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Case Report

Systemic manifestation of necrotic erythema nodosum leprosum: A case report of a fatal leprosy

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Abstract

Necrotic erythema nodosum leprosum (ENL) is an uncommon manifestation of type 2 lepra reaction, encountered in lepromatous and borderline lepromatous cases of leprosy. Necrotic ENL is associated with the involvement of multiple organs, therefore delayed diagnosis and treatment will lead to complications and poor prognosis. The aim of this case report was to report a challenging case of necrotic ENL misdiagnosed with multiple cellulitis since there were no signs of prior leprosy nor had any antimycobacterial treatment. A 45-year-old man was presented to the surgery department of Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, with complaints of fever, joint pain, and painful tender skin lesions with ulceration over the trunk, extremities, and ears for one month. The patient was diagnosed clinically with multiple cellulitis and underwent a debridement procedure. Clinical improvement was absent, the patient was then consulted to the dermatology department. Physical examination showed normal vital signs, madarosis, inguinal lymphadenopathy, thickening of nerves, and sensation of numbness in both hands and feet. Laboratory examinations on admission showed leucocytosis, anemia, thrombocytopenia, hypoalbuminemia, hypocalcemia, and elevated creatinine and ureum level. A slit skin smears examination yielded positive acid-fast bacilli (AFB) with a bacteriological index (BI) value of 3+ and morphological index (MI) of 72%. The patient was diagnosed with lepromatous leprosy with necrotic ENL reaction. Intravenous methylprednisolone and cefoperazone-sulbactam were given. Multidrug therapy mulitbacillary (MDT-MB) without dapsone, and ofloxacin 400 mg was initiated. On day 17, the patient had septic shock. The patient became unconscious and experienced death. This case highlights that medical professionals should be aware of the various manifestations of necrotic ENL to correctly diagnose and provide treatment as soon as possible to prevent mortality, especially in leprosy-endemic country, Indonesia.

Keywords: Erythema nodosum leprosum, necrotic ENL, leprosy, cellulitis, lepra reaction

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Introduction

Erythema nodosum leprosum (ENL) is a type 2 lepra reaction, an immune complex-mediated reaction that may occur in borderline lepromatous and lepromatous leprosy [1,2]. The classic

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presentation of ENL includes vesicular, pustular, bullous, and necrotic lesions, while histopathology results show pan vasculitis originating from the hypodermis. Severe ENL lesions manifest differently by breaking down lesions to produce ulceration, generally called necrotic ENL, which is seen in 8% of patients [3,4]. On histopathology, ENL is characterized by pan vasculitis starting in the hypodermis [4]. Necrotic ENL is a rare and atypical form of ENL. It usually heal with fibrotic, hypertrophic, or radiating scars. Other atypical types of ENL that been identified in the literature including Sweet's syndrome-like, erythema multiforme-like, Lucio phenomenon, and reactive perforating type vesiculobullous [4,5]. Apart from ulceronecrotic and pustular lesions presented in atypical ENL, systemic manifestation with constitutional features, visceral damage, and neuritis differentiate necrotic ENL from other types [4].

Necrotic ENL is often misdiagnosed due to its clinical presentation widely similar to other diseases, such as cutaneous vasculitis [6], systemic onset juvenile idiopathic arthritis [7], or acute febrile neutrophilic dermatosis (Sweet's syndrome) [8,9]. This type 2 lepra reaction usually appears during or after leprosy treatment, but it can also represent the first manifestation of the disease, making the diagnosis more difficult [9]. This diagnostic delay accelerates the nerve damage progression resulting in significant deformities or mortality. Therefore, a comprehensive understanding of necrotic ENL is important to ensure early diagnosis and treatment to prevent complications leading to poorer diagnosis. Here, we present a challenging case of necrotic ENL misdiagnosed with multiple cellulitis since there were no signs of prior leprosy nor had any antimycobacterial treatment.

Case

In December 2022, a 45-year-old man presented to the surgery department of Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, with complaints of fever, joint pain, and painful tender skin lesions with ulceration over the trunk, extremities, and ears for one month. The lesions initially appeared on the right leg and gradually increased in size and spread to the trunk, hands, and ears. The patient was diagnosed clinically with multiple cellulitis and underwent a debridement procedure. Since no clinical improvement, the patient was then consulted to the dermatology department at the same hospital.

The patient had no other medical history of diseases and no family history of similar complaints. The patient had never been presented with pre-existing evidence of leprosy nor had any antimycobacterial treatment. Physical examination revealed that the patient was in ill condition but had normal vital signs; madarosis, inguinal lymphadenopathy, thickening of nerves, and sensation of numbness in both hands and feet. There were multiple ulcers with necrotic tissue bases, varying sizes, some with bleeding and granulation tissues in the region of the ears, thoracoabdominal, and all extremities. The skin lesions are presented in **Figure 1**.

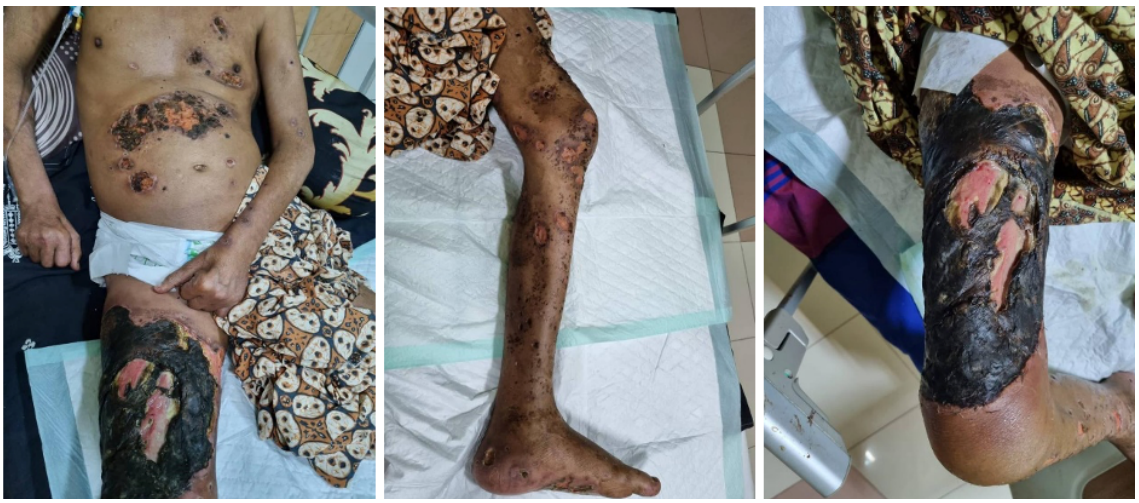

Figure 1. Multiple ulcers with necrotic tissues, varying sizes, some with bleeding and granulation tissues.

Laboratory examinations on admission showed leucocytosis, anemia, thrombocytopenia hypoalbuminemia, hypocalcemia, and elevated creatinine and ureum level. Venereal disease research laboratory (VDRL) and *Treponema pallidum* hemagglutination assay (TPHA) tests revealed negative results, ruling out syphilitic gumma. After one week of being consulted to the dermatology department, an examination of slit skin smears in the earlobes was conducted, yielding positive acid-fast bacilli (AFB) with a bacteriological index (BI) value of 3+ and morphological index (MI) of 72% (**Figure 2A**). A blood test workup was performed to evaluate the therapy but the results showed no significant improvements. Elevated liver function, hyponatremia, and hypokalemia occurred on day 12 of treatment. The skin biopsy revealed necrosis and fibromyxoid tissue with polymorphonuclear neutrophils, neutrophils, and lymphocytes indicating an acute inflammatory process following the appearance of an ulcer (**Figure 2B**).

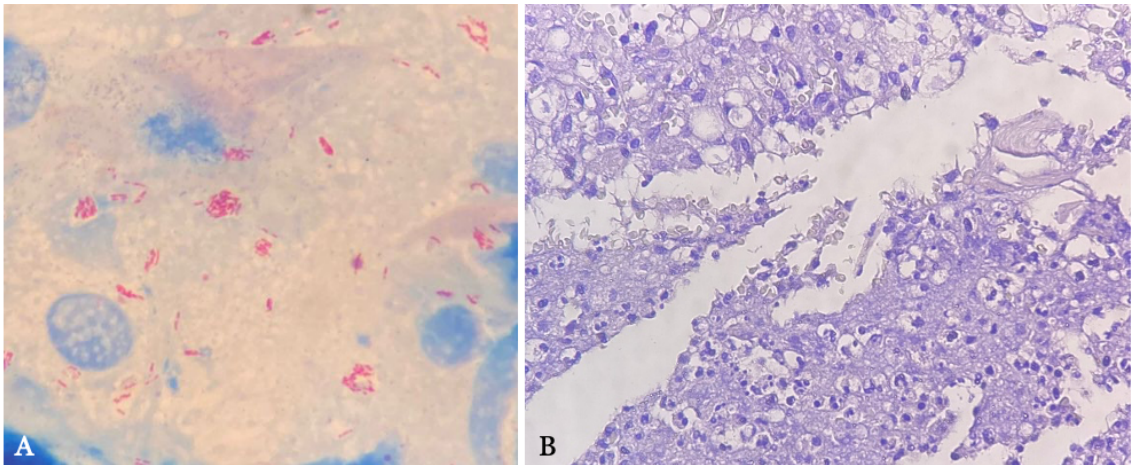

Figure 2. Acid-fast bacilli (AFB) test and histopathology of the patient. (A) Numerous acid-fast bacilli (AFB) are found in slit skin smears (Ziehl-Neelsen staining, 100x magnification). (B) Histopathology of the lesion shows necrosis and fibromyxoid tissue with polymorphonuclear inflammatory cells, neutrophils, and lymphocytes (hematoxylin-eosin staining, 400x magnification).

Based on the clinical manifestation and slit skin smear results, the patient was diagnosed with leprosy lepromatous with necrotic ENL reaction. The treatment was initiated with multibacillary multidrug therapy (MB-MDT) without dapsone, and ofloxacin 400 mg once daily. Systemic antibiotic meropenem 1 g every 8 hours was given at first but shifted to intravenous (IV) cefoperazone-sulbactam 2 g every 12 hours after the blood culture results came out. Other medications included IV methylprednisolone 62.5 mg was given every 24 hours with gradual tapering off, sodium chloride 0.9% 500 ml every 8 hours, nutrients as much as 1600 kcal (26 kcal/kg body weight), and 48 grams of protein (0.8 grams/kg body weight). The patient was also further consulted to the internal medicine department and was diagnosed with sepsis, anemia, severe hypoalbuminemia, thrombocytopenia, and hypocalcemia. The patient received calcium gluconate 1 g every 12 hours, albumin 25% for three days, packed red cells (PRC), and a thrombocyte concentrate (TC) transfusion. On the 17th day of admission, the patient's condition and vital signs worsened; mean arterial pressure (MAP) of 55 mmHg with adequate fluid resuscitation, heart rate 128 x/minute, respiratory rate 26 x/minute, body temperature 38.9°C and leukocyte count 21.92x10^{3}/mm^{3}. As a result, the patient had septic shock. Two days afterward, the patient became unconscious and died on the 19th day of admission.

Discussion

ENL is an immune-mediated inflammatory complication that affects 10% of patients with borderline lepromatous and 50% of patients with lepromatous leprosy and could occur before, during, or after MDT-MB has been completed [10]. ENL is characterized by painful nodules or plaques that are vividly erythematous in color [8]. Severe ENL may present two types of reactions:

lepromatous leprosy and necrotic ENL [11]. Necrotic ENL occurs mostly during the course of anti-leprosy treatment. Recent case reports have shown diagnosis delays; and the necrotic ENL occurred before leprosy reaction, initial treatment, or during extraordinary manifestations [3,12].

The patient in the present case report was initially diagnosed with multiple cellulitis due to its similar clinical manifestations. The diagnosis was significantly late since necrotic ENL cases have never been reported in Dr. Zainoel Abidin Hospital. The reassessment revealed cardinal signs of leprosy, AFB positive on skin slit smear, an ulcer and skin necrosis. In addition, the patient also had systemic manifestations such as anemia, leukocytosis, arthritis, swollen lymph nodes, kidney failure, and hepatic damage. The presence of ulceration or skin necrosis along with constitutional and systemic manifestations is indicative of necrotic ENL [13].

Other associated clinical manifestations of necrotic ENL include myositis, arthritis, synovitis, and painful dactylitis. Periosteal pain, tender and swollen lymph nodes, nephritis and proteinuria, renal failure, hepatosplenomegaly, and anemia may also be present [3]. Laboratory examinations always exhibit leukocytosis during reaction and anemia due to bone marrow depression [3]. Occasionally, this may lead to a hemolytic crisis as a result of the significant fall of leucocyte and hemoglobin [3]. The histopathology features of ENL are characterized by an influx of large numbers of neutrophils in the dermis, which are absorbed by clusters of vacuolated histiocytes containing bacilli [14]. Neutrophils are distributed mainly in the reticular part of the dermis, at the dermo-hypodermic junction, and in the subcutaneous tissue [14]. In the present case, AFB were detected in the Ziehl-Neelsen stain, and a large number of neutrophils were also found in the skin biopsy, thereby confirming the diagnosis.

Thalidomide is the preferred drug for ENL and received approval from the United States Food and Drug Administration (US FDA) for the acute treatment of moderate to severe ENL and the prevention of further episodes [8]. With its teratogenic properties and possible neurotoxicity, its use is severely constrained and prohibited in many countries [15]. Since thalidomide was not available at our health center (Dr. Zainoel Abidin Hospital), systemic corticosteroid was used to control the inflammation. The patient was given methylprednisolone, MDT-MB therapy, and ofloxacin 400 mg instead of dapsone.

The patient's death was a consequence of sepsis and multiorgan failure. Secondary infection and sepsis are the main causes of death in patients with leprosy reactions. Adverse effects from the anti-leprosy drug, steroid, and other drugs; toxemia from severe reactions; and hypoxia from glottic edema could all lead to an increase in mortality in necrotic ENL patients [16].

Conclusion

This case highlights that dermatologists and other medical professionals should be aware of the various manifestations of necrotic ENL in order to be able to correctly diagnose and provide treatment as soon as possible to prevent morbidity and mortality. It is crucial to have a high level of suspicion of skin abnormalities, especially in leprosy-endemic countries, such as Indonesia.

Ethics approval

The wife of patient provided written informed consent to be published as a case report.

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

All data are available as part of the article and no additional data are required.

How to cite

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