Case Report

Reactive Perforating Leprosy, Erythema Multiforme-Like Reactions, Sweet’s Syndrome-Like Reactions as Atypical Clinical Manifestations of Type 2 Leprosy Reaction

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Abstract

Type 2 leprosy reactions commonly known as erythema nodosum leprosum, but various clinical manifestations of type 2 leprosy reaction were exist. The highlight of this case series was to report various atypical clinical manifestations of type 2 leprosy reaction such as reactive perforating leprosy, erythema multiforme-like reaction, and sweet’s syndrome (SS)-like reaction.

Keywords: Atypical type 2 leprosy reaction, erythema multiforme-like reaction, reactive perforating leprosy, SS-like reaction

Introduction

The course of leprosy may be interrupted by acute phenomena called leprosy reactions. Type 2 leprosy reactions are mediated by immune complexes, occur in multibacillary (MB) patients, being stereotypical clinical manifestation as the erythema nodosum leprosum (ENL). We report three cases of atypical clinical manifestation of type 2 leprosy reaction. The diagnosis of this serial case of leprosy reaction based on clinical manifestation and histopathological examination.

Case Reports

Case 1

A 39 year-old-male, on the 2nd month multidrug therapy-MB (MDT-MB) treatment presented with painful punched-out ulcers over the back, arms, and legs of 1 week duration. Three months before consultation, he complained about numbness on his feet. Physical examination showed thickening of both ulnar, great auricular, and peroneus communis nerves. Multiple punched-out ulcers were found on the arms and legs [Figure 1a-c]. Slit-skin smear (SSS) examination revealed a bacterial index (BI) of 4, 67+ with globi and morphological index (MI) 10%. Histopathological examination on the punched-out ulcer found on the left arm showed invagination of the epidermis filled with numerous neutrophil infiltrates [Figure 1d]. The dermis was infiltrated with lymphocytes and foamy histiocytes [Figure 1e]. He was diagnosed as lepromatous leprosy (LL) with type 2 reaction manifested as reactive perforating leprosy (RPL). The patient received 40 mg prednisone/day and MDT-MB was continued. Significant improvement of skin lesions was observed within 2 weeks after the start of treatment.

Case 2

A 30-year-old-female was diagnosed as borderline lepromatous (BL) leprosy in July 2015 and released from 12 months treatment with MDT-MB. She presented with generalized pruritic erythematos lesions with intermittent fever of 2 weeks duration. The patient had a history of recurrent ENL which improved using oral prednisone, but the lesions worsened during the tapering off. General physical examination was normal with no neurological deficit. Skin examination showed disseminated wheal-like erythematos papules [Figure 2a-c]
with some central vesicles [Figure 2d] over the body. Blood count showed 13,600 leukocytes with 75% neutrophils. Liver and renal function tests, and urinalysis were normal. Ziehl-Neelsen examination showed no acid fast-bacilli (AFB). Histopathological examination of wheal-like erythematous papules from left upper arm revealed marked edema of papillary and reticular dermis, foamy macrophages [Figure 2e], and infiltration of inflammatory cells around neurovascular bundles [Figure 2f]. This result supported the diagnosis of type 2 leprosy reaction with erythema multiforme-like reaction (EMLR) form. She was treated with 40 mg prednisone/day and 400 mg pentoxifylline 3 times/day. Clinical improvement was achieved after 2 weeks treatment.

**Case 3**

A 31 year-old-male was diagnosed as BL leprosy in June 2010 and released from 12 months treatment with MDT-MB. In 2014, the patient presented with multiple painful, red and fluid-filled lesions over the face, stomach, arms, and legs and also multiple ulcers on the right arms. This symptoms were accompanied by fever, arthralgia, vomit, and malaise. Four months before consult, erythematous macules were emerged on the chest, back, arms, and legs. Some of blisters were developed on erythematous macules, then it ruptured became painful ulcers on right arms and thighs. Moon face and central obesity were found on examination. Both ulnar and right peroneus communis nerves were thickened. Erythematous macules, bullae, papules, plaques with pseudo-vesicular and central pallor were seen over face, stomach, arms, and legs [Figure 3a-c]. There were ulcers with clean base, sharply defined borders, and erythema along the margin [Figure 3d]. SSS showed BI of 2+ and MI 16,9%. Histopathological examination revealed granulomatous reaction that composed of foam cells, epitheloid cells, neutrophils, and a few lymphocytes infiltration [Figure 3e]. Fite-Faraco stain was positive for AFB [Figure 3f]. Blood test showed leucocytosis (28.100/mm³) with 92% neutrophils. We concluded that this is a case of BL leprosy relapse with a type 2 reaction presenting as a sweet’s syndrome-like (SS-like) manifestation. The patient was readministered MDT-MB and 40 mg prednisone/day. After 2 weeks of treatment, the skin lesions were markedly improved.

**Discussion**

Leprosy reactions could cause disability if not diagnosed and treated early. There are atypical forms of type 1 and type 2 reactions. Type 2 leprosy reaction is a type 3 hypersensitivity reaction based on Coombs and Gell. This reaction occurs exclusively in LL, occasionally in BL leprosy. The presence of high levels of proinflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin (IL)-1 in the sera of ENL patients, may be partly responsible for the clinical manifestations of type 2 reaction. RPL or pustular ENL is an atypical form of type 2 leprosy reaction. RPL was first reported by Ghorpade in 2014 in India. There was only one case of RPL that has been reported. The clinical features are multiple punch-out ulcers. The histopathological result shows a dense inflammatory infiltrate with numerous neutrophils that perforate the epidermis to form a subcorneal pustule. In this serial case, the patient presented with painful punch-out ulcers. The histopathological examination showed invagination of the epidermis filled with numerous neutrophil infiltrates and there were lymphocytes infiltration with foamy histiocytes in dermis that supported the diagnosis of RPL.
Erythema multiforme defined as the diversity in the clinical pattern. The typical pattern is wheal-like erythematous papules or plaques. Often, the center become purpuric or necrotic and transforms into a tense vesicle or bulla, which gives rise to concentric rings of color (classic target or iris lesion). [8] Miranda et al. reported that 4, 5% of type 2 leprosy reactions occur as EMLR. [9] It presented as typical vesico-bullous target lesions, whereas the other clinical manifestation as erythematous patches, plaques, papules, or ulcers. The skin lesions could be pruritic [9] or painful. [10] In general, histopathologic feature of EMLR resemble ENL. [9] In this case, the patient presented with pruritic wheal-like erythematous papules and some with central vesicles. The histopathological examination showed foamy macrophages that confirmed the diagnosis.

SS is a neutrophilic dermatoses, characterized by papules, plaques, and erythematous or violaceous painful nodules, some with pseudo-vesicular appearance and central pallor. [11] Vesicles, bullae, sterile pustules, and ulcerated lesions were found in some cases. Systemic manifestations are fever, arthralgia, malaise, headache, and myalgia. [11, 12] Blood examination shows leukocytosis with high neutrophilia. The histopathological results reveal diffuse infiltration of matured neutrophils, upper dermal edema, endothelial cells swelling, and blood vessels dilatation. [11] Clinical manifestations of type 2 leprosy reaction may resembles SS. [12, 13] This SS-like reaction was firstly reported by Kuo dan Chan in 1987. [14] Das et al. reported a case of leprosy reaction that resembles SS. There were pustules and painful violaceous nodules on the face and thigh. The laboratory results were leucocytosis (18.200/mm³), neutrophils (82%), and increased erythrocyte sedimentation rate. [13] Chiaratti et al. reported a case of leprosy reaction that resembles SS presented with papules and erythematous edematous plaques, some with a pseudo-vesicular appearance with central pallor. Histopathological examination confirmed the diagnosis. Clinically, SS-like reaction could not be distinguished from SS. SS-like reaction established only with histopathological evaluation. [14] In our case, the patient developed painful erythematous macules, papules, and plaques with pseudo-vesicular and central pallor, on the chest, stomach, back, arms, and legs. There were bullae and ulcers on some erythematous macules. The symptoms were accompanied by high fever, vomiting, and malaise. Blood examination showed leucocytosis with neutrophilia (92%). Histopathological examination revealed foamy macrophages, infiltration of neutrophils, and blood vessels congestion. Fite’s stain was positive for AFB. Hence the diagnosis of SS-like leprosy reaction was established.

Histopathological examination and polymerase chain reaction (PCR) assay play an important role to confirm the diagnosis of leprosy, especially in difficult and atypical cases. [15] PCR is a highly sensitive, specific, and reliable diagnostic method for early detection of Mycobacterium leprae (M. leprae) using different gene targets, such as RLEP, 16s rRNA, rpoT, and sod A genes. [16] A new multiplex PCR assay could assist the diagnosis of leprosy with limited clinical manifestation. [15] PCR could be useful to determine strains of M. lepra in order to trace out the transmission pattern. [17]

Systemic corticosteroid as the first line and effective treatment for severe type 2 leprosy reaction. [18] In some cases, the patient appear to be steroid dependence (the leprosy reaction occur when the dose is tapered), so the patient need a sparing agent to reduce the risk of long term side effect of corticosteroid. [19] In our cases, all the patients received the corticosteroid for antireaction treatment and one of them was combined with sparing agent.

**Conclusion**

Type 2 leprosy reaction is a serious condition, presented with various clinical manifestation, and require long term therapy. Therefore, the clinicians should be recognized that atypical forms of type 2 leprosy reaction. The histopathological examination is an important tool to confirm the diagnosis of atypical leprosy reactions.

**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 understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

**Consent and ethical clearance**

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical clearance number: LB.04.01/A05/EC/315/XI/2017. A copy of the written consent and ethical clearance is available for review by the Editor-in-Chief of this journal.
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Conflicts of interest
There are no conflicts of interest.

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