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Ramona D. Lubis
Department of Dermatology & Venereology, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, North Sumatera, Indonesia

Mila Darmi
Department of Dermatology & Venereology, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, North Sumatera, Indonesia

Rudi Chandra
Department of Dermatology & Venereology, Medical Faculty of Universitas Prima Indonesia, Medan, North Sumatera, Indonesia

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Case Report

Childhood-onset borderline tuberculoid leprosy with reversal reaction

Ramona D Lubis[1], Mila Darmi[1], Rudi Chandra[2]

[1]Department of Dermatology & Venereology, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, North Sumatera, Indonesia
[2]Department of Dermatology & Venereology, Medical Faculty of Universitas Prima Indonesia, Medan, North Sumatera, Indonesia

Email: Ramona_lubis@yahoo.com

Abstract

Background: Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae* that predominantly affects the skin and peripheral nerves. Leprosy among children is still common in endemic countries.
Case Illustration: A 12-year-old girl complained about a hypopigmented anesthetic patch on her face for 11 years, which became larger and spread slowly to her arms and legs. She had a history of close contact with her aunt, who was diagnosed with multibacillary leprosy. On *slit-skin-smear* test, acid-fast-bacilli (bacteriologic index +1) were found. She was diagnosed with multibacillary leprosy and treated with children's multidrug therapy-multibacillary (MDT-MB) regimen. After 2 months of MDT-MB treatment, she complained that the hypopigmented patches became reddish and swollen with enlarged peripheral nerves. She underwent a reversal reaction (RR) and was treated with 40 mg prednisone daily and continued the MDT regimen.
Discussion: RR is found less frequently in children than the adult. Accurate diagnosis is vital because of its psychosocial impact on the family. One of the most prominent features of borderline tuberculoid leprosy is its susceptibility to RR. It is characterized by rapid changes from existing plaques to edematous lesions with or without abrupt neuritis.
Conclusion: We reported a girl with borderline tuberculoid leprosy with developed RR after taking MDT-MB for 2 months. The risk factors for developing RR were being diagnosed with borderline tuberculoid leprosy, female, multiple and disseminated patches involving larger body areas and multiple nerve involvement, large facial patches, and starting treatment. These risk factors were found in our patient.

***Keywords**: borderline tuberculoid, leprosy, reversal reaction*

Background

Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae* that predominantly affects the skin and peripheral nerve. *Mycobacterium leprae* is a non-cultivable, Gram-positive, obligate intracellular, and acid-fast bacillus.[1] In 2011, about 83% of the new cases were detected in three major countries worldwide, in which India, Brazil, and Indonesia were responsible for 58%,16%, and 9%, respectively.[2]

Leprosy commonly affects adults, but the increasing reports of leprosy in children and adolescents showed an active transmission of bacillus, a significant reservoir of undiagnosed cases in the community, and the health system's failure to control this disease.[2,3] Leprosy among children (under 15 years old) is still common in countries where it continues to be endemic. The global figures for 2012 reported about 21,349 (9%) new cases in children, with 76.5% of these residing in the South-East Asian region.[4] Children's proportion of leprosy cases in the South-East Asian region ranged from 2.99% in Thailand to 11.4% in Indonesia.[5] Wulan *et al.*[6] had reported the profile of new leprosy in childhood at Dr. Soetomo general hospital in Surabaya from January 2009 until December 2011, where they found 37 (5,5%) new cases of leprosy in children out of 677 new leprosy

cases. Most of the children diagnosed with leprosy cases aged from 10 to 14 years old.

The presence of household or neighborhood contact increases the risk for infection of leprosy. The risk rises fourfold when there is a neighborhood contact and ninefold if the contact case is within the immediate household.[3,5] The risk for developing leprosy increases up to fourteen times when multibacillary (MB) leprosy, especially lepromatous type, is found in the family, or when the index case is the mother, or multiple cases are found in the family. The detection of childhood leprosy cases may provide an opportunity for early detection of the index case, usually within the family and even in the community. The prevalence of familial contact in childhood leprosy ranged from 10% to 36%, as observed in different studies.[3]
Type 1 reaction of leprosy commonly occurs in the borderline tuberculoid (BT), mid-borderline (BB), and borderline lepromatous (BL) forms. It is characterized by erythema and swelling in the pre-existing lesions and manifestation of novel lesions (papules and plaques).[7] Generally, children under 15 years old do not experience leprosy reactions. Some studies showed a low frequency of leprosy reactions, ranging between 1.36% to 8.33%. However, some authors have found it to occur more than expected, with rates varying from 18% to 29.7%. In these studies, the type 1 reaction was the most commonly found among children, in which the most frequent clinical form was borderline tuberculoid.[2]

Leprosy with reaction in children must be handled seriously because of its potential to cause physical deformity and psychosocial damage on the child and family. Disabilities are recognized as major contributing factors of the stigma associated with leprosy, and they may impact psychological development in children.[5]

Case Illustration

A 12-year-old girl presented to the hospital with hypopigmented patches on her face, arms, and legs for 11 years. The hypopigmented macule on her face had appeared since she was 1 year old and became more extensive and slowly multiplied. The patient denied any symptoms like fever, itchy, or joint pain. She had been treated by several doctors taking the disease as an allergic disease, but her condition never improved. The patient was raised by her aunt when she was a baby who was diagnosed with MB leprosy 2 years ago and had finished her treatment with 12 packages of multidrug therapy. The patient's family had been examined and declared not suffering from leprosy.

We found normal vital signs, body weight 59 kg, height 147 cm, and no peripheral nerve enlargement on physical examination. Multiple (a total of 8 lesions) ill-defined xerotic hypopigmented macules with irregular patterns, scales, and loss of sensation were found on her face, right forearm, elbow, the front side of right thigh, and both posterior thighs (figure 1).

On *slit skin smear* examination from the lesions of the arm and thigh, acid-fast bacilli were found with bacteriological index (BI) +1 (figure 2) and morphological index (IM) 72.7%. The patient was diagnosed with MB leprosy and treated with multidrug therapy (MDT) regimen from World Health Organization (WHO) for children. This regimen consists of 50 mg dapsone daily, 450 mg rifampicin monthly, and 150 clofazimine monthly, followed by 50 mg clofazimine every other day for 12 months.

After 2 months of treatment, the patient complained that the patches became reddish and swollen. On physical examination, the sensory nerves on the lesions improved (no anesthesia), but enlargement and tenderness of the peripheral nerves were found on the right ulnar nerve and both common peroneal nerves. We found shiny erythematous and edematous large plaques on the left face and erythematous plaques with peripheral edematous margins at the right forearm, elbow, left leg, and posterior thighs (figure 3). The patient was diagnosed with MB leprosy with reversal reaction and treated with 40 mg prednisone daily for 2 weeks, then tapered off until 12 weeks and continued the MDT regimen.

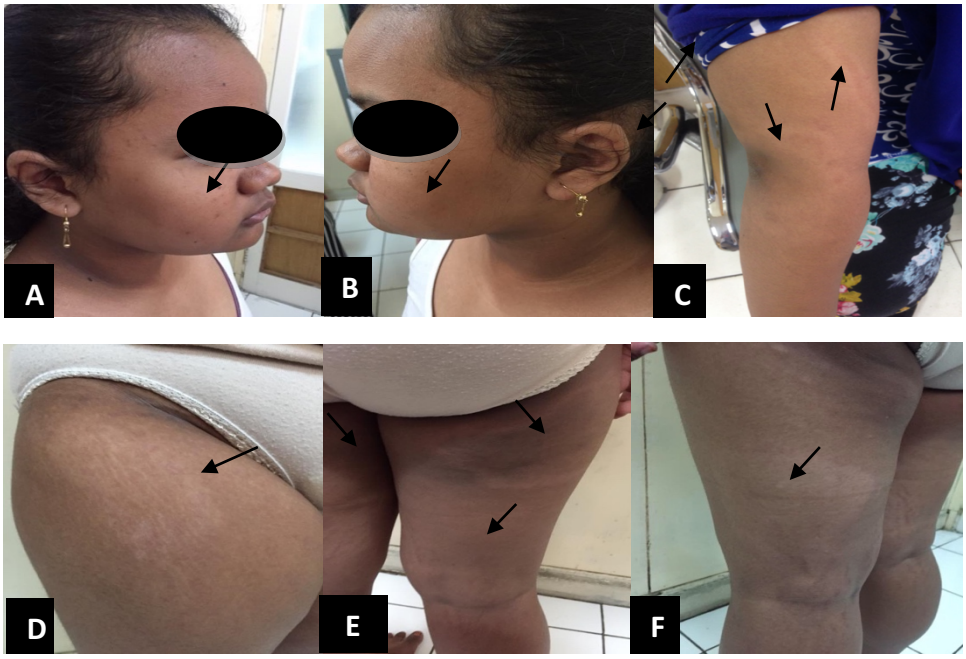

Figure 1. Hypopigmented macules with anesthesia; right (A) and left (B) face, right forearm and cubital (C), the front side of the right thigh (D), and both posterior thighs (E) & (F)

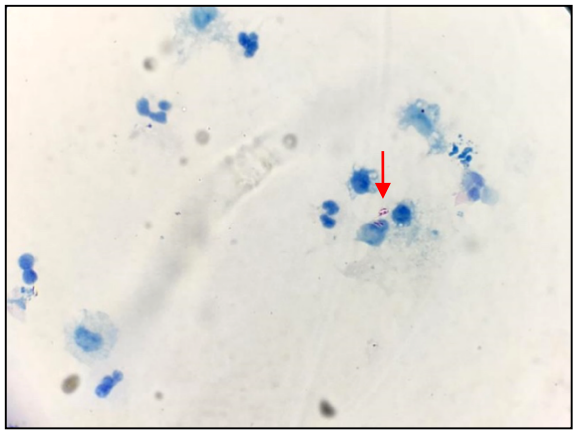

Figure 2. Slit skin smear examination showed acid-fast bacilli with BI+1 (Ziehl-Neelsen stain, magnified 10x)

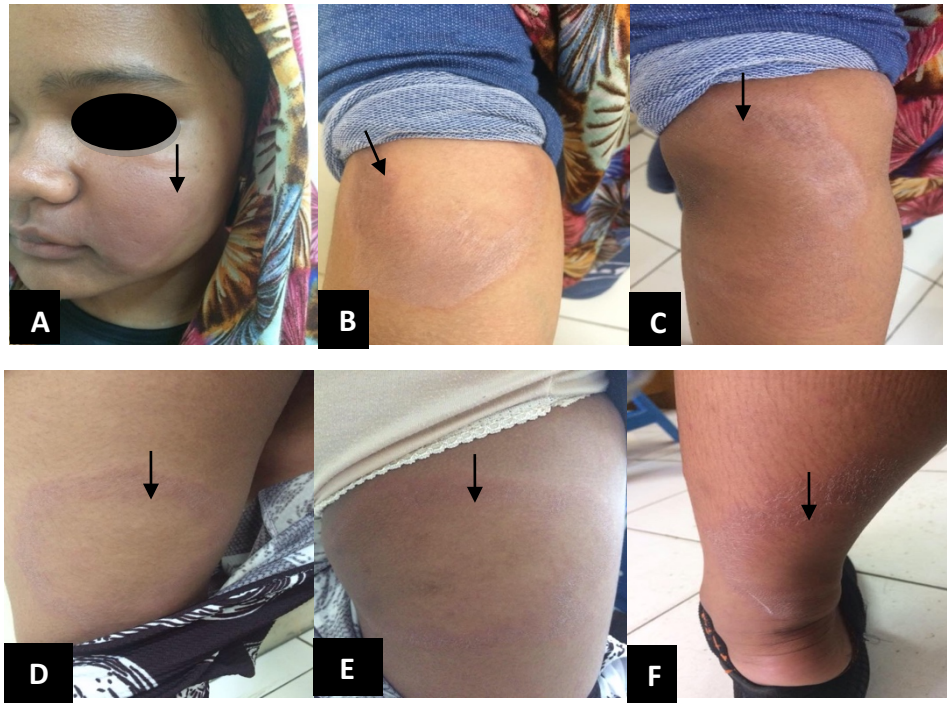

Figure 3. Large erythematous plaques; left face (A), right forearm (B) and cubital (C), left posterior thigh (D) and right posterior thigh (E), and left leg (F)

Discussion

In our case, the source of the infection is most likely from the patient's aunt, who raised her since she was a baby. The patient's family was examined and declared not suffering from leprosy. The presence of household or neighborhood contact of leprosy increased the risk for infection. The risk for leprosy transmission was higher with neighborhood contact and immediate household contact.[3,5] The higher risk for developing leprosy was associated with multibacillary leprosy cases, especially lepromatous disease in the family. The prevalence of familial contact in childhood leprosy ranged from 10% to 36%, as observed in different studies.[3] Wulan *et al.*[6] reported that leprosy in children was primarily transmitted from household contact (68,8%), neighborhood contact (18,7%), and others (12,5%).

In our case, the patient presented with multiple hypopigmented macules (a total of 8 lesions) and a positive result of slit skin smear. Thus, this case was classified as an MB case. WHO recommended using purely clinical classification. They established it as a paucibacillary (PB) case for those with less than 5 skin lesions and or only one nerve trunk involvement, whereas as MB case for those with up to 5 skin lesions and or more than one nerve trunk involvement. However, if the microscopic examination of skin smear is available, patients with positive results are considered MB, regardless of the number of lesions.[8]

Based on the classification proposed by Ridely & Jopling (1966), our case was categorized as BT leprosy. The patient presented with multiple large ill-defined xerotic hypopigmented macules with irregular patterns, scales, and loss of sensation at the region of the face, right forearm and cubital fold, the front side of right thigh, and both posterior thighs. The borderline tuberculoid form is the commonest; its prevalence ranged from 55–78.7% of all childhood cases of leprosy in various studies.[5] BT leprosy is characterized by skin lesions resembling tuberculoid leprosy with ill-defined margins; in some parts, it may start sloping outwards and even fade imperceptibly into normal skin. The number of lesions may vary from 3 to 10 with variation in size and contour. Large hypopigmented macules with nerve involvement in BT leprosy are often called maculoanesthetic. Lesions tend to be large and asymmetrical in their distribution and are more commonly found on the face, lateral aspect of the extremities, buttocks, and scapulae. The lesions showed a dry and rough surface with loss of sensation to touch and temperature. Also, there may be areas of sensory

loss on extremities following the course of large cutaneous nerves.[5,8]

In our case, the patient demonstrated a reversal reaction (RR) after 2 months of treatment with MDT. We found that previous hypopigmented skin lesions became reddish and swollen, a new tumid lesion arising from previously normal skin on the left leg, and enlargement and tenderness of the right ulnar nerve and both common peroneal nerves. The most striking feature of BT leprosy is the susceptibility to type 1 reaction.[5] Reversal reaction usually occurs during the first six months of the MDT regimen in BT and BB leprosy. In 2003, the Indian Association of Leprologists (IAL) reported 42% of all type 1 reaction cases presented at the time of registration and initiation of therapy and 33% developed within the first 6 months after starting MDT.[7] Gitte *et al.*[9] reported 33 (10%) out of 330 PB cases and 56 (25.3%) out of 221 MB cases of child leprosy experienced type 1 reaction. Clinically, reversal reaction is characterized by the abrupt change of previously passive plaques to swollen lesions and new swollen lesions arising in clinically normal skin with or without an abrupt onset of neuritis. A purplish dusky erythematous color is typical in RR. Neuritis also ranged from mild to severe and is potentially disastrous, particularly if involving multiple nerves.[1,7,10]

In this case, the leprosy reaction appeared on a 12-year-old girl with borderline tuberculoid leprosy treated with MDT. Leprosy reactions are rarely found in children compared to adults. The low prevalence of leprosy reactions in children is probably due to the lower incidence of nerve involvement. Nevertheless, there are several risk factors for developing reversal reactions, such as (1) patient of the borderline group (BT, BB, and BL leprosy) are the most vulnerable group; (2) female gender carries a higher risk than men, probably due to hormonal fluctuations; (3) patients with multiple and disseminated patches involve larger body areas and multiple nerves involvement; (4) patients with extensive facial patches; (5) starting the treatment may precipitate the reaction due to increased breakdown and release of bacterial antigens.[7] All of these risk factors were found in our patient.

In our case, the patient was treated with the MDT regimen from WHO for children. This regimen consists of 50 mg dapsone daily, 450 mg rifampicin monthly, and 150 clofazimine monthly, followed by 50 mg clofazimine every other day for 12 months. MDT was the cornerstone of the leprosy elimination strategy to cure the patients, reduce the reservoir of infection, and interrupt its transmission. Early cure with MDT also prevents disabilities. Fortunately, the intolerance to anti-leprosy drugs in children was low; most cases responded well to the MDT regimen of WHO.[5] After taking MDT for 2 months, our patient was diagnosed with a reversal reaction. It was stated that the starting of MDT treatment precipitated the reaction due to increased breakdown and release of bacterial antigens.[7] MDT regimen consisted of rifampicin, clofazimine, and dapsone acted as bactericidal agents to *M. leprae*. The mechanism of action of rifampicin was through its ability to inhibit bacterial DNA-dependent RNA polymerase. The mechanism of action of clofazimine was unclear, but aminophenazone dye was shown to bind to mycobacterial DNA and caused a bactericidal effect. Meanwhile, dapsone was an inhibitor of dihydropteroate synthase that needed for folate synthesis in M. leprae.[11]

As the reversal reaction occurred in this case, we gave 40 mg prednisone daily and continued MDT. Along with the initiation of prednisone treatment, the swollen reddish plaques and the enlargement and tenderness of the right ulnar nerve and both common peroneal nerves subsided after 2 weeks of treatment. WHO recommended a standard regimen (1-2 mg/Kg body weight) of prednisone for adult patients for 12 weeks. We provided our patient with the adult dose of prednisone because of the patient's body weight. Corticosteroid (prednisone) was still the cornerstone therapy and considered the drug of choice for reversal reaction.[10]

Conclusion

We reported a BT leprosy case with a reversal reaction in a child after starting 2 months of treatment of MDT. Leprosy reactions were much less frequently in children. Risk factors for developing reversal reactions such as BT type, female gender, multiple and disseminated patches involving larger body areas, multiple nerve involvement, extensive facial patches, and the starting of MDT were found in our patient.

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Conflict of Interests

The authors declared to have no conflict of interests.

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