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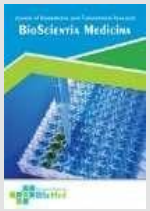

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A Rare Presentation of Type 2 Lepra Reaction: Necrotizing Erythema Nodosum Leprosum with Extensive Ulceration

Tutty Ariani[1*], Clarissa Maharani Putri[1]

[1]Department of Dermatology, Venereology and Esthetics, Faculty of Medicine, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia

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***Corresponding author:**
Tutty Ariani

E-mail address:
tuttyariani@med.unand.ac.id

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A B S T R A C T

Background: Leprosy, primarily caused by *Mycobacterium leprae*, is a chronic infectious disease that mainly affects the skin and peripheral nerves. Type 2 leprosy reaction (ENL) is an immune complex-mediated complication characterized by inflammation of the skin, nerves, and other organs. A less common manifestation of ENL is necrotizing ENL, which presents with extensive skin necrosis and ulceration. This case report describes a rare presentation of necrotizing ENL with extensive ulceration in a young woman with borderline lepromatous leprosy. **Case presentation:** A 20-year-old female presented with multiple, progressively enlarging, painless ulcers on her right leg and painful reddish nodules on her left arm and left leg. She had a history of borderline lepromatous leprosy. Dermatological examination revealed madarosis, infiltration, nodules, hyperpigmentation macules, ulcers, and blackish crusts. Sensory testing showed hypoesthesia in the abdomen and back, and anesthesia in both lower arms and legs. Histopathological examination confirmed the diagnosis of necrotizing ENL. **Conclusion:** Necrotizing ENL is a rare and severe complication of leprosy. This case highlights the importance of early diagnosis and appropriate management with multi-drug therapy and corticosteroids to prevent significant morbidity and disability.

1. Introduction

Leprosy, a chronic infectious disease primarily caused by *Mycobacterium leprae,* continues to pose a significant global health challenge. This insidious disease predominantly affects the skin and peripheral nerves, leading to a spectrum of clinical manifestations and potential long-term complications. Despite significant advancements in treatment and control efforts, leprosy remains endemic in many parts of the world, particularly in resource-limited settings. The global burden of leprosy underscores the need for continued research and clinical vigilance to effectively manage this disease and minimize its impact on individuals and communities. *Mycobacterium leprae*, the causative agent of leprosy, is an acid-fast bacillus with a predilection for cooler body tissues, such as the skin, peripheral nerves, upper respiratory tract, eyes, and testes. The bacterium's unique tropism for these tissues contributes to the characteristic clinical features of leprosy, including skin lesions, nerve damage, and involvement of other susceptible organs. The ability of *M. leprae* to invade and reside within Schwann cells, the myelin-producing cells of the peripheral nervous system, plays a crucial role in the pathogenesis of nerve damage, a hallmark of leprosy. The clinical manifestations of leprosy are diverse, ranging from paucibacillary forms with limited skin lesions and minimal bacterial load to multibacillary

forms characterized by extensive skin involvement and a high bacterial burden. This spectrum of clinical presentations reflects the complex interplay between the host's immune response and the pathogen's virulence factors. The Ridley-Jopling classification system, widely used to categorize leprosy, recognizes five major forms: tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), borderline borderline leprosy (BB), borderline lepromatous leprosy (BL), and lepromatous leprosy (LL). This classification system aids in guiding treatment decisions and predicting disease progression.[1-3]

Type 2 leprosy reaction (T2LR), also known as erythema nodosum leprosum (ENL), is an immune-mediated complication that occurs in individuals with lepromatous or borderline lepromatous leprosy. ENL is characterized by the sudden onset of painful, erythematous nodules on the skin, often accompanied by systemic symptoms such as fever, malaise, and joint pain. This inflammatory reaction can also involve other organs, including the nerves, eyes, and testes, potentially leading to significant morbidity and disability. Necrotizing ENL (NENL) is a rare and severe form of T2LR characterized by extensive skin necrosis and ulceration. This aggressive manifestation of ENL is thought to result from a complex interplay of immune complex deposition, vasculitis, and thrombosis, leading to tissue ischemia and necrosis. NENL presents a diagnostic and therapeutic challenge due to its rapid progression and potential for severe complications, including secondary bacterial infection, sepsis, and permanent scarring. The diagnosis of NENL relies on a combination of clinical and histopathological findings. Clinically, NENL typically presents with well-defined, necrotic ulcers surrounded by erythema and edema. These lesions may be painful or painless and can occur on any part of the body. Systemic symptoms, such as fever, malaise, and arthralgia, may also be present. Histopathological examination of skin biopsies from NENL lesions typically reveals a dense dermal infiltrate composed of lymphocytes, histiocytes, and neutrophils, along with evidence of vasculitis, fibrinoid necrosis of vessel walls, and thrombosis.[4-6]

The treatment of NENL requires a multi-pronged approach, including multi-drug therapy (MDT) to eradicate the underlying *M. leprae* infection and corticosteroids to suppress the inflammatory response driving the reaction. MDT, recommended by the World Health Organization (WHO), consists of a combination of antibiotics, typically rifampicin, dapsone, and clofazimine, administered over a period of 6 to 12 months depending on the type of leprosy. Corticosteroids, such as prednisone, are essential in managing NENL to reduce inflammation and prevent further tissue damage. High doses of corticosteroids are often required initially, followed by a gradual taper to minimize the risk of side effects. In some cases of NENL, additional immunosuppressive agents, such as thalidomide or azathioprine, may be necessary to control the inflammatory process. Thalidomide, an immunomodulatory drug with anti-inflammatory properties, has been shown to be effective in treating severe ENL, including NENL. However, its use is limited due to its potential teratogenic effects and other serious side effects. Azathioprine, a purine synthesis inhibitor, can also be used as an adjunctive immunosuppressant in NENL, but its use requires careful monitoring due to its potential for bone marrow suppression and other adverse effects. The prognosis of NENL is variable and depends on several factors, including the extent of skin involvement, the presence of systemic complications, and the individual's overall health status. Early diagnosis and prompt initiation of appropriate treatment are crucial to minimize morbidity and disability associated with NENL. Complications of NENL can include secondary bacterial infection, sepsis, and permanent scarring, which can lead to functional impairment and social stigma.[7-10] This case report describes a rare presentation of NENL with extensive ulceration in a young woman with borderline lepromatous leprosy.

2. Case Presentation

This report details the case of a 20-year-old unmarried Indonesian woman who presented with a

complex and concerning dermatological condition. She was a high school graduate, currently unemployed, and resided with her parents in Parak Gadang, Indonesia. The patient's primary reason for seeking medical attention was the development of multiple, progressively enlarging, painless ulcers on her right leg. These ulcers had emerged approximately two weeks prior to her presentation. Concurrently, she reported painful, reddish nodules on her left arm and left leg, also of recent onset (approximately two weeks). A detailed exploration of the patient's medical history revealed a series of dermatological events preceding her current condition. Approximately two months before the appearance of the leg ulcers, she had noticed reddish, painful nodules on both heels. These nodules eventually progressed to form ulcers. A month later, similar lesions appeared on both legs, accompanied by systemic symptoms including fever, fatigue, and joint pain. The painless ulcers on her right leg, which prompted her to seek medical attention, had developed two weeks prior. She had initially sought treatment at a local clinic, where she received antibiotics and topical medications. However, these interventions failed to yield any improvement. Further investigation revealed a longer history of dermatological concerns. Two years prior, the patient had noticed reddish patches accompanied by numbness. However, she did not seek medical attention at that time. An incident involving a hot oil burn, which she was unaware of until blisters formed, suggested a possible impairment of sensation. Recurrent episodes of painful, red patches on her arms and legs had been occurring for the past three years, with the lesions eventually spreading to her chest, abdomen, and back. Additionally, she reported experiencing eyebrow hair loss (madarosis) and swollen ears over the same three-year period. The patient denied any previous history of similar ulcers or other significant medical conditions. A pertinent family history of leprosy was disclosed. The patient's father had been diagnosed with leprosy in 2019. He received a one-year course of treatment and was subsequently declared cured. The patient lived with her parents in a house measuring approximately 10 x 11 square meters. The house was described as having adequate ventilation. Her father worked as a delivery driver, while her mother was unemployed. Upon examination, the patient was conscious, alert, and appeared moderately ill. Her vital signs were within normal limits: blood pressure 110/70 mmHg, pulse 88 bpm, respiratory rate 20 breaths/min, and temperature 36.6°C. Her height was 150 cm, and her weight was 45 kg, resulting in a normal BMI of 20. A comprehensive dermatological examination revealed a multitude of skin findings. Madarosis (loss of eyebrows) was noted, along with skin infiltration, nodules, hyperpigmentation macules, ulcers, and blackish crusts. These lesions were distributed across various areas of her body, including the ears, abdomen, back, left arm, and both legs. The ulcers varied in size, with the largest measuring 2 x 1.5 x 0.5 cm and the smallest measuring 1.5 x 1 x 0.3 cm. The ulcers were characterized by irregular edges, a non-indurated base with granulation tissue, and surrounding skin that was edematous and erythematous. Sensory testing revealed hypoesthesia (decreased sensation) in the abdomen and back, and anesthesia (complete loss of sensation) in both lower arms and legs. Enlargement of the great auricular nerve (N. Auricularis Magnus) was also observed. Slit skin smears were obtained from several sites. The right earlobe showed a Bacteriological Index (BI) of -3, the left earlobe -3, the back lesion +3, and the leg ulcer +2. The total BI was +9, with a calculated BI of +2.75 and a Morphological Index (MI) of 30%. Gram staining of the smears revealed the presence of a few Gram-positive rods. Complete blood count revealed a hemoglobin level of 12.1 g/dL (normal range: 12.0-14.0 g/dL), a leukocyte count of 9,270/mm³ (normal range: 5,000-10,000/mm³), and a platelet count of 341,000/mm³ (normal range: 150,000-450,000/mm³). Hematocrit was 36% (normal range: 37-43%). Coagulation studies showed a prothrombin time (PT) of 11.5 seconds (normal range: 9.98-11.85 seconds) and an activated partial thromboplastin time (APTT) of 34 seconds (normal range: 23.32-30.92

seconds). Liver function tests were within normal limits, with SGOT at 15 U/L (normal: <32) and SGPT at 6 U/L (normal: <31). Random blood glucose was 107 mg/dL (normal range: 50-200 mg/dL). Renal function was also normal, with urea at 8 mg/dL (normal range: 10.0-50.0 mg/dL) and creatinine at 0.7 mg/dL (normal range: 0.6-1.1 mg/dL). No imaging studies were performed in this case. A skin biopsy was taken from the ulcer on the right leg. Histopathological examination revealed a dense dermal infiltrate composed of lymphocytes, histiocytes, and neutrophils. There was evidence of vasculitis with fibrinoid necrosis and thrombosis, indicating an intense inflammatory process. A separate biopsy was taken from a nodule on the left leg. This biopsy showed a granulomatous reaction with epidermal hyperplasia. Granulomas containing epithelioid histiocytes, foamy macrophages, and lymphocytes were observed, along with dilated blood vessels in the dermis. A clear "grenz zone" was identified in the superficial dermis, a characteristic finding in some types of leprosy. Based on the comprehensive clinical, laboratory, and histopathological findings, the following diagnoses were made; Primary Diagnosis: Borderline lepromatous leprosy with necrotizing erythema nodosum leprosum (NENL). This diagnosis reflects the patient's underlying leprosy infection and the severe, necrotizing form of type 2 leprosy reaction she was experiencing; Secondary Diagnosis: Keloid. This diagnosis indicates the presence of a hypertrophic scar, likely related to the patient's previous skin lesions. This case represents a rare and challenging presentation of leprosy, highlighting the potential for severe complications such as NENL. The extensive ulceration and systemic symptoms underscore the importance of early diagnosis and aggressive management to prevent significant morbidity and disability (Table 1).

The management of this patient with necrotizing erythema nodosum leprosum (NENL) secondary to borderline lepromatous leprosy involved a multi-faceted approach encompassing patient education, general supportive measures, specific pharmacological interventions, and a comprehensive follow-up plan. Recognizing the critical role of patient understanding and compliance in successful leprosy management, a comprehensive educational session was conducted. The patient and her family were provided with detailed information about leprosy, encompassing its etiology, modes of transmission, and the potential for contracting the infection from her father, who had a history of leprosy. The importance of adhering to the prescribed multi-drug therapy (MDT) regimen for the full 12-month duration was emphasized. The rationale behind this extended treatment, even after apparent clinical improvement, was explained to ensure complete eradication of *Mycobacterium leprae* and prevent relapse. The need for regular follow-up appointments until officially declared cured was also stressed. Furthermore, the patient was educated about the use of high-dose corticosteroids in managing ENL. The rationale for this treatment, which aims to suppress the inflammatory response driving the reaction, was clearly conveyed. The importance of regular follow-up to monitor for potential side effects of corticosteroid therapy and adjust the dosage accordingly was also highlighted. Given the potential for leprosy transmission within households, the possibility of transmission to family members was discussed. The need for prophylactic treatment with Rifampicin for close contacts was explained to mitigate the risk of further spread. In addition to specific pharmacological interventions, general supportive measures were implemented to enhance the patient's overall well-being and facilitate recovery. These included; Rest: The patient was advised to prioritize rest to conserve energy and support the body's healing processes. Adequate rest is crucial during the acute phase of NENL, as the inflammatory response can be physically taxing; Hydration: Maintaining adequate hydration was emphasized, particularly in light of the potential for fever and fluid loss associated with NENL. Proper hydration supports optimal physiological function and aids in the body's natural detoxification processes; Nutrition: A balanced and nutritious diet was

encouraged to provide the necessary nutrients for tissue repair and immune system function. Nutritional support is essential in promoting recovery from both leprosy and its associated reactions; Wound Care: Proper wound care techniques were demonstrated to prevent secondary infection and promote healing of the ulcers. This included regular cleaning of the ulcers with antiseptic solutions and application of sterile dressings; Pain Management: Analgesics were prescribed to manage pain associated with NENL. Pain relief is crucial in improving the patient's quality of life and facilitating adherence to treatment. The specific pharmacological treatment for this patient comprised a combination of MDT and corticosteroids; Multi-Drug Therapy (MDT): The patient was initiated on the World Health Organization (WHO) recommended MDT regimen for multibacillary leprosy (MB). This regimen consists of a combination of three antibiotics: rifampicin, dapsone, and clofazimine. Rifampicin, a bactericidal drug, acts by inhibiting bacterial RNA synthesis. Dapsone, a bacteriostatic agent, interferes with bacterial folate synthesis. Clofazimine, with both bactericidal and anti-inflammatory properties, disrupts bacterial DNA function and modulates the immune response; Corticosteroids: Prednisone, a potent anti-inflammatory corticosteroid, was prescribed at a high initial dose of 40 mg/day for two weeks. This high-dose therapy aimed to rapidly suppress the inflammatory cascade driving the NENL reaction. Following the initial two weeks, the prednisone dose was gradually tapered to minimize the risk of long-term side effects associated with corticosteroid use; Adjunctive Medications: In addition to MDT and prednisone, several adjunctive medications were prescribed to address specific symptoms and potential complications; Paracetamol: This analgesic and antipyretic was prescribed at a dose of 500 mg three times a day to manage pain and fever associated with NENL; Lansoprazole: This proton pump inhibitor was prescribed at a dose of 30 mg once a day to prevent gastrointestinal side effects associated with corticosteroid use; Zinc: This essential mineral was prescribed at a dose of 20 mg once a day to support wound healing and immune function; Vitamin B Complex: This supplement was prescribed once a day to address potential vitamin deficiencies and support overall health. A comprehensive follow-up plan was established to monitor the patient's clinical progress, prevent leprosy reclassification, and manage any further reactions. This included; Monthly Clinical Evaluation: The patient was scheduled for monthly follow-up appointments to assess her clinical response to treatment, monitor for any signs of leprosy reclassification, and address any new or recurring symptoms. These appointments provided an opportunity to evaluate the efficacy of the treatment regimen and make any necessary adjustments; Skin Smear Monitoring: Periodic slit skin smears were planned to monitor the bacteriological index (BI) and assess the effectiveness of MDT in eradicating *Mycobacterium leprae*; Neurological Assessment: Regular neurological examinations were scheduled to monitor for any signs of nerve damage or progression of neuropathy. Early detection of nerve involvement is crucial in preventing permanent disability; Ophthalmological Evaluation: Given the potential for ocular involvement in leprosy, periodic ophthalmological examinations were recommended to detect and manage any eye complications; Patient Counseling: Ongoing patient counseling was provided to address any concerns, reinforce adherence to treatment, and provide psychological support throughout the recovery process. The patient's prognosis was assessed based on various factors, including her overall health status, the extent of skin involvement, and the presence of systemic complications. The following prognostic indicators were considered; Quo ad vitam: Bonam (good). This suggests a good prognosis for life, indicating that the patient's overall health and life expectancy were not significantly compromised by her condition; Quo ad sanam: Bonam (good). This indicates a good prognosis for cure, suggesting that with appropriate treatment and adherence, the patient had a high likelihood of achieving complete eradication of *Mycobacterium*

leprae and resolution of NENL; Quo ad cosmeticum: Dubia ad bonam (doubtful to good). This reflects some uncertainty about the cosmetic outcome, acknowledging the potential for residual scarring due to the extensive ulceration; Quo ad functionam: Bonam (good). This indicates a good prognosis for functional capacity, suggesting that the patient was likely to maintain good physical function and quality of life despite the challenges posed by her condition. Overall, the patient's prognosis was considered favorable, with a high likelihood of achieving a cure and maintaining good functional capacity. However, the potential for residual scarring and the need for long-term follow-up were acknowledged (Table 2).

Table 1. Anamnesis, clinical findings, dermatology findings, laboratory, imaging, and clinical diagnosis.

Category	Subcategory	Details
Anamnesis	**Demographics**	Age: 20 years old. Gender: Female. Occupation: High school graduate, unemployed. Marital Status: Single
	Presenting Complaint	Painless, enlarging ulcers on the right leg, painful reddish lumps on the left arm and left leg (2 weeks)
	History of Present Illness	Reddish, painful nodules on both heels (2 months prior), developed into ulcers. Similar lesions on both legs (1 month prior), accompanied by fever, fatigue, and joint pain. Painless ulcers on the right leg (2 weeks prior), treated with antibiotics and topical medications at a local clinic with no improvement. Reddish patches with numbness (2 years prior), no treatment sought. Injury with hot oil, unaware of the burn until blisters formed. Recurrent episodes of painful red patches on arms and legs (3 years), spreading to the chest, abdomen, and back. Eyebrow hair loss and swollen ears (3 years)
	Past Medical History	No history of similar ulcers
	Family History	Father diagnosed with leprosy, treated for 1 year and declared cured (2019)
	Social History	Lives with her parents in Parak Gadang, Indonesia. House size: approximately 10 x 11 m^2, with adequate ventilation. Father is a delivery driver, mother is unemployed
Clinical Findings	**General Examination**	Conscious, alert, appears moderately ill. Blood pressure: 110/70 mmHg. Pulse: 88 bpm. Respiratory rate: 20 breaths/min. Temperature: 36.6°C. Height: 150 cm. Weight: 45 kg. BMI: 20 (normal)
	Dermatological Examination	Madarosis, infiltration, nodules, hyperpigmentation macules, ulcers, blackish crusts on the ears, abdomen, back, left arm, and both legs. Largest ulcer size: 2 x 1.5 x 0.5 cm. Smallest ulcer size: 1.5 x 1 x 0.3 cm. Ulcer characteristics: irregular edges, non-induration, granulation tissue base, surrounding skin edematous and erythematous (Figure 1-4). Hypoesthesia in the abdomen and back, anesthesia in both lower arms and legs. Enlarged N. Auricularis Magnus auricular
Laboratory Findings	**Slit Skin Smears**	Right earlobe: +3. Left earlobe: +3. Back lesion: +3. Leg ulcer: +2. Total: +9. Bacteri Index: +2.75. Morphology Index: 30%
	Gram Stain	Few Gram-positive rods (Figure 5)
	Hematology	Hemoglobin: 12.1 g/dL (normal: 12.0-14.0 g/dL). Leukocytes: 9,270/mm^3 (normal: 5,000-10,000/mm^3). Thrombocytes: 341,000/mm^3 (normal: 150,000-450,000/mm^3). Hematocrit: 36% (normal: 37-43%)
	Clinical Chemistry	PT: 11.5 seconds (normal: 9.98-11.85 seconds). APTT: 34 seconds (normal: 23.32-30.92 seconds). SGOT: 15 U/L (normal: <32). SGPT: 6 U/L (normal: <31). Random blood glucose: 107 mg/dL (normal: 50-200 mg/dL). Urea: 8 mg/dL (normal: 10.0-50.0 mg/dL). Creatinine: 0.7 mg/dL (normal: 0.6-1.1 mg/dL)
Imaging	**Histopathology**	Skin biopsy from the right leg: dense dermal infiltrate with lymphocytes, histiocytes, and neutrophils. Vasculitis with fibrinoid necrosis and thrombosis. Biopsy from the left leg nodule: granulomatous reaction, epidermal hyperplasia, granulomas with epithelioid histiocytes, foamy macrophages, lymphocytes, and dilated blood vessels in the dermis. Greenzone in the superficial dermis (Figure 6).
Diagnosis		Primary Diagnosis: Borderline lepromatous leprosy with necrotizing erythema nodosum leprosum. Secondary Diagnosis: Keloid

Table 2. Treatment and follow-up.

Category	Subcategory	Details
Treatment	**General Measures**	Patient education about leprosy, its cause, transmission, and the possibility of contracting it from her father. Explained the need for adherence to MDT for 12 months and regular follow-up until declared cured. Explained the use of high-dose corticosteroids for ENL and the importance of regular follow-up. Discussed the possibility of transmission to family members and the need for prophylactic treatment with Rifampicin.
	Specific Treatment	Multi-drug therapy (MDT) MB regimen. Prednisone 40 mg/day for 2 weeks, followed by a taper. Paracetamol 500 mg three times a day. Lansoprazole 30 mg once a day. Zinc 20 mg once a day. Vitamin B complex once a day.
Follow-up	**Clinical Evaluation**	Monthly follow-up appointments to monitor clinical improvement, prevent leprosy reclassification and manage any further reactions.
	Prognosis	Quo ad vitam: Bonam (good). Quo ad sanam: Bonam (good). Quo ad cosmeticum: Dubia ad bonam (doubtful to good). Quo ad functionam: Bonam (good). This suggests a good prognosis for life, functional capacity, and potential for cure, with some uncertainty about the cosmetic outcome due to potential scarring.

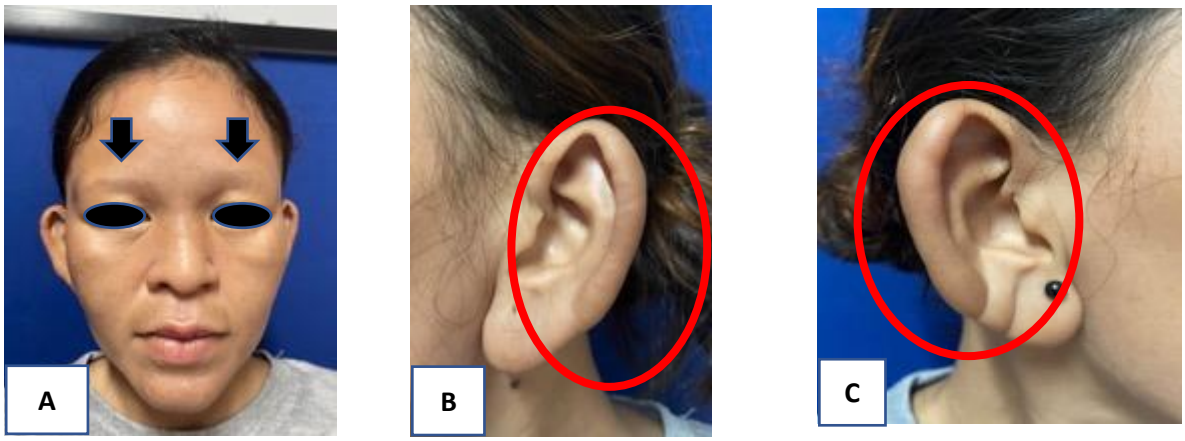

Figure 1. A. Madarosis (Black arrow). B and C. Infiltrate (Red circle).

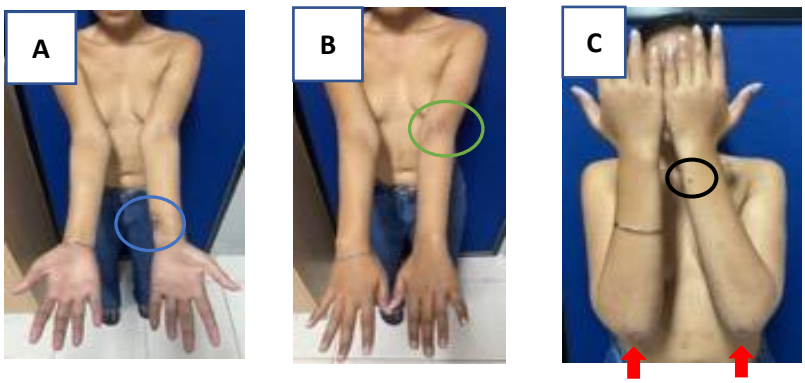

Figure 2. (A-C) Keloid (blue circle), hyperpigmentation macule (green circle), nodule (black circle), and blackish crust (red arrow).

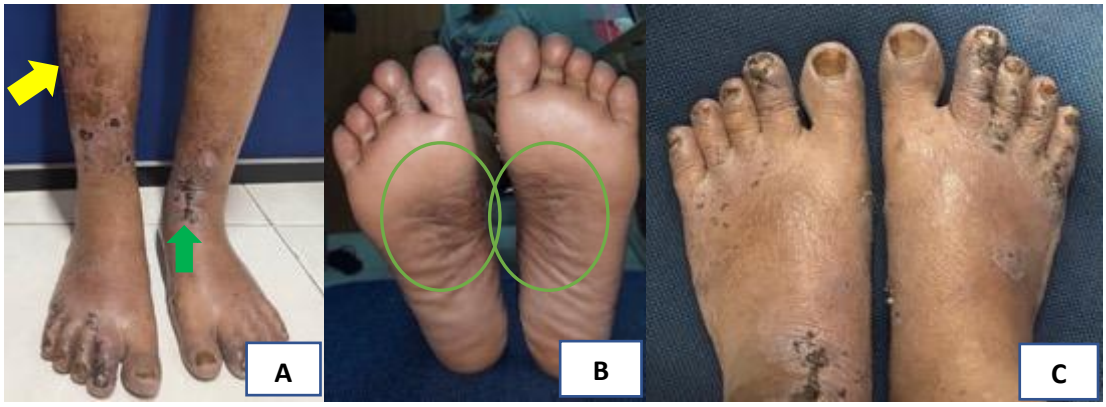

Figure 3. (A-C) Ulcer (yellow arrow), blackish crust (green arrow), and hyperpigmentation macule (green circle).

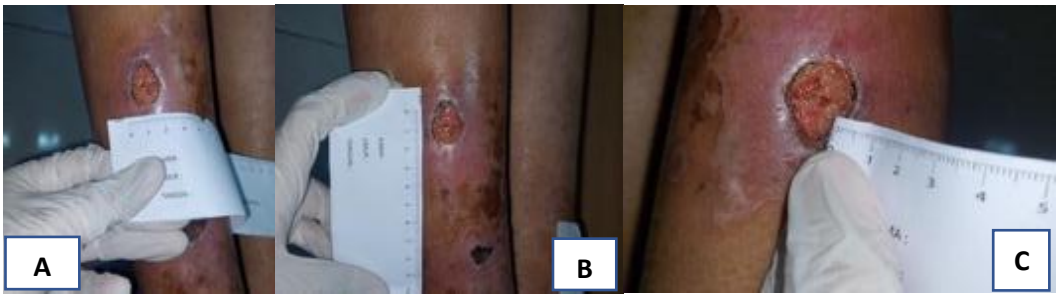

Figure 4. (A-C) Ulcer measuring 2 x 1.5 x 0.5 cm, with a flat edge, surrounded by edematous and erythematous skin, and a granulation tissue base.

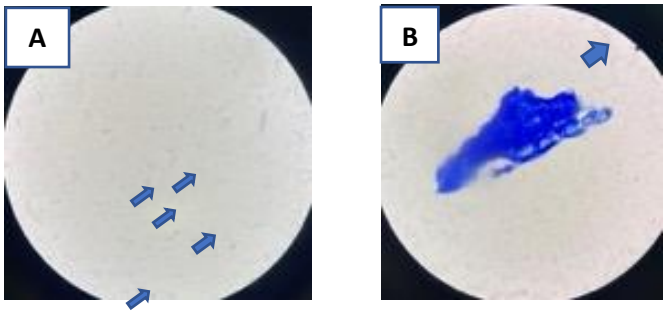

Figure 5. *Mycobacterium leprae* bacteria in the lesion (A) and in the ulcer on the leg (B) (blue arrows).

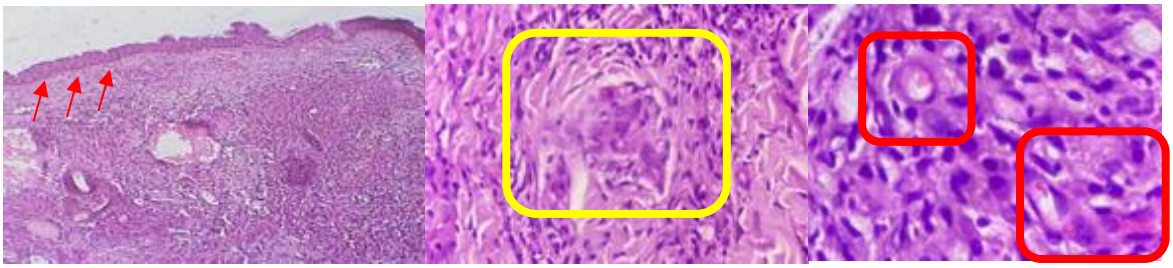

Figure 6. Histopathological examination reveals a green zone (red arrow), granuloma (yellow box), and hyperemic blood vessels (red box).

3. Discussion

Necrotizing erythema nodosum leprosum (NENL) represents a particularly severe and rare variant of type 2 leprosy reaction (ENL). It is characterized by extensive areas of skin necrosis and ulceration, posing significant challenges in both diagnosis and treatment due to its rapid progression and potential for severe complications. These complications can include secondary bacterial infections, sepsis, and permanent scarring, all of which can contribute to significant morbidity and disability. The development of NENL typically occurs in individuals with lepromatous or borderline lepromatous leprosy, underscoring the importance of early diagnosis and appropriate management to mitigate these risks. While the exact mechanisms underlying the pathogenesis of NENL remain incompletely understood, it is widely believed to involve a complex interplay of immune complex deposition, vasculitis, and thrombosis. These processes ultimately lead to tissue ischemia and the characteristic necrosis observed in NENL. The initial trigger for the immune response in ENL, including NENL, is thought to be the release of antigens from *Mycobacterium leprae*, the causative organism of leprosy. These antigens stimulate the host's immune system, leading to the formation of immune complexes. These complexes, consisting of antibodies bound to antigens, circulate in the bloodstream and have a propensity to deposit in the walls of blood vessels. The deposition of immune complexes in the vascular walls initiates a cascade of inflammatory events. One of the key players in this cascade is the complement system, a part of the innate immune system that enhances the ability of antibodies and phagocytic cells to clear microbes and damaged cells. Activation of the complement system leads to the generation of various complement proteins that contribute to the inflammatory response. These proteins can directly damage blood vessels, attract neutrophils to the site of inflammation, and stimulate the release of additional inflammatory mediators. The vasculitis associated with NENL is a hallmark of the disease process. It is characterized by inflammation of the blood vessel walls, leading to damage and compromising their integrity. This inflammation is often accompanied by fibrinoid necrosis, a form of tissue necrosis characterized by the deposition of fibrin-like material in the vessel walls. The damage to the blood vessels, combined with the ongoing inflammatory response, creates a conducive environment for thrombosis, or the formation of blood clots within the vessels. These thrombi further obstruct blood flow, exacerbating the tissue ischemia caused by the initial vasculitis. The combined effect of vasculitis and thrombosis significantly compromises the delivery of oxygen and nutrients to the tissues, ultimately leading to necrosis. Tissue ischemia, or the restriction of blood supply to tissues, is the critical event that leads to the extensive skin necrosis observed in NENL. The complex interplay of immune complex deposition, vasculitis, and thrombosis culminates in a severe compromise of blood flow to the affected areas. The lack of adequate blood supply deprives the tissues of essential oxygen and nutrients, leading to cell death and the formation of necrotic lesions. These lesions are often characterized by well-defined areas of ulceration surrounded by erythema and edema. The extensive skin necrosis can result in significant disfigurement and functional impairment, underscoring the need for prompt and effective treatment.[11-13]

Necrotizing erythema nodosum leprosum (NENL) presents a distinctive clinical picture, yet its diagnosis often requires careful differentiation from other conditions with similar skin manifestations. Understanding the characteristic features of NENL, along with the appropriate use of histopathological examination, is crucial for accurate diagnosis and timely management. NENL typically manifests with well-defined necrotic ulcers that are often surrounded by erythema and edema. The ulcers can vary in size and depth, and their appearance may evolve over time. The necrotic tissue within the ulcer may appear black, brown, or gray, and the surrounding skin may be red, swollen, and tender. The lesions can occur on any part of the body but are often found on the extremities,

particularly the lower legs. The presence of pain associated with the lesions can vary. Some individuals with NENL may experience significant pain, while others may report only mild discomfort or even no pain at all. The pain may be constant or intermittent and may be exacerbated by movement or pressure on the affected area. In addition to the skin lesions, individuals with NENL may also present with systemic symptoms. These symptoms reflect the underlying inflammatory process driving the reaction and can include fever, malaise, and arthralgia (joint pain). The severity of these systemic symptoms can vary, and their presence may provide important clues in distinguishing NENL from other skin conditions. The clinical diagnosis of NENL can be challenging due to its resemblance to other skin conditions that can also present with necrotic ulcers. Pyoderma gangrenosum is a rare inflammatory skin condition characterized by painful ulcers that often start as small pustules or nodules. The ulcers can enlarge rapidly and may have a violaceous border. Vasculitis refers to a group of disorders characterized by inflammation of the blood vessels. Vasculitis can affect various organs, including the skin, and may present with skin lesions such as palpable purpura, nodules, or ulcers. Certain bacterial, fungal, or viral infections can also cause skin ulcers, particularly in individuals with compromised immune systems. The presence of systemic symptoms, such as fever, malaise, and arthralgia, may help distinguish NENL from some of these conditions. However, definitive diagnosis often requires histopathological examination of skin biopsies. Histopathological examination of skin biopsies from NENL lesions is essential for confirming the diagnosis. The dermis, the layer of skin beneath the epidermis, is typically infiltrated by a dense collection of inflammatory cells. This infiltrate is composed predominantly of lymphocytes, histiocytes (macrophages), and neutrophils. Evidence of vasculitis, or inflammation of the blood vessels, is a key feature of NENL. This may manifest as fibrinoid necrosis of the vessel walls, where the walls of the blood vessels are damaged and replaced by a fibrin-like material. Thrombosis, or the formation of blood clots within the blood vessels, is another common finding in NENL. The thrombi can further obstruct blood flow, contributing to tissue ischemia and necrosis. The presence of these histopathological findings, in conjunction with the clinical presentation, helps differentiate NENL from other skin conditions with similar clinical manifestations.[14-16]

The effective management of necrotizing erythema nodosum leprosum (NENL) necessitates a multifaceted treatment approach, targeting both the underlying *Mycobacterium leprae* infection and the intense inflammatory response driving the reaction. This approach typically involves a combination of multi-drug therapy (MDT) to eradicate the infection and corticosteroids to suppress the inflammation, with the potential addition of other immunosuppressive agents in severe cases. MDT is the cornerstone of leprosy treatment and is crucial in managing NENL to eliminate the underlying *Mycobacterium leprae* infection. The World Health Organization (WHO) recommends MDT regimens consisting of a combination of antibiotics, typically rifampicin, dapsone, and clofazimine, administered over a period of 6 to 12 months, depending on the classification of leprosy. Rifampicin is a bactericidal drug that acts by inhibiting bacterial RNA synthesis, effectively killing *Mycobacterium leprae.* A bacteriostatic agent, dapsone interferes with bacterial folate synthesis, halting the growth and multiplication of *Mycobacterium leprae*. Clofazimine drug possesses both bactericidal and anti-inflammatory properties. It disrupts bacterial DNA function and also modulates the immune response, contributing to the control of both the infection and the inflammatory reaction. Adherence to the full course of MDT is critical, even after apparent clinical improvement, to ensure complete eradication of *Mycobacterium leprae* and prevent relapse. Corticosteroids, such as prednisone, are essential in managing NENL to reduce inflammation and prevent further tissue damage. They work by suppressing the immune response and inhibiting the production of inflammatory mediators.

Due to the severity of the inflammatory response in NENL, high doses of corticosteroids are often required initially, followed by a gradual tapering of the dose to minimize the risk of long-term side effects associated with corticosteroid use. The optimal dose and duration of corticosteroid therapy are not well-defined and need to be individualized based on the severity of the NENL reaction and the patient's response to treatment. Close monitoring for potential side effects of corticosteroid therapy, such as hyperglycemia, hypertension, and osteoporosis, is essential, and the dosage should be adjusted accordingly. In some cases of NENL, where the inflammatory response is particularly severe or resistant to corticosteroids alone, additional immunosuppressive agents may be necessary. These agents further suppress the immune system and help control the inflammatory process. Thalidomide is an immunomodulatory drug that has anti-inflammatory properties and has been shown to be effective in treating severe ENL, including NENL. However, its use is restricted due to its potential for serious side effects, including teratogenicity (causing birth defects) and peripheral neuropathy. Azathioprine is a purine synthesis inhibitor can also be used as an adjunctive immunosuppressant in NENL. It works by interfering with DNA synthesis, thereby inhibiting cell division and suppressing the immune response. However, its use requires careful monitoring due to its potential for bone marrow suppression and other adverse effects, such as hepatotoxicity and pancreatitis.[17,18]

Necrotizing erythema nodosum leprosum (NENL) is a rare and severe complication of leprosy that can significantly impact a patient's health and well-being. The prognosis of NENL is variable and depends on several factors, including the extent of skin involvement, the presence of systemic complications, and the individual's overall health status. Early diagnosis and prompt initiation of appropriate treatment are crucial to minimize morbidity and disability associated with NENL. Several complications can arise from NENL, each with its own set of challenges and potential long-term consequences. The extensive necrosis and ulceration characteristic of NENL disrupt the skin's protective barrier, providing an entry point for bacteria and increasing the risk of secondary infections. These infections can range from localized skin infections to more serious systemic infections, potentially leading to sepsis. Sepsis is a life-threatening condition that arises when the body's response to an infection becomes dysregulated, leading to widespread inflammation and organ damage. In NENL, sepsis can occur if a secondary bacterial infection is not adequately controlled, posing a significant threat to the patient's life. Even with appropriate treatment, NENL can result in permanent scarring due to the extensive skin necrosis. These scars can be disfiguring and may lead to functional impairment, particularly if they involve joints or other areas critical for movement. The physical complications of NENL, such as scarring and disfigurement, can have a significant psychological impact on patients. The visible nature of these complications can lead to social stigma and discrimination, affecting the patient's self-esteem, body image, and overall quality of life. The extent and severity of skin necrosis can significantly impact the prognosis. More extensive involvement is associated with a higher risk of complications and a longer recovery time. The presence of systemic complications, such as sepsis or organ damage, can worsen the prognosis and increase the risk of mortality. The individual's overall health status plays a crucial role in their ability to recover from NENL. Patients with underlying health conditions or weakened immune systems may have a poorer prognosis. Early diagnosis and prompt initiation of appropriate treatment are crucial for improving the prognosis of NENL. Delays in diagnosis and treatment can lead to more severe complications and a longer recovery time. Early diagnosis and prompt initiation of appropriate treatment are essential for minimizing the morbidity and disability associated with NENL. Early diagnosis allows for timely intervention with MDT and corticosteroids, which can help control the infection, reduce inflammation, and prevent further tissue

damage. Prompt treatment can also help prevent or minimize the risk of complications, such as secondary bacterial infection, sepsis, and permanent scarring. By addressing the underlying infection and inflammation early on, the extent of skin necrosis can be limited, reducing the likelihood of disfigurement and functional impairment.[19,20]

4. Conclusion

This case report presents a rare and severe manifestation of type 2 leprosy reaction (ENL), known as necrotizing ENL (NENL), in a young woman with borderline lepromatous leprosy. NENL is characterized by extensive skin necrosis and ulceration, resulting from a complex interplay of immune complex deposition, vasculitis, and thrombosis. This case highlights the importance of early diagnosis and appropriate management of NENL to prevent significant morbidity and disability. The patient's clinical presentation, with multiple progressively enlarging painless ulcers and painful reddish nodules, underscores the diverse and often subtle manifestations of NENL. The diagnosis was confirmed through histopathological examination, revealing a dense dermal infiltrate with lymphocytes, histiocytes, and neutrophils, along with vasculitis, fibrinoid necrosis, and thrombosis. The management of NENL requires a multi-pronged approach, including multi-drug therapy (MDT) to address the underlying *Mycobacterium leprae* infection and corticosteroids to suppress the inflammatory response. In severe cases, additional immunosuppressive agents may be necessary to control the inflammation. Early diagnosis and prompt treatment are critical to minimize the potential complications of NENL, such as secondary bacterial infection, sepsis, and permanent scarring. Regular follow-up is essential to monitor the patient's clinical progress, prevent leprosy reclassification, and manage any further reactions. This case emphasizes the need for healthcare professionals to be vigilant in recognizing and managing NENL, particularly in patients with lepromatous or borderline lepromatous leprosy. By increasing awareness of this rare and severe complication, we can strive to improve patient outcomes and reduce the burden of leprosy worldwide.

5. References

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