doi: 10.5123/S2176-6223202501604

Reactional state in an atypical borderline tuberculoid leprosy: a spectrum of type 2 leprosy reaction?

Estado reacional em uma hanseníase tuberculoide atípica limítrofe: um espectro de reação hansênica tipo 2?

Felipe Marinho Rocha de Macêdo[1], Carolina Barbosa Farias[1], Maria Cecilia Leal Ardito[1], Luiza Gonçalvez de Arruda Ferraz[1], Tárcio dos Santos Pereira[1], Márcio Martins Lobo Jardim[1]

[1] *Santa Casa de Misericórdia do Recife, Centro de Estudos Dermatológicos do Recife, Recife, Pernambuco, Brasil*

ABSTRACT

Leprosy is a chronic granulomatous neurocutaneous disease with a wide clinical, histopathological, and immunological spectrum. Leprosy reactions can occur at any stage of the disease, even in untreated individuals, reflecting abrupt immunological shifts. This report describes a case of an otherwise healthy female patient referred to the dermatology outpatient service due to an isolated, asymptomatic, long-standing single lesion on her left thigh for five years. A diagnosis of borderline tuberculoid (BT) leprosy was made. Within 30 days, the patient complained of a sudden onset of systemic symptoms and showed multiple hemorrhagic bullae on her lower limbs, prompting suspicion of an atypical type 2 leprosy reaction. BT leprosy is typically characterized by a few scattered infiltrated plaques with asymmetrical and irregular nerve thickening. Histopathology often shows granulomas composed of epithelioid cells and an admixture of macrophages and lymphocytes. Type 2 leprosy reactions usually manifest as painful erythematous papules, plaques, and nodules. Although several type 2 reaction patterns have been described in literature, diagnosis remains challenging.

Keywords: Leprosy; Leprosy, Borderline; Leprosy, Paucibacillary.

RESUMO

A hanseníase é uma doença granulomatosa, crônica e neurocutânea, com largo espectro de características clínicas, histopatológicas e imunológicas. Reações hansênicas podem acontecer em qualquer estágio da doença, mesmo em indivíduos não tratados, refletindo mudanças abruptas no equilíbrio imunológico do hospedeiro. Relata-se o caso de uma paciente do sexo feminino, previamente hígida, encaminhada ao serviço de dermatologia devido queixa de lesão única, assintomática, localizada na coxa esquerda há cerca de cinco anos. O diagnóstico de hanseníase borderline-tuberculoide (BT) foi feito. Nos 30 dias seguintes, a paciente apresentou sintomas sistêmicos e múltiplas bolhas hemorrágicas nos membros inferiores, levando à suspeita imediata de reação hansênica tipo 2 atípica. A forma BT é caracterizada por poucas placas infiltradas dispersas, associadas a espessamento nervoso assimétrico e irregular. A histopatologia normalmente evidencia granuloma composto por células epitelioides e uma mistura de macrófagos e linfócitos. As reações hansênicas tipo 2 geralmente se manifestam como pápulas, placas e nódulos dolorosos. Apesar dos diversos padrões já descritos na literatura, o diagnóstico dessas reações permanece desafiador.

Palavras-chave: Hanseníase; Hanseníase Dimorfa; Hanseníase Paucibacilar.

INTRODUCTION

Leprosy is a chronic granulomatous neurocutaneous disease caused by *Mycobacterium leprae*, with a wide spectrum of clinical, histopathological, and immunological characteristics[1,2,3,4]. Acute or subacute inflammatory episodes, known as leprosy reactions, can occur at any stage of the disease, even in untreated individuals[4,5,6]. These reactions are not uncommon, affecting up to one-third of patients[4,5]. They result from abrupt immunological shifts and are classified into type 1 (reversal), type 2 (erythema nodosum leprosum, T2R/ENL), and type 3 (Lucio phenomenon) reactions[5,6].

Type 2 leprosy reactions typically feature tender erythematous papules, plaques, and nodules, followed by systemic symptoms[6,7]. Atypical morphological patterns, including bullous lesions, have been reported[6,7,8,9]. These variants can reassemble other dermatological conditions, making diagnosis a daunting task.

Correspondence / Correspondência:
Felipe Marinho Rocha de Macêdo
Santa Casa de Misericórdia do Recife, Centro de Estudos Dermatológicos do Recife
Av. Cruz Cabugá, 1563. Bairro: Santo Amaro. CEP: 50040-000 – Recife, Pernambuco, Brazil
E-mail: fmarinhomacdo@gmail.com

Herein, we report a case of a clinically atypical, long-standing single lesion in an immunocompetent patient, histopathologically classified as borderline tuberculoid (BT) leprosy. Conversely, the patient's reactional state shared no expected immunological patterns of this form of leprosy.

CASE REPORT

A 50-year-old otherwise healthy female from Recife, Pernambuco State, Brazil, was referred by a general practitioner (GP) to a dermatology outpatient clinic due to a single, asymptomatic, erythematous lesion on her left thigh, persisting for five years. The GP's primary diagnostic hypothesis was cutaneous sarcoidosis, as the patient denied contact with leprosy cases.

On examination, a well-defined, erythematous-infiltrated, tumid plaque measuring 1.0 cm in diameter was observed on the medial thigh (Figure 1). Thermal and tactile sensitivity were significantly reduced, but no systemic symptoms were present. A biopsy revealed aggregates of vacuolated histiocytes surrounded by lymphocytes along neurovascular bundles, extending through the papillary and reticular dermis. Slit-skin smear examination showed a bacterial index (BI) of +2, with few acid-fast bacilli (AFB) detected on Fite-Faraco staining (Figure 2). Routine biochemical panel did not detect leukocytosis or raised erythrocyte sedimentation rate (ESR), and antinuclear antibodies (ANA) were also negative. The patient was diagnosed with BT leprosy.

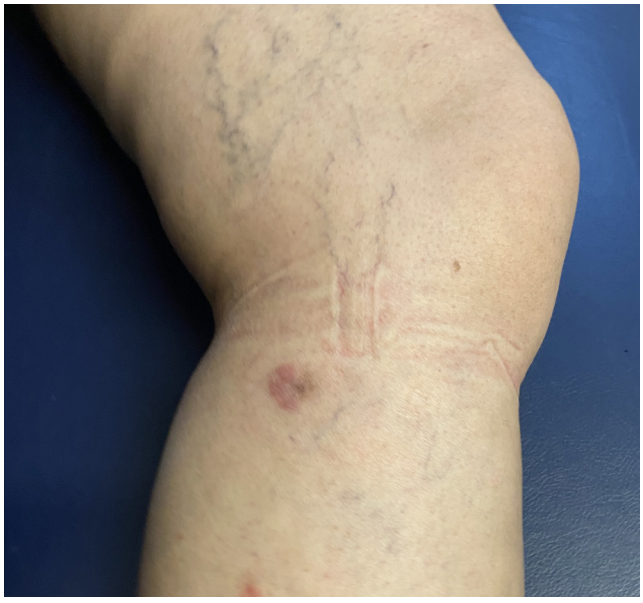

Photo: Marília de Moraes Delgado.

Figure 1 – Single, tumid, erythematous-infiltrated, well-defined plaque on the medial thigh region

Thirty days after the initial consultation, the patient complained of a sudden onset of fever, myalgia, joint stiffness, malaise, and the skin lesion had become tender and painful. Simultaneously, multiple hemorrhagic bullae appeared on her lower limbs (Figure 3). A biopsy of these new lesions revealed a superficial perivascular neutrophilic infiltrate with fibrinoid necrosis and leukocytoclasia (Figure 4), leading to a diagnosis of an atypical type 2 leprosy reaction.

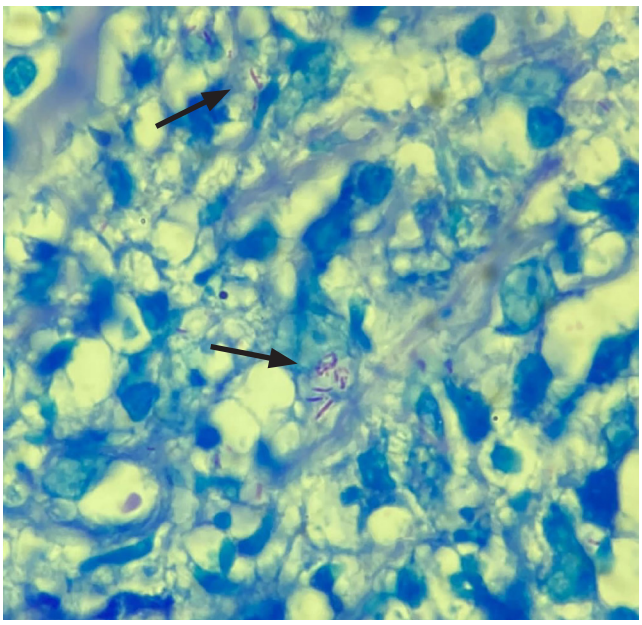

Photo: Marília de Moraes Delgado.

Figure 2 – Fite stain showing solid-staining and fragmented AFB (black arrow) (AFB, fite stain, × 1,000)

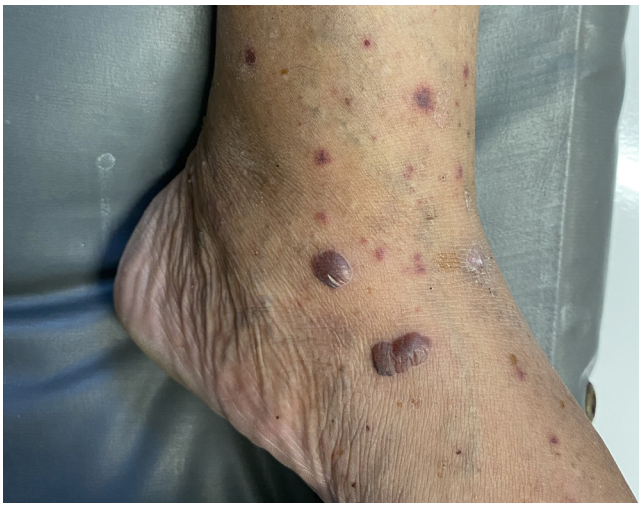

Photo: Marília de Moraes Delgado.

Figure 3 – Multiple erythematous-violaceous papules and hemorrhagic bullae on the distal extremity of left leg

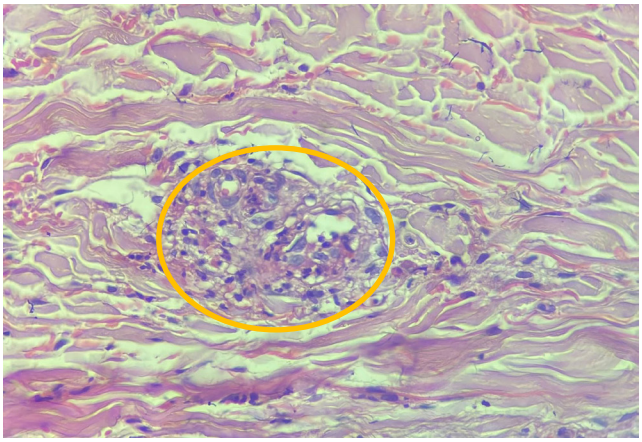

Photo: Marília de Moraes Delgado.

Figure 4 – Superficial perivascular neutrophilic infiltrate with fibrinoid necrosis and leukocytoclasia (yellow circle) (H&E, x 400)

Treatment was initiated with prednisolone 60 mg daily, with a stepped-down dose of 5 mg per week. Significant and sustained improvement in skin lesions was observed within three weeks. The patient was discharged after safe corticosteroid discontinuation and advised to consult a GP for initiation of anti-leprosy therapy.

DISCUSSION

Leprosy, a neglected tropical disease, remains associated with poverty, with approximately 200,000 new cases detected annually over the last decade[1,2,3,4]. Southeast Asia and the Americas reported the highest prevalence rates, with Brazil, India, and Indonesia accounting for nearly 80% of cases worldwide[1,2,3,4]. In Brazil, the incidence rate is 15.32 per 100,000 inhabitants, but the North and Northeast regions reported rates nearly twice the national average, with hyperendemic areas primarily in Pernambuco[3]. Socioeconomic disparities, unequal urbanization, and household crowding contribute to increased leprosy risk and poor disease control in the Brazilian scenario[1,2,3,4].

According to the Ridley and Jopling classification, most cases fall within the borderline leprosy spectrum, which is subdivided into borderline tuberculoid (BT), borderline borderline (BB), and borderline lepromatous (BL) forms, depending on the patient's immune response. The hallmark of borderline leprosy is immune instability, which may cause untreated patients to shift toward the lepromatous pole over time as bacterial levels rise[5,9]. BT leprosy is typically characterized by a few scattered infiltrated plaques with asymmetric nerve thickening. Histopathological examination reveals epithelioid granulomas with a mix of macrophages and lymphocytes, while AFB staining often shows fragmented or sparse bacilli[5,9].

T2R, an immunological complication primarily affecting BL groups, accounts for over a quarter of leprosy reactions in Brazilian referral centers[10,11,12]. Typical T2R presents as painful erythematous papules, plaques, or nodules, frequently among BL patients[5,10,11,12]. Nonetheless, atypical forms, such as pustular, hemorrhagic, and bullous variants, can turn into necrotic ulcers. Although several T2R patterns have been described, it remains a difficult diagnosis as there is a lack of reviews addressing atypical variants. Bullous eruptions are rarely observed in leprosy and might be associated with severe forms of ENL[6]. Moreover, vesiculobullous lesions are ENL's most common atypical clinical presentation form, with blisters varying from tense and flaccid to hemorrhagic[7,8].

Histologically, T2R is marked by intense dermal and perivascular neutrophilic infiltration, especially during acute stages[7,8,10,11]. A dermal infiltrate of foamy histiocytes and epithelioid cells are also evident. Vascular changes are common, and it seems leukocytoclastic vasculitis is the major pathological event of early ENL cases[10,11]. There is limited data on the early histological features of ENL and its atypical variants[8].

Biopsies from this patient showed no epithelioid histiocytes, indicating a lack of Th1 immune response and suggesting an abrupt immunological shift toward the lepromatous pole. The initial BT diagnosis appears unusual, given the quick progression to an unexpected type 2 reactional state without any clinical change in a previously chronic and stable lesion.

CONCLUSION

These findings reinforce the spectrum-like nature of leprosy rather than seemingly straightforward classifications. Dermatologists and public health professionals should consider the role of socioeconomic determinants in disease prevalence and recognize the importance of early histological features and clinicopathological correlations.

INSTITUTIONAL REVIEW BOARD STATEMENT

This case report was approved by the Research Ethics Committee of the Hospital do Câncer de Pernambuco (HCP) / Santa Casa de Misericórdia do Recife, on April 29, 2024 (CAAE No. 77617223.5.0000.5205), in compliance with the Declaration of Helsinki, the Nuremberg Code, and the National Health Council Resolution No. 466/12.

INFORMED CONSENT STATEMENT

Written informed consent was obtained from the study participant to publish this case report.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTION

All authors played an equal role in discussing and contributing to the final manuscript. They were involved in curating data, managing the clinical aspects of the case, critically reviewing the relevant literature and data, writing the manuscript, and approving the final version submitted to the journal.

REFERENCES

1 Grijsen ML, Nguyen TH, Pinheiro RO, Singh P, Lambert SM, Walker SL, et al. Leprosy. Nat Rev Dis Primers. 2024 Nov;10(1):90.

2 Nery JS, Ramond A, Pescarini JM, Alves A, Strina A, Ichihara MY, et al. Socioeconomic determinants of leprosy new case detection in the 100 million Brazilian Cohort: a population-based linkage study. Lancet Glob Health. 2019 Sep;7(9):e1226-36.

3 Barbosa CC, Bonfim CV, Brito CMG, Souza WV, Melo MFO, Medeiros ZM. Spatial analysis of epidemiological and quality indicators of health services for leprosy in hyperendemic areas in Northeastern Brazil. Rev Inst Med Trop S Paulo. 2020 Nov;62:e93.

4 Fogagnolo L, Souza EM, Cintra ML, Velho PENF. Vasculonecrotic reactions in leprosy. Braz J Infect Dis. 2007 Jun;11(3):378-82.

5 Chen KH, Lin CY, Su SB, Chen KT. Leprosy: a review of epidemiology, clinical diagnosis, and management. J Trop Med. 2022 Jul:2022(1):8652062.

6 Vashisht D, Das AL. Bullous erythema nodosum leprosum. Med J Armed Forces India. 2013 Jan;69(1):71-3.

7 Alakad R, Nofal A, Assaf M. Atypical presentations of erythema nodosum leprosum: diagnostic and therapeutic aspects. J Dtsch Dermatol Ges. 2021 Aug;19(8):1133-43.

8 Chatterjee D, Saikia UN, Narang T, Dogra S. The diagnostic dilemma of erythema nodosum leprosum - a clinicohistological study. Lepr Rev. 2017 Jun;88(2):217-26.

9 Talhari C, Talhari S, Penna GO. Clinical aspects of leprosy. Clin Dermatol. 2015 Jan-Feb;33(1):26-37.

10 Serrano-Coll H, Wan EL, Restrepo-Rivera L, Cardona-Castro N. Leprosy reactions: unraveling immunological mechanisms underlying tissue damage in leprosy patients. Pathog Dis. 2024 Feb;82:ftae013.

11 Antunes DE, Santos DF, Lima MIS, Caixeta LP, Correa MBC, Moraes ECS, et al. Clinical, epidemiological, and laboratory prognostic factors in patients with leprosy reactions: a 10-year retrospective cohort study. Front Med (Lausanne). 2022 Jul;9:841030.

12 Ambrosano L, Santos MAS, Machado ECFA, Pegas ES. Epidemiological profile of leprosy reactions in a referral center in Campinas (SP), Brazil, 2010-2015. An Bras Dermatol. 2018 May-Jun;93(3):460-1.

Received / Recebido em: 7/5/2024
Accepted / Aceito em: 3/3/2025

How to cite this article / Como citar este artigo:

Macêdo FMR, Farias CB, Ardito MCL, Ferraz LGA, Pereira TS, Jardim MML. Reactional state in an atypical borderline tuberculoid leprosy: a spectrum of type 2 leprosy reaction? Rev Pan Amaz Saude. 2025;16:e202501604. Doi: https://doi.org/10.5123/S2176-6223202501604