Clinical Case Reports

WILEY

Clinical Case Reports Open Access

CASE REPORT OPEN ACCESS

Borderline Lepromatous Leprosy With Type 1 Reaction: A Challenging Diagnostic Case

Polanco Llanes Alondra Saray[1] | Zajdman Faitelson Dalit[2] | Figueroa Basurto Carla Itzel[1] | Rodríguez Escamilla Irene Montserrat[1] | Vega Memije María Elisa[2] | Arenas Guzmán Roberto[3]

[1]National Autonomous University of Mexico, Mexico City, Mexico | [2]Dermatology Department, "Manuel Gea Gonzalez" General Hospital, Mexico City, Mexico | [3]Micology Department, "Manuel Gea Gonzalez" General Hospital, Mexico City, Mexico

Correspondence: Polanco Llanes Alondra Saray (alondra93_saray@hotmail.com)

Received: 29 April 2024 | **Revised:** 9 October 2024 | **Accepted:** 5 November 2024

Funding: This work was supported by Universidad Nacional Autónoma de México (UNAM).

Keywords: borderline lepromatous leprosy | case | dermatology | type 1

ABSTRACT

Borderline lepromatous leprosy with Type 1 reaction poses significant diagnostic challenges due to overlapping clinical features. Early recognition and differentiation are crucial, especially in endemic regions like Mexico, to ensure prompt, appropriate management and prevent complications. Accurate diagnosis requires a multidisciplinary approach integrating clinical, histopathological, and microbiological data.

Taxonomy Classification: Dermatology, Chronic Diseases, Acute Medicine, Global Health

1 | Introduction

Leprosy, or Hansen's disease, is a chronic granulomatous infection caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*, primarily affecting the skin and peripheral nerves [1].

Borderline lepromatous leprosy (BL) presents with a wide variety of cutaneous lesions, with the most characteristic being nodules and irregular erythematous infiltrated plaques with poorly defined outer edges. Due to the diversity of clinical manifestations, classifying borderline patients is difficult as cutaneous manifestations may not fit into described clinical patterns, or histopathological examination may not be compatible with clinical classification [2].

We present a case of borderline lepromatous leprosy with a subsequent Type 1 reaction, whose classification posed a challenge and required collaboration among the fields of dermatology, leprology, and dermatopathology. Our goal is to demonstrate that this pathology remains prevalent in our environment and should be considered a possible diagnosis in suspicious clinical cases.

1.1 | Case History/Examination

A 57-year-old male, native and resident of Pungarabato, Tierra Caliente, Altamirano City, Guerrero, Mexico. Previously healthy, presented to the Dermatology service with a generalized dermatosis affecting all body segments, characterized by erythematous, isolated, and confluent plaques of 2–20 cm in diameter, infiltrated, covered with fine scales, and with regular edges (Figure 1); of 4 years of evolution.

One month before coming to our service, he experienced induration and decreased sensitivity in the skin lesions, as well as

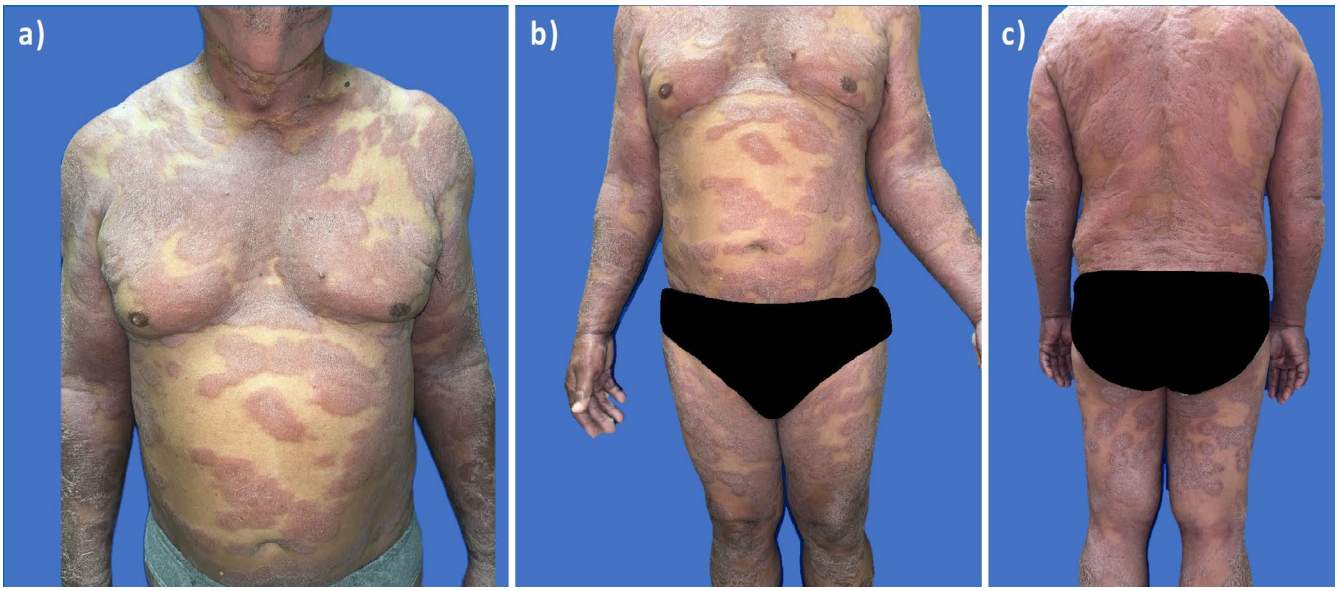

FIGURE 1 | (a, b, and c) Dermatosis affecting the chest, abdomen, back, and the entire circumference of the 4 limbs. It is characterized by multiple plaques with infiltrative appearance, erythematous-violaceous, with irregular but precise borders and a fine whitish scale on the surface. Some of these plaques converge.

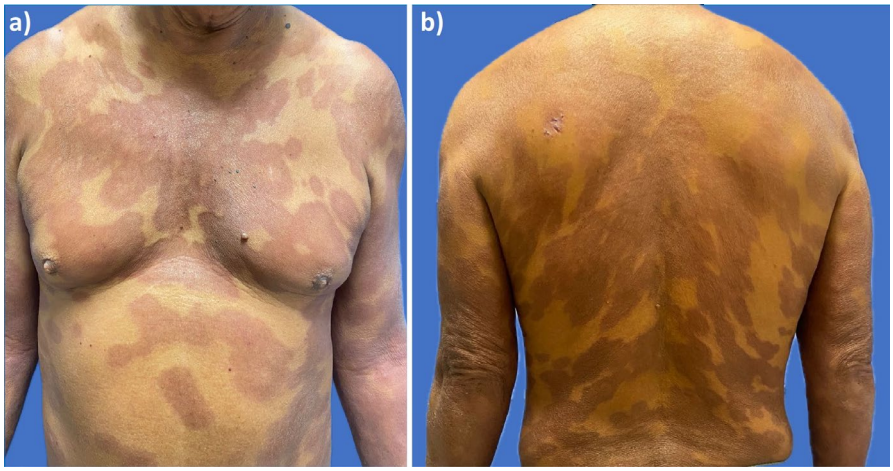

FIGURE 2 | (a and b) Dermatosis after 2 weeks of treatment with WHO regimen and 40 mg of prednisone. It shows involvement of the chest and back characterized by multiple brown macules with irregular borders, some merging, indicative of hyperpigmentation post inflammatory.

facial edema and edema of all four limbs, along with asthenia and general malaise. The examination of the lesions by touch and pinprick was nonspecific.

2 | Methods (Differential Diagnosis, Investigations, and Treatment)

Slit skin smear involving Ziehl–Neelsen staining of smears from the earlob lymphshowed the presence of multiple acid-alcohol-resistant bacilli with a BI (bacteriological index) of2+ and IM (morphological index) of 75%–100%. granulomas of histiocytes with foamy cytoplasm (Virchow cells), as well as multinucleated giant cells and lymphocytes. Fite-Faraco staining showed abundant bacilli (Figure 2). Based on clinical, bacilloscopy, and histopathology findings, the diagnosis of Borderline Lepromatous Leprosy was established.

Treatment began with the World Health Organization's multidrug therapy regimen (dapsone 100 mg, rifampicin, and clofazimine 50 mg), in addition to general skin care measures.

3 | Conclusion and Results (Outcome and Follow-Up)

One week after starting the multidrug therapy regimen, the patient experienced general discomfort, asthenia, and fever. Suspecting a Type 1 reaction, prednisone 50 mg/day was initiated. The patient showed an appropriate response to the treatment, achieving clinical improvement of symptoms and lesions. A gradual tapering of the steroid dose began. Currently, the patient is on a dose of 10 mg of prednisone, a reduction of 5 mg every 2 weeks will be performed, in 2 weeks the steroid will be suspended, and the patient will continue

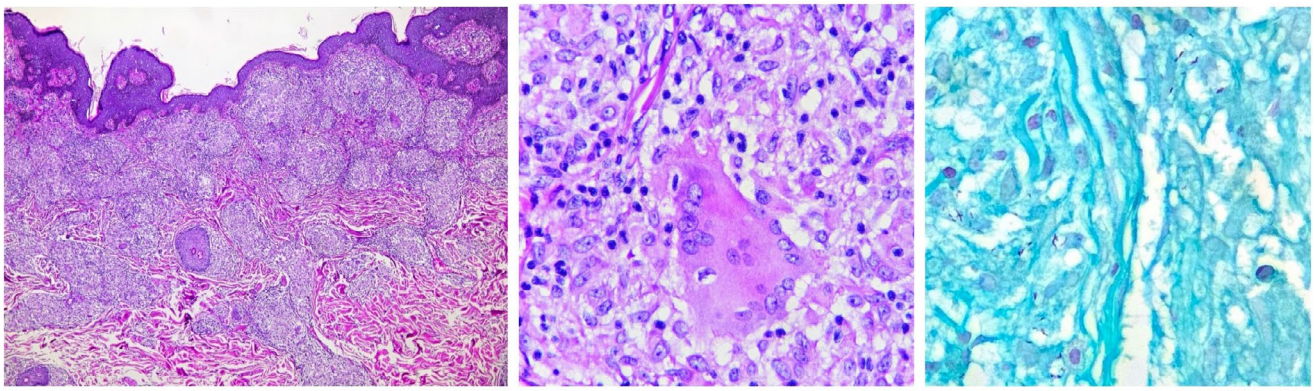

FIGURE 3 | (a) 4X HE, Histological section of skin showing a multinodular inflammatory infiltrate of variable sizes, predominantly around adnexal structures and vessels (b) 40X HE, The infiltrate is composed of histiocytes with foamy cytoplasm (Virchow cells), as well as some multinucleated giant cells and lymphocytes. (c) 40X Fite-Faraco stain, highlighting numerous bacilli.

with the WHO regimen (dapsone 100 mg, rifampicin 600 mg once a month, and clofazimine 50 mg), since it was a paucibacillary presentation, treatment will be continued for 1 year along with general skin care measures. The patient is experiencing a favorable clinical evolution, which has persisted without new symptoms or skin lesions. Only residual macules are present, erythematous with irregular but precise borders, without signs of infiltration, consistent with sequelae of previous lesions (Figure 3).

4 | Discussion

Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*, a bacillus that cannot be cultured in any medium. It grows in the paws of mice and in the nine-banded armadillo, with slow growth facilitated by low temperatures [3]. Due to the slow growth of *Mycobacterium spp*. and the prolonged incubation period, individuals may harbor subclinical leprosy for years, making it challenging to estimate its true incidence [4].

According to information from the Epidemiological Bulletin of Mexico's Epidemiological Surveillance System, there is an accumulated total of 125 leprosy cases in the year 2022, and during this year 2023, a total of 107 cases have been reported, with 64 belonging to males and 43 to females. The state with the highest prevalence is Sinaloa with 15 reported cases, followed by Nuevo León and Michoacán with 12 cases each [5].

Regarding the classification of the disease, it is based on clinical, bacilloscopic, immunological and histopathological parameters. It encompasses two polar types: lepromatous and tuberculoid and two group of cases: one at the onset of leprosy (indeterminate cases) and cases of changing immunology (borderline or dimorphic). The polar types are stable, while the case groups are unstable. The dimorphic group, based on its behavior in the immunological spectrum, can be Borderline Tuberculoid (BT) if it is close to the tuberculoid pole, Borderline Lepromatous (BL) when it is close to the lepromatous pole, and Borderline Borderline if it is located in the center of this spectrum (BB) [6, 7].

Within the clinical spectrum of Hansen's disease, borderline leprosy is a highly unstable form, as it can transition from one pole to another during the course of the disease. The clinical classification of borderline patients is often challenging, as cutaneous manifestations may not conform to known clinical patterns, and histopathological examination may not conclusively match the clinical classification [8].

BL is closer to the lepromatous pole and clinically presents with erythematous-violaceous infiltrated macular or plaque-like skin lesions, with a respected central region and poorly defined outer edges blending with the surrounding skin. These lesions are symmetrical and pauci-symptomatic, similar to the lesions observed in our clinical case. They increase in number as they approach the lepromatous pole, due to lack of treatment [8]. While there are generally alterations in sensitivity, it can be preserved in some cases, making touch and pinprick examination nonspecific, as observed in our clinical case [9].

Histopathological findings of BL are characterized by the presence of vacuolated histiocytes mixed with lymphocytes, sometimes predominating over macrophages, as seen in the histopathological result of our patient; in these cases, the diagnosis can be challenging [10].

Up to 30% of patients develop severe acute exacerbations and, at times, potentially life-threatening, either spontaneously, during, or after treatment; these outbreaks are known as leprosy reactions. They represent a manifestation of a sudden imbalance in the immune balance between the pathogen and the patient, requiring early diagnosis and treatment to prevent deterioration of nerve function and permanent disability [3]. Leprosy reactions are classified as Type I or reversal reaction, occurring in dimorphic cases, and Type II or lepromatous reaction, observed in lepromatous cases, including three dermatological syndromes: erythema nodosum, erythema multiforme, and Lucio's phenomenon. In Type II reaction, the patient presents an acute febrile state, occurring in 60% of lepromatous leprosy patients; it can occur once or have repetitive episodes. In addition to neurological manifestations, the patient experiences general symptoms such as asthenia, adynamia, anorexia, fever, headache, arth

ralgia, and weight loss; the treatment of choice for Type II reaction is thalidomide [11].

Regarding Type I leprosy reaction, such as the one presented by our patient, it is a hypersensitivity reaction Type IV hypersensitivity response, occurring in borderline forms due to an increase in cellular immunity. It occurs in up to 30% of borderline leprosy patients, generally within 12 months after the start of treatment. Possible triggers include pregnancy, comorbidities, and leprosy treatment medications [11]. In a case reported by Asz et al. described a patient with BL who developed a Type 1 reaction immediately after initiating multiple drug therapy, like our patient [12].

Although its pathophysiology is not clearly understood, Type I reaction lesions demonstrate an influx of CD4 T cells and a strong Th1 helper T cell response with high levels of interferon-gamma, interleukin (IL)-2-induced nitric oxide synthase, TNF-alpha, and interferon-gamma-induced protein 10 (IP-10). Increased expression of TNF-alpha, transforming growth factor-beta, and CXCL10 has also been observed in skin biopsy samples. Innate immunity also plays a significant role, as Schwann cells express toll-like receptor (TLR)2, and their activation by *M. leprae* antigens results in Schwann cell death, which may explain nerve damage in these reactions [13–15]. Clinically, Type I reaction causes sudden inflammation of lesions, along with general discomfort, fever, asthenia, and adinamia [13].

The neuronal damage experienced by patients with leprosy is due to the reversal reaction, which can lead to permanent disability if not treated promptly [15]. The patient may present neuritis manifested with pain, sensitivity, and paresthesia, while impaired nerve function is observed with reduced motor or sensory function. The ulnar, median, common peroneal, facial, and posterior tibial nerves are most affected, leading to foot drop, wrist drop, and facial paralysis. Patients may progress to loss of protective pain sensation, increasing the risk of injury [11]. Although the histopathologic study is not essential for the diagnosis of reverse reaction, key histological features can aid in diagnosis. The main findings include edema in the superficial dermis, granulomas with Virchow cells, foreign body giant cells, and a significant lymphocytic infiltrate; these findings are similar to those presented [11].

Due to the impact of the reversal reaction on neuronal function, it's treatment is crucial. The objectives include relieving pain, controlling inflammation, and preventing deterioration of nerve function. The treatment of choice is corticosteroids; prednisone at a dose of 1 mg/kg/day provides rapid symptomatic relief and helps reverse nerve function deterioration. The duration is a matter of debate, but the regimen should be individually tailored based on nerve sensitivity and motor or sensory deficits. Symptoms should be reassessed every 2 weeks, and a gradual reduction of the steroid (5–10 mg every 14 days) is initiated, dose reduction is not standardized, depending on the regression of symptoms. Drug de-escalation should start at 9 months, the average time for lesion resolution. Treatment may last up to 6 months or even years for patients with neuritis [16].

However, because prolonged use of corticosteroids carries the risk of adverse effects, other therapies have been explored. Azathioprine (3 mg/kg/day) combined with low doses of prednisolone, cyclosporine (5 mg/kg/day), methotrexate, and tacrolimus have been used, but more clinical studies are needed to improve treatment [17, 18].

In conclusion, leprosy remains a stigmatized disease, so recognizing it as a present disease in our environment is crucial for timely diagnosis and treatment initiation. Identifying the immunological reactions of this pathology is fundamental because they dramatically worsen its clinical course, can occur before the start of therapy, and are not necessarily a consequence of it. Physicians should educate newly diagnosed leprosy patients about the signs and symptoms of these reactions, so they can seek immediate medical attention. Early recognition of these reactions ensures a rapid start of treatment to reduce the likelihood of associated complications and disability, aiming to minimize the sequelae that this pathology can leave behind; thereby improving the quality of life and social development of patients.

Author Contributions

Polanco Llanes Alondra Saray: conceptualization, formal analysis, investigation, methodology, supervision, validation, visualization, writing – original draft, writing – review and editing. **Zajdman Faitelson Dalit:** conceptualization, investigation, supervision, validation, visualization, writing – original draft, writing – review and editing. **Figueroa Basurto Carla Itzel:** investigation, methodology, writing – original draft, writing – review and editing. **Rodríguez Escamilla Irene Montserrat:** conceptualization, formal analysis, investigation, resources, writing – review and editing. **Vega Memije María Elisa:** conceptualization, investigation, project administration, supervision, validation, writing – original draft, writing – review and editing. **Arenas Guzmán Roberto:** conceptualization, investigation, methodology, software, supervision, validation, writing – original draft.

Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

References

1. M. R. Mungroo, N. A. Khan, and R. Siddiqui, "Mycobacterium leprae: Pathogenesis, Diagnosis, and Treatment Options," *Microbial Pathogenesis* 149 (2020): 104475, https://doi.org/10.1016/j.micpath.2020.104475.

2. M. Palombo, R. Achenbach, G. F. Sánchez, and S. Dupuy, "Lepra Dimorfa Lepromatosa (Borderline Lepromatosa, BL)," *Revista Argentina de Dermatologia* 93, no. 1 (2012), https://www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S1851-300X2012000100005&lng=es&tlng=es.

3. M. Fischer, "Leprosy-An Overview of Clinical Features, Diagnosis, and Treatment," *JDDG: Journal der Deutschen Dermatologischen Gesellschaft* 15, no. 8 (2017): 801–827, https://doi.org/10.1111/ddg.13301.

4. K. Eichelmann, S. E. González González, J. C. Salas-Alanis, and J. Ocampo-Candiani, "Lepra: Puesta Al Día. Definición, Patogénesis, Clasificación, Diagnóstico Y Tratamiento," *Actas Dermo-Sifiliográficas* 104, no. 7 (2013): 554–563, https://doi.org/10.1016/j.ad.2012.03.003.

5. Sistema Nacional de Vigilancia Epidemiologica, https://www.sinave.gob.mx.

6. M. Romero-Navarrete, R. Arenas, X. Y. Han, M. E. Vega-Memije, and A. D. Castillo-Solana, "Leprosy Caused by Mycobacterium lepromatosis," *American Journal of Clinical Pathology* 158, no. 6 (2022): 678–686, https://doi.org/10.1093/ajcp/aqac110.

7. E. Torres-Guerrero, F. Vargas- Martínez, C. E. Atoche-Diéguez, J. Arrazola, and G. R. Arenas, "Lepra. Clasificación Y Cuadro Clínico," *Dermatologia Revista Mexicana* 56, no. 1 (2012): 47–54.

8. C. Matsuo, C. Talhari, L. Nogueira, R. F. Rabelo, M. N. dos Santos, and S. Talhari, "Hanseníase Borderline Virchowiana," *Anais Brasileiros de Dermatologia* 85 (2010): 921–922, https://doi.org/10.1590/S0365-05962010000600026.

9. N. M. Elwan and Y. M. E. H. Neinaa, "Borderline Lepromatous Leprosy: Uncommon Clinical Presentation," *American Journal of Dermatopathology* 41, no. 3 (2019): 211–213, https://doi.org/10.1097/dad.0000000000001262.

10. C. Massone, W. A. Belachew, and A. Schettini, "Histopathology of the Lepromatous Skin Biopsy," *Clinics in Dermatology* 33, no. 1 (2015): 38–45, https://doi.org/10.1016/j.clindermatol.2014.10.003.

11. S. Kamath, S. A. Vaccaro, T. H. Rea, and M. T. Ochoa, "Recognizing and Managing the Immunologic Reactions in Leprosy," *Journal of the American Academy of Dermatology* 71, no. 4 (2014): 795–803, https://doi.org/10.1016/j.jaad.2014.03.034.

12. D. Asz-Sigall, L. López-García, Y. Neme-Yunes, R. Yuen-Palos, M. E. Vega-Memije, and R. Arenas, "Type I Reaction in a Borderline Leprosy Case Successfully Treated With Multidrug Therapy and Ofloxacin," *International Journal of Dermatology* 47, no. 10 (2008): 1084–1086, https://doi.org/10.1111/j.1365-4632.2008.03399.x.

13. D. N. J. Lockwood, L. Suneetha, K. D. Sagili, et al., "Cytokine and Protein Markers of Leprosy Reactions in Skin and Nerves: Baseline Results for the North Indian INFIR Cohort," *PLoS Neglected Tropical Diseases* 5, no. 12 (2011): e1327, https://doi.org/10.1371/journal.pntd.0001327.

14. A. L. Cogen, S. L. Walker, C. H. Roberts, et al., "Human Beta-Defensin 3 Is Up-Regulated in Cutaneous Leprosy Type 1 Reactions," *PLoS Neglected Tropical Diseases* 6, no. 11 (2012): e1869, https://doi.org/10.1371/journal.pntd.0001869.

15. E. A. Misch, M. Macdonald, C. Ranjit, et al., "Human TLR1 Deficiency Is Associated With Impaired Mycobacterial Signaling and Protection From Leprosy Reversal Reaction," *PLoS Neglected Tropical Diseases* 2, no. 5 (2008): e231, https://doi.org/10.1371/journal.pntd.0000231.

16. I. P. Kahawita, S. L. Walker, and D. N. J. Lockwood, "Leprosy Type 1 Reactions and Erythema Nodosum Leprosum," *Anais Brasileiros de Dermatologia* 83, no. 1 (2008): 75–82, https://doi.org/10.1590/s0365-05962008000100010.

17. D. P. Legendre, C. A. Muzny, and E. Swiatlo, "Hansen's Disease (Leprosy): Current and Future Pharmacotherapy and Treatment of Disease-Related Immunologic Reactions," *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 32, no. 1 (2012): 27–37, https://doi.org/10.1002/phar.1009.

18. M. E. Schram, "Off-Label Use of Azathioprine in Dermatology," *Archives of Dermatology* 147, no. 4 (2011): 474–488, https://doi.org/10.1001/archdermatol.2011.79.