Case Report

Erythema Nodosum Leprosum Presenting as Sweet's Syndrome-Like Reaction in a Borderline Lepromatous Leprosy Patient

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Abstract

Erythema nodosum leprosum (ENL) is characterized by tender erythematous nodules, accompanied by fever, malaise, arthralgia, and systemic complications. Atypical clinical manifestations have been reported such as pustular, bullous, ulceration; livedo reticularis; erythema multiforme-like reaction; and Sweet's syndrome (SS)-like presentation. We reported a case of ENL reaction presenting as SS-like reaction in a borderline lepromatous leprosy patient.

Keywords: Atypical leprosy reaction, erythema nodosum leprosum, Sweet's syndrome-like reaction

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, characterized by involvement of the skin and peripheral nerves.[1] In the course of leprosy, a patient could obtain an acute inflammatory episode called leprosy reaction. This result can occur before, during, or after the treatment of multiple drug therapy (MDT). There are three types of leprosy reactions: type 1 reaction (reversal reaction/RR), type 2 reaction (erythema nodosum leprosum/ENL), and Lucio's phenomenon. RR mainly occurs in borderline-type leprosy, whereas ENL is more common in borderline lepromatous (BL)-type leprosy and lepromatous-type leprosy.[2]

ENL is characterized by tender erythematous nodules accompanied by constitutional symptoms such as fever, malaise, arthralgia, as well as systemic complications.[2] There are reports of atypical and rare clinical manifestations such as pustular,[3,4] bullous,[1,5] ulceration;[6] livedo reticularis;[7] erythema multiforme (EM)-like reaction;[4,8] or Sweet's syndrome (SS)-like presentation.[1,4,9-11] This article will present a case of ENL presenting as SS-like reaction in a BL leprosy patient.

Case Report

A 37-year-old Javanese male complained of painful red bumps all over the body with fever and joint pain since 3 days before the hospitalization. The lumps began at the face and spread almost the entire body. A year earlier, he was diagnosed with BL-type leprosy. He received treatment of MDT package for 8 months, but the medications were terminated by himself.

Upon examination, the general condition was weak but fully conscious (*compos mentis*). His blood pressure was 120/80 mmHg and his temperature was 38°C. His respiration rate was 20 times per minute. Dermatological status showed edematous appearance of the face, accompanied by papules and multiple erythematous plaques with vesicles in the middle, some with pus. Numerous erythematous nodules measuring 0.5–1 cm, erythematous papules, and erythematous plaques with vesicles in the middle were present in the body and extremities [Figure 1a-e]. On physical examination, madarosis, tenar and hypothenar atrophy, and enlargement of auricularis magnus nerve and ulnar nerve were found.

Blood test results showed leukocytosis of 28.860/μL, neutrophilia of 88.4%, anemia (hemoglobin) of 8 g/dL, and erythrocyte sedimentation rate of 110 mm/h. His random blood glucose was 124 mg/dL, and 2-h postprandial blood

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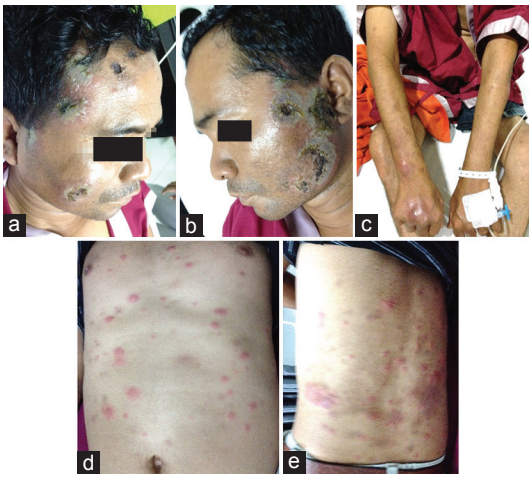

Figure 1: (a) Clinical manifestation of the patient, there were multiple papules, nodules, and erythematous plaques with edematous skin, some parts with pseudovesicles, pustules, and erosions covered with hemorrhagic crusts (right face). (b) Clinical manifestation of the patient, there were multiple papules, nodules, and erythematous plaques with edematous skin, some parts with pseudovesicles, pustules, and erosions covered with hemorrhagic crusts (left face). (c) Clinical manifestation of the patient, there were multiple papules, nodules, and erythematous plaques with edematous skin, some parts with pseudovesicles (hands). (d) Clinical manifestation of the patient, there were multiple papules, nodules, and erythematous plaques with edematous skin, some parts with pseudovesicles (abdomen). (e) Clinical manifestation of the patient, there were multiple papules, nodules, and erythematous plaques with edematous skin, some parts with pseudovesicles (back and waist)

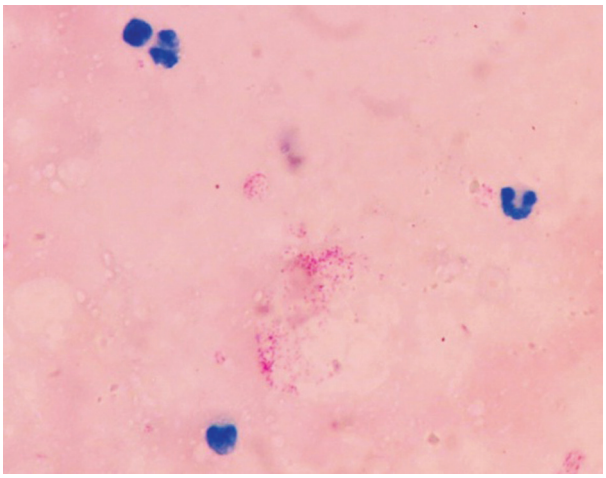

Figure 2: Examination of acid-fast bacilli showed bacillus with bacterial index +4

glucose was 150 mg/dl. His liver and kidney function tests were within normal limits. Urine test presented leukocytes 3–6 per high-power field and bacteria. Examination of pus showed leukocytes 1–2 per high-power field and Gram-positive cocci with the result of pus culture revealing *Staphylococcus epidermidis*. Peripheral blood smear test showed microcytic normochromic anemia, with leukocytosis and reactive thrombocytosis. Acid-fast bacillus test showed bacillus with bacterial index (BI) of + 4 [Figure 2].

Histopathological examination showed edema of the papillary dermis and intraepidermal vesicles [Figure 3a]. There were neutrophilic infiltrates and nuclear dust that diffusely scattered around eccrine glands and blood vessels and extravasation of erythrocytes [Figure 3b and c]. There were lymphocyte, eosinophil, and histiocyte infiltrates, with some of the histiocytes appearing as phagocyting nuclear debris and rod-shaped bacteria. Some parts of the histiocytes presented in cluster arrangement/granuloma [Figure 3d]. Electromyogram examination result presented mixed polyneuropathy (axonal and demyelinating).

The diagnosis of this patient revealed ENL reaction presenting as SS-like reaction and anemia of chronic disease. The patient's condition had improved with methylprednisolone therapy 8 mg three times per day, cefotaxime 1 g three times per day (intravenously), and the provision of MDT for 12 months.

Discussion

ENL is a type III hypersensitivity reaction (Coombs and Gell) associated with bacterial destruction and the release of large quantities of antigen, which induces antibody production. Antigens from dead bacterial products react with antibodies and form antigen–antibody complexes. These antigen–antibody complexes will activate complementary reaction which causes acute inflammation of tissue in the form of erythema nodules.[2] The clinical signs of ENL are tender erythematous nodules with constitutional symptoms, but there are reports of atypical and rare clinical manifestations such as pustular,[3,4] bullous,[1,5] ulceration;[6] livedo reticularis;[7] EM-like reaction;[4,8] or SS-like reaction.[1,4,9-11]

SS or acute febrile neutrophilic dermatosis is a condition characterized by papules, tender erythematous nodules, and plaques with or without pseudo-vesiculation with constitutional symptoms such as fever and malaise. Characteristics of SS are the positive finding of leukocytosis with neutrophilia, histopathologic examination of neutrophilic infiltrates in the dermis without evidence of leukocytoclastic vasculitis, and good response to corticosteroids [Table 1].[12]

SS-like leprosy presentation is rarely reported, making it difficult to diagnose, especially in patients who have not been diagnosed with leprosy previously.[12] Kun and Chan reported this variant for the first time in 1987, which described patients that clinically and histopathologically consistent with lepromatous leprosy and SS.[13] After that, only some cases have been reported with this type of reaction.[4,10,14,15] SS-like leprosy reactions are classified as type 2 leprosy reactions and may occur in borderline-type leprosy or lepromatous type,[10,11,14,15] but they were reported more commonly in borderline-type leprosy due to instability of immune system in the body.[10]

Clinical diagnosis of SS-like leprosy reaction is difficult to enforce if edematous plaques dominate the skin lesions, often difficult to distinguish it from type 1 reactions. SS-like reaction has characteristic histopathology such as neutrophilic

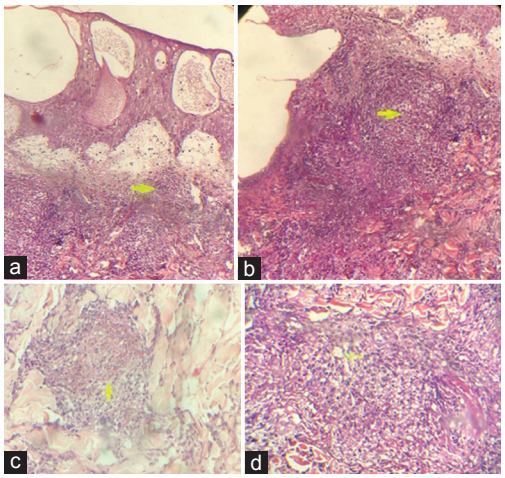

Figure 3: (a) Histopathologic result showing edema of the papillary dermis and intraepidermal vesicles. (b and c) There were neutrophilic infiltrates and nuclear dust that diffusely scattered around eccrine glands and blood vessels, with extravasation of erythrocytes. (d) There were lymphocyte, eosinophil, and histiocyte infiltrates, with some of the histiocytes appearing as phagocyting nuclear debris and rod-shaped bacteria. Some parts of histiocytes presented in cluster arrangement/granuloma

Table 1: Diagnostic criteria for Sweet's syndrome

Classic SS
Major
1. Abrupt onset of painful erythematous plaques or nodules
2. Histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis
Minor
1. Pyrexia >38°C (100.4°F)
2. Association with an underlying hematologic or visceral malignancy, inflammatory disease, pregnancy, or preceded by an upper respiratory or gastrointestinal infection or vaccination
3. Excellent response to treatment with systemic steroids or potassium iodide
4. Abnormal laboratory values at presentation (three of four): Erythrocyte sedimentation rate >20 mm/h, positive C-reactive protein, >8000 leukocytes, >70% neutrophils
Drug-induced SS
A. Abrupt onset of painful erythematous papules or nodules
B. Histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis
C. Pyrexia >38°C (100.4°F)
D. Temporal relationship between drug ingestion and clinical presentation or temporally related resolution of lesions after drug withdrawal
Presence of both major and two of the four minor criteria is required to establish the diagnosis of Classic SS. All five (A, B, C, D, E) are required for the diagnosis of drug-induced SS. SS: Sweet's syndrome

infiltrates, especially in the dermal papilla, accompanied by pronounced edema that resembles SS, resulting in frequent misdiagnosis of SS. To have a proper diagnosis, pathologists should look for the presence of Virchow's cells in staining with hematoxylin-eosin and Fite-Faraco.[10] In this case, the diagnosis of SS-like leprosy reaction was based on the patient's history of leprosy with previous inadequate therapy, the discovery of leprosy symptoms such as madarosis, nerve thickening, and atrophic muscles of the tenar and hypothenar, the detection of acid-resistant bacilli, and supported by histopathologic results.

In ENL reaction, there were significantly increased interleukin (IL-4), IL-5, IL-10, IL-7, and tumor necrosis factor (TNF)-α levels. The most severe reaction was associated with increased production of TNF-α and interferon-ɣ. There is an imbalanced in Th 17 and Treg populations, which shows the important role of Treg in controlling the inflammatory response during leprosy reactions.[16] Vieira *et al.* stated Tregs down modulation may affect the development of Th-17 response that characterizes this reactions.[17] A study by Hungria *et al.* (2017) showed anti-LID-1 (leprosy IDRI diagnostic-1) serology at diagnosis has shown prognostic value for ENL development in BI positive patients with a sensitivity level of 71% and a specificity of 80%.[18]

SS-like leprosy responds well to corticosteroid therapy, but it is advisable to administer thalidomide to prevent worsening of lesions and prevent the onset of corticosteroid withdrawal.[10] Thalidomide is the drug of choice for severe ENL due to its anti-Tumor Necrosis Factor-α (TNF-α) effect.[11,19,20] Patients with chronic ENL reactions may be susceptible to corticosteroids dependence, therefore thalidomide is the best option to prevent long-term corticosteroid side effects.[10,20]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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