Case Report

Reversal reaction with nodules that initially diagnosed as erythema nodosum leprosum in borderline lepromatous leprosy

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Abstract

Background: The reversal leprosy reaction generally manifest as larger, swollen, red and shiny the pre-existing skin lesions which are accompanied with pain. This reaction can be manifest as infiltration and nodules which resembles the features of erythema nodosum leprosum (ENL) leprosy reaction.
Case Illustration: We present a case of 26-year-old woman with erythematous nodules on almost all the body since two weeks ago. She had pre-existing erythema plaque on the right elbow became more erythematous and arouse with partially felt pain, fever, and malaise. Nodule lesions in BL leprosy with reaction need to be distinguished between ENL and reversal reaction because they may affect therapy and prognosis.
Discussion: The patient was diagnosed as BL leprosy with ENL reaction erythematous nodules on the face, both upper and lower arms, upper and lower limbs, knees, that partially felt pain, but after more careful history and histopathologic examination of the lesions, the nodules didn't match to the histopathologic features of ENL reaction. Correlation between the clinical and histopathological findings in the form of acid fast bacilli (AFB) and granulomatous inflammation grenz zone with epithelioid cells and lymphocyte cells infiltrations in the dermis established the diagnosis of BL leprosy with reversal reaction.
Conclusion: Erythema nodule lesions in leprosy can be an ENL or reversal reaction or a leprosy lesion in type BL leprosy. Reversal reaction should always be considered when diagnosing a skin-colored nodule in leprosy. Appropriate clinical and histopathological findings of the skin-colored nodules are needed to establish the definite diagnosis of reversal reaction.

Keywords: *leprosy, borderline lepromatous, nodule, reversal reaction, erythema nodosum leprosum*

Background

Leprosy is a chronic granulomatous infectious disease caused by Mycobacterium leprae (M. leprae).[1,2,3] This disease has various morphological clinical variations in skin lesions so it is also called a great imitator of other skin diseases. As a dermatovenereologist, we require deep history taking and physical examination to diagnose this disease.[4] In 1966, Ridley and Jopling classified the leprosy and included borderline lepromatous (BL) type.[5,6] Nodular lesions are one of the clinical features of BL type leprosy with discrete distribution and tend to be symmetrical.[3,7] Angoori et al. reported a case of BL type leprosy in a man with multiple dome-shaped nodule lesions on the chest, forehead, and back. Beside BL type leprosy, nodule lesions are one of the clinical features of lepromatous leprosy (LL) type leprosy.[3] Nodule in LL type leprosy had erythema-colored with shiny[6] and smooth[5] surface which numb, and bilateral symmetrical distributions. The location of lesions in LL leprosy type generally on the face, arms, buttocks, and legs.[3]

The clinical manifestations of reversal reaction on BL type leprosy are the pre-existing lesions became larger, swollen, red and shiny with pain. Even new lesions in the form of infiltrations of the entire body and erythematous nodules can arise. This complaint accompanied with painful enlargement of peripheral nerves, malaise, body weakness, and edema especially on the hands, feet, or face.[8] While the clinical picture of the ENL reaction are painful firm superficial or subcutaneous erythema nodules on the face and extensor areas of the limb.[9] This complaint can be accompanied by nerve inflammation and non-pitting edema of the hands and feet. There is one case report of BL type leprosy that reacted with a clinical picture of painful nodules so that an ENL reaction was initially diagnosed. But from the histopathological pictures, there were high T cell activities which is a picture of reversal reaction.[10] Here, we present a case of reversal reaction with nodules that initially diagnosed as ENL in borderline lepromatous leprosy which is an unusual manifestation of BL leprosy of a female patient. In this report, the diagnosis of reversal reaction and BL leprosy was established based on the clinical and histopathological findings.

Case Illustration

A 26-years-old Papua woman was presented with erythematous nodules on the face, both upper and lower arms, upper and lower limbs, knees, that partially felt pain. Four months before consultation she complained erythematous macules on the right elbow and 3rd right toe that numb. The lesions enlarged gradually, so she came to primary healthcare and diagnosed with leprosy. She had multibacillary multidrug therapy (MB-MDT). Three months before the consultation, the erythematous macules became redder and thicker associated with fever, erosions on the lips, jaundice, and icteric. Then she got hospitalized and diagnosed with “liver disease” and drug allergy. She stops to consumed the white tablet from MB-MDT. Two weeks before the consultation, there were new erythematous nodules on the face, both upper and lower extremities, knees, and feet with pain associated with fever, malaise, and arthritis. She came to dermatovenereologist and was referred to Hasan Sadikin Hospital.

She was born and raised in Papua. She had a brother with leprosy and neighbours with leprosy. From the area where the patient lived in Jayapura, there were 4 from 10 neighbours who had leprosy. No history of alopecia, madarosis, facies leonina, ear infiltrations, eyesight disturbance, lagofthalmus, nasal congestion, saddle nose, nosebleeds, hoarse, and deformities of fingers or toes. From the physical examination, the vital sign within normal limits. From the general examination, there was non-pitting edema on the left dorsum pedis. From the dermatological examination, there were erythematous plaque on the right elbow, erythematous macules on the left foot, erythematous nodules on the face, both arms, hands, and feet. (Figure 1). From the neurological examination, there were enlargement on the right ulnaris nerve and peroneous communis nerve which are rubbery and tender. There were hypesthesia on the lesion at the right elbow and left plantar pedis from sensory nerve function, strong motor nerve function, and dryness skin from autonomy nerve function but the Gunawan test didn’t perform. Skin slit smears examination of the skin lesion on the right elbow and both earlobes revealed +1,6 as bacterial index (BI) and 0 as morphological index (MI) of acid fast bacilli (AFB).

Excision biopsy was performed on the erythematous plaque on the right elbow as the primary lesion of leprosy and punch biopsy on the erythematous nodules on the right lower arm as the reaction lesion. From histopathology features with hematoxylin-eosin stains, there were granulomatous inflammation, grenz zone with epithelioid cells and lymphocyte cells infiltrations in the dermis. There were lymphocytes cell in connective tissue. There were no granulomatous caseation necrosis and malignant cells (Figure 2A&B). From Fite Faraco stains, there were AFB (Figure 2C). Anti-PGL-1 serology from the serum was performed with 2107 U/mL (cut off: 605 U/mL) for IgM anti-PGL-1 and 507 U/mL (cut off: 630 U/mL) for IgG anti-PGL-1.

Rifampicin 600 mg/month, clofazimine 300 mg/month, clofazimine 50 mg/day, dapson 100 mg/day from the government program MDT-MB for leprosy was given orally for 19 days. Then the patient asked to change the regimen because she

worried to had recurrent “liver disease” and drug allergy. On 20th day, she had rifampicin 600 mg/month, Ofloxacin 400 mg/month, and minocycline 100 mg/month (ROM regimen) for MDT-MB. She also had prednisone from 40 mg/day from the beginning that tapered off every two weeks for the severe reaction. After 41 days, the patient showed great improvement. The lesion did not became redder, thicker, and enlarged. No history of fever, arthritis, neuritis, and new lesion with reduction of the dorsum pedis edema.

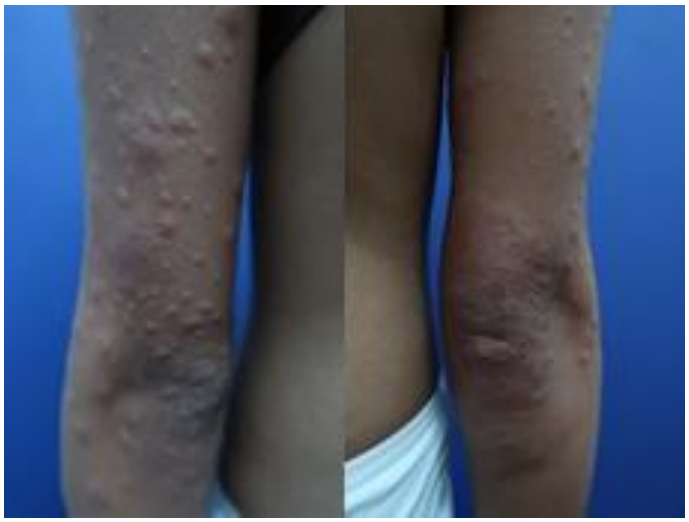

Figure 1. Clinical findings of erythematous nodules on both upper and lower arms that partially felt pain before treatment

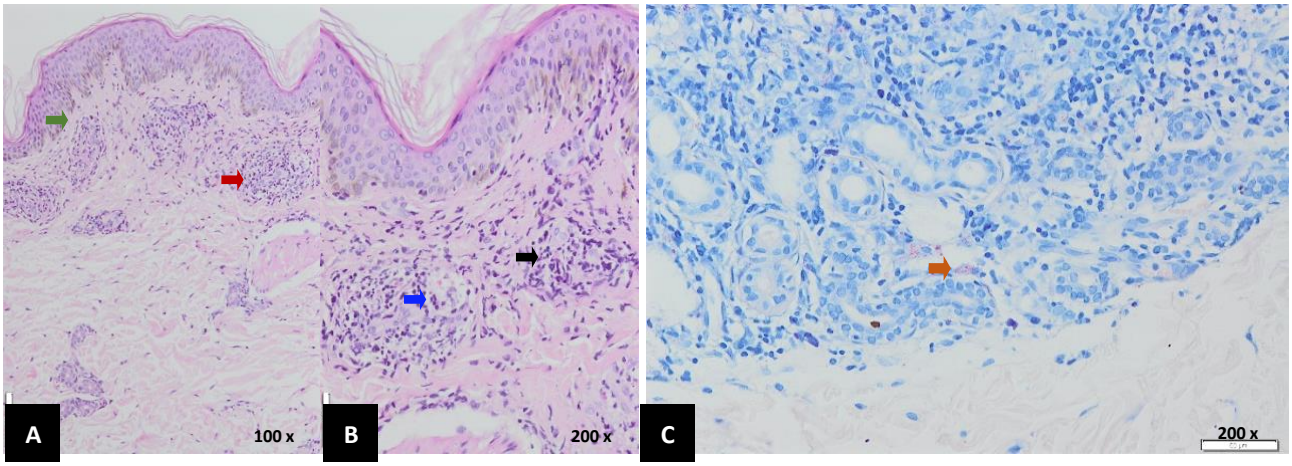

Figure 2. Histopathological features with hematoxylin-eosin stains. A. 100 times, B. 200 times magnification. There were granulomatous inflammation (red arrow) grenz zone (green arrow) with epithelioid cells (black arrow) and lymphocyte cells (blue arrow) infiltrations in the dermis. C. Histopathological features with Fite Faraco stains. There was acid-fast bacillus (brown arrow)

Discussion

Leprosy can be diagnosed based on one or more of three cardinal signs such as numbness of the skin lesions, enlargement of the peripheral nerve with nerve function disorders, or presence AFB from skin slit smear.[11] BL leprosy is one type of leprosy. One of the clinical pictures of BL leprosy is erythematous nodules[9] which firm,[6,7] round or oval,[9] with 2-3 cm for diameters and well-defined border.[6,7] The lesions are numerous[9] but less than lepromatous leprosy (LL) leprosy[7] which tend to symmetry[6] and discretely distributed with well define border.[9] Neurological disorders can occur in BL leprosy such as loss of sensation and reduced sweating in the lesion[6] with enlargement peripheral nerve enlargement.[12]

Leprosy reactions can occur in BL leprosy which is an acute episode during the course of chronic leprosy. There were 2 type of leprosy reactions such as type 2 or type 1 reaction. Type 2 or ENL reaction can occur because of antigen derived from dead M. leprae will react with antibodies to form an antigen-antibody complex which deposit in the blood vessel. This immune complex further was phagocytized by macrophages and activate complement system which caused the tissue damage. This reaction can occur at the beginning of therapy until MDT treatment has been completed (generally at the first three years after the treatment of leprosy) because the body needs a long time to clean the bacilli in the macrophages. The clinical features of this reaction were the presence of hard erythematous nodules that arise acutely, multiple, bilaterally, and symmetrically on cold parts of the body such as facial skin and painful limb extensor areas.[2] On severe ENL reactions, there were nerve inflammations such as painful enlargement of peripheral nerves, disorders of nerve functions, and edema non pitting of the hands and feet.[13] ENL reaction can be triggered by physical stress, psychology, infection, trauma, or surgical procedures.[14] The histopathological features of type 2 leprosy included a picture of inflammatory cells that spread in the papilla and reticular dermis to subcutaneous, edema in the dermal papillae, neutrophil infiltrates, increased lymphocyte counts, lobular panniculitis, fibrosis,[1] and vasculitis.[5] There were fragment AFB[5] and AFB in the macrophage in the dermis[15] was found in Fite Faraco stain.

Type 1 reactions also called reversal reactions can generally occur within the first few months after MDT MB treatment. This immunological reaction is associated with a sudden increase in cell-mediated immunity to antigens in AFB, especially protein antigens resulting from the destruction of M. leprae during therapy. Reversal reactions provide a clinical picture of skin lesions become more inflamed, swollen, shiny, and warm. In severe reversal reactions can occur new lesions, hand or foot edema, nerve function disorders, fever, and malaise.[8,9] There was a case report reversal reaction with a clinical picture of painful erythematous nodules that initially diagnosed as ENL reaction in BL leprosy. In this case, the complaints begin with the appearance of painful erythematous nodules on both forearms and numbness on the right hand, two months later the nodules return to multiply. Biopsy of nodules arising in the first episode and nodules arising two months later. Comparison of the histopathological picture between the two nodule lesions showed an increase in cellular immunity and no ENL picture was obtained, so the patient was diagnosed as a reversal reaction.[10] Histopathological features in reversal reactions were obtained, among others, edema, increased number of cells that differentiated into epithelioid cells, and increase in the number of lymphocyte cells.[1,14]

Laboratory investigation that are generally used to diagnose leprosy is skin slit smear.[19] Based on some researchers, this examination is the simplest but most valuable examination of leprosy.[20] This examination has a low sensitivity (55.8%) with a high specificity of 100%.[18] Skin slit smear of BL leprosy are BI +4 to +5.[5] The BI score was +1.6, this might be due to the low sensitivity of this examination and MDT-MB therapy for 3 months. Giving MDT-MB therapy can cause a decrease in BI and MI scores. MI reduction was found to be faster than BI after effective MDT-MB administration.[19,20] Based on Gayatri et al.[21] BI in leprosy patient who had one year MDT-MB therapy could decrease around IB +1 to +2 and MI 0% (which indicates no viable AFB). The AFB could disappear within a few months in BB leprosy, one

to two years in BL leprosy, and six to ten years in LL leprosy.[2]

The histopathological examination from skin biopsy tissue can support the diagnosis of leprosy.[22] Determined the location of a biopsy is very important. The skin lesions taken for biopsy should be representative of leprosy lesions and reaction lesions.[23] From various studies there was a mismatch of clinical features and histopathological features.[17,18] The histopathological features can incompatibility in BL leprosy around 43%. Based on that study, Job et al.[17] found 10 cases from 109 cases of clinically BL leprosy with histopathological features of BB leprosy. Failure or usefulness of histopathological examination are based on several factors such as the type and depth of biopsy, the quality of skin lesions taken for biopsy, and tissue bacterial staining.[17] BL leprosy can provide 2 types of histopathological features based on Makino et al.[5] the first type there was a diffuse proliferation of histiocyte cells which differentiate to the epithelioid cells, no foam cells, and few lymphocyte cells. In the second type, there were not so many foamy macrophages, no differentiation cells to epithelioid cells, and there was an infiltration of lymphocytes in the perineural membrane area. There were many AFB from the histopathological features in BL leprosy.[5]

Conclusion

Erythematous nodules lesions in leprosy can be considered as ENL reaction or reversal reaction or leprosy lesion in BL leprosy. Appropriate and careful anamnesis, physical examination, skin slit smear examination, and histopathological examination of the erythematous nodules lesions are needed to establish a definite diagnosis. Only scarce reports of a case of reversal reaction with nodules that were initially diagnosed as erythema nodosum leprosum in borderline lepromatous leprosy have been reported.

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