed or subclinical leprosy, exacerbating its clinical presentation and dissemination. Treatment protocols for *M. leprae* typically involve multidrug therapy (MDT) with rifampicin, dapsone, and clofazimine.[11] In HIV-positive patients, the addition of corticosteroids is often necessary to manage IRIS.[10]

In this patient who presented with HIV and bone marrow involvement without skin lesions, the treatment approach would likely involve a combination of antiretroviral therapy (ART) for HIV and multidrug therapy (MDT) for *M. leprae*. Given the bone marrow involvement, it is crucial to monitor for signs of leprosy reactions and adjust the treatment

regimen accordingly. The use of corticosteroids may be necessary to manage any inflammatory reactions seen.[12]

In summary, the management of leprosy in HIV-positive patients requires a comprehensive approach involving multidrug therapy (MDT), antiretroviral therapy (ART), and corticosteroids. In this case, the lack of clinical suspicion of leprosy due to its atypical presentation and the low local incidence led to a delay in diagnosis and treatment. Although available literature may propose reasons for such atypical presentations, it remains essential to always consider potential co-infections, such as other mycobacterial and opportunistic infections. This case reiterates the importance of enhancing awareness and training among healthcare providers regarding the potential for leprosy in HIV-positive patients, which can improve early detection and survival outcomes.

CONCLUSION

This case illustrates the unusual presentation of lepromatous leprosy in an immunodeficient patient. The complexity of the disease is now being realised as more and more studies shed light on the immunopathological mechanism of the condition. Although rare, leprosy should be considered as a possible diagnosis in an immunocompromised patient with cytopenia presenting with hepatosplenomegaly. Relevant clinical signs associated with the disease should be carefully looked for, and appropriate investigations should be considered. Treatment should be comprehensive, involving MDT, ART, and corticosteroids for IRIS.

REFERENCES

1. World Health Organization. Global Strategy for Further Reducing the Leprosy Burden and Sustaining Leprosy Control Activities. *Lepr Rev*, 2006;77(IX, X), 1-50.
2. Ustianowski A P, Lawn S D, & Lockwood D N. Interactions between HIV infection and leprosy: A paradox. *Lancet Infect Dis*, 2006;6(6), 350–360.
3. World Health Organization Expert Committee on Leprosy. Eighth Report. *WHO Tech Rep Ser*. 2012; (968), 1–61.
4. Yap F B, Kiung S T, Yap J B. Quality of life in patients with erythema nodosum leprosum in Kuala Lumpur, Malaysia. *Indian Dermatol Online J*. 2016 Jul-Aug;7(4):255-8.
5. Ridley D S, Jopling W H. Classification of leprosy according to immunity. A five-group system. *Int J of Lepr Other Mycobact Dis*, 1996; 34(3): 255–273.
6. Guilherme J M S C, Goulart L R, Goulart I M B. Pathogenesis of Leprosy: Immunogenetics and Immunopathology of Infection. In: *International Textbook of Leprosy*. 2017.
7. Belgaumkar V A, Chavan R B, Deshmukh N S, Ponathil A P. Lepromatous leprosy as a presenting feature of HIV. *Indian J Sex Transm Dis AIDS*. 2021 Jul-Dec;42(2):162-165.
8. Santana M A O, da Costa W V T, Celestino I C, dos Santos D F, Dornelas B dC, Pavelka M M, Luppi A D M, & Goulart I M B. Fever of unknown origin, wasting syndrome, and bone marrow involvement: A leprosy case report. *Front Immunol*, 2022: 13, 916319.
9. Saini S T, Jain S, Narang T, Yadav R, Rastogi P. Bridging dermatology and hematology: A case of lepromatous leprosy with bone marrow involvement and pancytopenia. *J Hematop*. 2024 Aug 7.
10. Centers for Disease Control and Prevention. Immune reconstitution inflammatory syndrome associated with Mycobacterium leprae infection in HIV-infected patients. *Emerg Infect Dis*. 2007;13(9):1371-1373.
11. World Health Organization. Guidelines for the diagnosis, treatment and prevention of leprosy (2nd ed). Geneva: WHO; 2018.
12. Mouchard A, Blaizot R, Graille J, Couppié P, Bertin C. Leprosy as immune reconstitution inflammatory syndrome in patients living with HIV: Description of French Guiana's cases over 20 years and systematic review of the literature. *PLoS Negl Trop Dis*. 2022 Mar 4;16(3).