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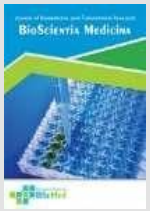

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Diagnosis and Treatment of Multibacillary Leprosy Borderline Lepromatous Type: A Case Report

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A B S T R A C T

Background: Leprosy is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*. This disease has a high transmission ability and can cause physical disability and have an impact on the social life of the sufferer because of the negative stigma about leprosy. This study aims to describe the examinations performed in the diagnosis and treatment of patients with multibacillary leprosy, borderline lepromatous type. **Case presentation:** A 43-year-old woman with a chief complaint of redness on the arm since 1 year ago. The patches are not itchy, painless, stiff, and numb. Since 3 months ago, the patient complained of red patches increasing and spreading to the trunk and legs. Dermatological examination found in the facial region et truncus anterior et posterior et superior, and inferior extremities bilateral showing multiple erythematous plaques, well-demarcated with scales in several parts. Sensory function examination revealed a decrease in lesions on the face, superior and inferior extremities, and anterior and posterior trunks. Negative AFB examination and biopsy results support the diagnosis of borderline lepromatous type (BL) multibacillary leprosy (MB). **Conclusion:** Clinical findings in the form of hypopigmented lesions that feel numb is a cardinal signs of leprosy. Asymmetrical distribution of lesions with a number of more than 5 lesions accompanied by impaired nerve function in the form of decreased sensibility is a characteristic of MB leprosy. Histopathological features support the diagnosis of MB type BL leprosy even though the results of the skin slit smear examination were negative.

1. Introduction

Leprosy or leprosy or morbus hansen is a chronic infectious disease caused by *Mycobacterium leprae (M. leprae). Mycobacterium leprae* infects the skin and nerves and causes clinical manifestations of skin and nerve disorders, including hypopigmented or erythematous lesions, peripheral nerve damage, and deformities in further infection.[1] Leprosy has a fairly high transmission rate. However, this disease has low morbidity.[2] Transmission *M. leprae* can be through the skin or nasal mucosa, with the incubation period of this bacterium varying from a few weeks to 30 years or more.[1]

Leprosy is a disease that is endemic in tropical countries, especially in underdeveloped and developing countries such as Southeast Asia, America, Africa, the East Pacific, and the Western Mediterranean.[3,4] The number of new cases of leprosy in the world in 2018, according to the World Health Organization (WHO), was recorded at more than 208,641 cases, while in the Southeast Asia region, there were 148,495 new cases.[5] New cases of leprosy in Indonesia, according to the Ministry of Health of the Republic of Indonesia 2017, were 10,477 cases, with the highest number being multi-bacillary (MB) type leprosy.[6]

According to WHO, leprosy is classified into bacillary (PB) and multibacillary (MB), while according to Ridley Jopling, it is classified into tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), mid borderline leprosy (BB), borderline lepromatous leprosy (BL) and lepromatous leprosy (LL).[4,7,8] Leprosy types TT and BT are included in the PB group, while BB, BL, LL, and some BT are in the MB group.[4] PB leprosy is characterized by the appearance of 1 to 5 skin lesions without *M. leprae* on a skin slit smear examination. In contrast, MB leprosy has the characteristics of the appearance of 6 or more skin lesions accompanied by nerve damage or the discovery of *M. leprae* bacilli on skin slit smears examination.[4,7]

The diagnosis of leprosy can be made by examining the skin and nerves. Cardinal symptoms include numbness of hypopigmented or erythematous skin lesions, thickening of the peripheral nerves with decreased sensation and weakness of the muscles innervated by these nerves, and acid-fast bacilli found on skin tissue smears or biopsies. The diagnosis of leprosy is made if there are one or more of these cardinal symptoms. Histopathological investigations with hemotoxylin-eosin (H&E) and Fite Faraco (FF) staining can be performed to support the diagnosis of leprosy.[2,3]

MB-type leprosy can be treated with MDT consisting of rifampin and dapsone. This therapy can be given for 12-18 months.[2] Leprosy can cause disability so it affects the activities and work of the sufferer and affects the social life of the sufferer due to the stigma of society towards this disease.[3,4] This study aims to describe the examinations performed in the diagnosis and treatment of patients with multibacillary leprosy, borderline lepromatous type.

2. Case Presentation

A 43-year-old woman came to the outpatient polyclinic of Dr. Moewardi General Hospital Surakarta with complaints of redness on her arm 1 year ago. The patches are not itchy, painless, stiff, and numb. Initially, the spots are small but gradually enlarge. Since 3 months ago, the patient complained of red patches increasing and spreading to the trunk and legs. The patient went to a general practitioner and received drug therapy once a day, and ketoconazole ointment was applied 2 times a day, but there was no improvement. The patient complained of white patches spreading to the back and fever and chills. Then, the patient went to a dermatologist and was given methylprednisolone 3x4 mg treatment, then the complaints improved.

Denied history of similar complaints, denied a history of taking medication before illness, denied contact history with similar complaints, denied a history of traveling in leprosy endemic areas, and denied a history of living near individuals with similar complaints. A family history of similar complaints and patches of numbness was denied.

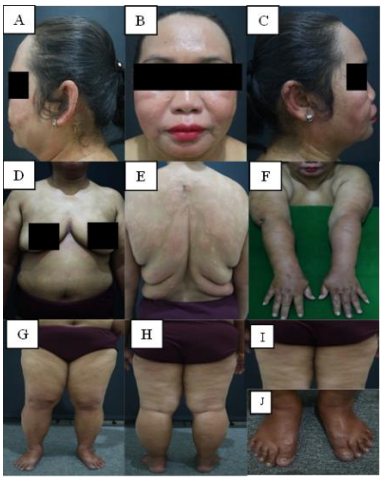

Figure 1. (A-J). In the facial region, erythematous plaques were seen, well-defined, raised at the edges, and atrophic in the middle with thin scales on top.

On physical examination, the patient's general condition was good, and consciousness was compos mentis, pain score was zero. Examination of vital signs showed blood pressure 120/60 mmHg, pulse 88 x/minute, respiratory rate 20 x/minute, and body temperature 36.5ºC. The patient's height is 156 cm, and her weight is 74 kg. Examination of the dermatological status showed that in the facial region et, truncus posterior et, superior, and inferior extremities, bilateral multiple erythematous plaques were seen, well-demarcated with scales in several parts (Figure 1). Peripheral nerve examination showed no thickening. On sensory examination, there was decreased sensibility in lesions on the face, superior and inferior extremities, and anterior and posterior trunks, while on motor examination, there were no abnormalities. AFB examination with slit skin smear showed that the lesions on the right hand, right, and left ear lobes were negative.

The differential diagnosis in this patient is tinea fascialis et corporis et cruris. Examination of skin scrapings with 10% potassium hydroxide (KOH) was performed to rule out this differential diagnosis. Examination of skin scrapings taken from the lesion on the back was then added with 10% KOH, and no spores or hyphae were found so that the diagnosis of tinea fascialis et corporis et cruris could be ruled out. A skin biopsy examination with hematoxylin & eosin (H&E) staining was performed to confirm the diagnosis of leprosy and determine its type. The skin biopsy with H&E staining showed that the epidermis was within normal limits, and the dermis showed a Grenz zone with tubercles of epithelioid cells and lymphocytes, and Langhans cells (Figure 2). The histopathological features support the diagnosis of type BL leprosy. Fite Faraco (FF) staining showed the presence of AFB bacteria stained red, in the globi, in granular form (Figure 3).

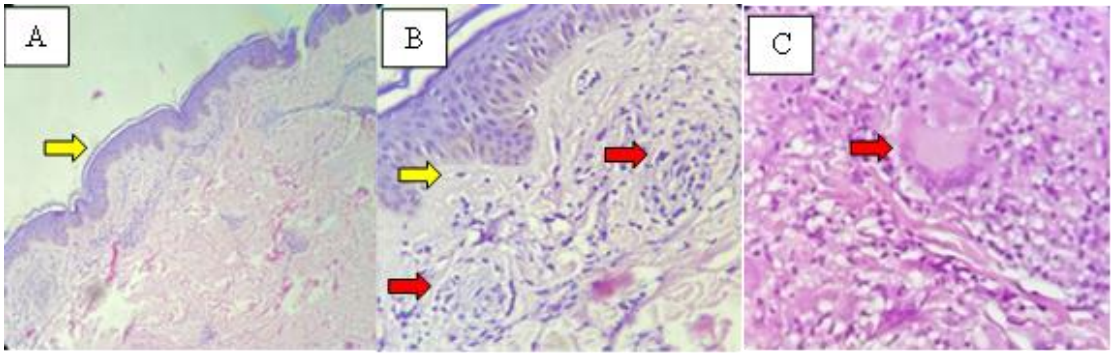

Figure 2. (A). Staining of H&E. Epidermis within normal limits (yellow arrow) (B). The dermis shows the Grenz zone (yellow arrow), tubercles of epithelioid cells, and lymphocytes (red arrows) (400X magnification). (C). The dermis shows Langhans cells (red arrows) (400X magnification).

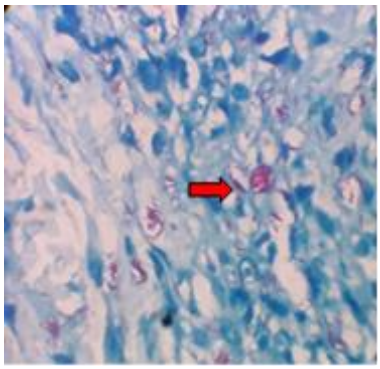

Figure 3. Fite Faraco staining shows AFB bacteria painted red inside the globi, granular (red arrow).

Based on the history, physical examination, and supporting examination, the patient was diagnosed with borderline lepromatous type MB leprosy. Patients are advised to go to the health center to get multi-drug therapy (MDT) PB, namely rifampin 600 mg per month, dapsone 100 mg, clofazimine 300 mg per month taken in front of health workers and dapsone 100 mg, and clofazimine 50 mg per day taken at home for 12 months.

3. Discussion

Leprosy is a chronic granulomatous infectious disease caused by the acid-fast bacillus *M. leprae.*[9] This bacterium infects Schwann cells of unmyelinated nerve fibers, macrophages, and endothelial cells of patients.[10] The incubation period of this bacterial infection varies from a few weeks to 30 years.[1] Clinical manifestation of leprosy includes skin lesions accompanied by peripheral nerve damage.[8] Most of the new cases were detected in India, Brazil, and Indonesia, and even the WHO reported that more than 90% of new cases were detected in these regions.[5] The prevalence of leprosy in Indonesia in 2017 was dominated by MB leprosy, which amounted to 9,015 cases from all 10,477 patients.[6]

Immunological and histopathological characteristics of borderline type leprosy vary between tuberculoid and lepromatous forms. Granulomatous lesions and the presence of a Th1 cellular immune response that inhibits the proliferation of bacilli are found in tuberculoid leprosy, whereas in lepromatous leprosy, there is a Th2 cellular immune response that contributes to the multiplication of bacilli in phagosome macrophages. There is a progressive decrease in the cellular immune response from the BT to the BL forms, accompanied by more and more lesions and nerve damage, as well as increased bacilli and antibody levels. Neurological manifestations in the borderline form result from immunological instability, which is characterized by nervous disorders and frequent reactions to leprosy, which will progress to neurological disorders that appear asymmetrical and deformed. This process is caused by an increase in the number of bacilli in the nerve branches near the Schwann cells.[11]

Lesions in type BL leprosy almost resemble those of type LL, which include the presence of hypochromic, erythematous, or light brown lesions in large numbers, asymmetrical distribution, and loss of sensation in several areas.[4] In this case, multiple erythematous patches were found with numbness with elevation at the edges with an asymmetrical distribution and loss of sensibility in several places. These clinical findings are consistent with the description of LL-type leprosy.

Another supporting examination is a slit skin smear. The slit skin smear procedure is an examination that can be used to help establish the diagnosis of leprosy, which includes taking a smear, fixation, staining, and reading the results.[12,13] The reading of the results of this examination is based on the bacteriological index (IB) and the morphological index of an acid-fast bacillus (AFB). The bacteriological index in this examination starts from a value range of 0 which means that AFB is not found and is usually found in tuberculoid leprosy up to 6+ which means that more than 1000 AFB is found per field of view that occurs in lepromatous leprosy.[14,15] In this patient, the IB value was 0, and the morphological index was 0%. A slit skin smear examination is easier, faster, and cheaper, but a biopsy is necessary, especially if the results of the slit skin smear examination are negative.[12]

Histopathological examination is the gold standard in diagnosing leprosy.[12] H&E staining and Fite Faraco (FF) were used as stains in the histopathological examination of leprosy. Classification of leprosy can be seen from the histopathological picture with H&E staining. The histopathological picture of TT-type leprosy is in the form of an epidermis that looks normal, and there is no clear zone in the subepidermal called the Grenz zone. There is a non-caseating granulomatous appearance and Langhans giant cells; usually, no smear is present. Histopathological appearance in BT type leprosy shows the presence of a Grenz zone, whereas, in BB type, there are aggregates of epithelioid cells, scattered and rare

lymphocytes, and no Langhans giant cells accompanied by an increase in the number of AFB. Histological features of type BL leprosy are the presence of a Grenz zone in the subepidermal, macrophage aggregates, epithelioid cells with abundant cytoplasm, several foam cells, and lymphocytes, and large amounts of AFB accompanied by globi. Type LL is characterized by flattening of the epidermis, the presence of a Grenz zone, and large amounts of AFB and Virchow cells, namely foamy macrophages in which there are globi.[14,16] Fite Faraco staining is used to see the presence of AFB, which will stain red.[16] In this case, a skin biopsy of the posterior trunk region with H&E staining showed no abnormalities in the epidermis and a Grenz zone with tubercles of epithelioid cells and lymphocytes, and Langhans cells. The histopathological features support the diagnosis of type BL leprosy. FF staining, in this case, showed the smear bacteria stained red, in the globi, in granular form, which is suitable for supporting BL-type leprosy. The results of the history, physical examination, slit skin smear examination, and histopathological examination in this patient support the diagnosis of MB type BL leprosy.

The differential diagnosis, in this case, is tinea fascialis et corporis et cruris. Tinea, also known as ringworm, is a dermatophyte infection that has characteristic circular lesions resembling a ring. This infection can occur in the epidermis (epidermomycosis), hair and hair follicles (tricomycosis), and nails (onychomycosis). Tinea fascialis is facial tinea, while tinea cruris occurs in the groin and can spread to the feet. Tinea corporis is tinea that occurs on the body, neck, and arms. Characteristics of lesions in tinea corporis are characterized by erythematous patches or in the form of solitary or multiple rings with well-defined edges with elevation and central healing. Lesions in the cruris region are red or brownish or dark plaques that are itchy with central healing. Lesions may extend to the thighs and buttocks. Lesions on the face can be in the form of papules or vesicles or pustules in small quantities.[17] Supporting examinations to help establish the diagnosis of tinea are skin scraping examinations with 10% KOH with microscopic images in the form of conceptual, branched, or unbranched hyphae which can also be found in short hyphae and spores.[18,19,20] Tinea generally has atypical histopathological features, but some characteristic features can be found, including the presence of neutrophils in the epidermis with orthokeratosis and/or parakeratosis or hyperkeratosis with a basket-weave. A sandwich sign, i.e., hyphae between the 2 zones of confined cells, can be seen. These features appear as orthokeratotic lamellae with underlying parakeratotic lamellae with fissure formation between them. There is marked papillary edema in the dermis. The results of the examination, in this case, did not match with tinea, so the diagnosis could be ruled out.[21]

Based on the MDT treatment regimen recommended by WHO, therapy for MB leprosy is differentiated according to the patient's age, namely adults or over 15 years, children aged 10-14 years, and children aged less than 10 years. Multi-drug treatment is a therapy that uses a combination of rifampin, dapsone, and clofazimine as the first choice of treatment for PB and MB leprosy. The mechanism of action of rifampin is through the inhibition of bacterial RNA polymerase. This drug also has a bactericidal effect against *M. leprosy*. Dapsone has the ability to inhibit bacterial folic acid synthesis. This drug is bacteriostatic against *M. leprae*. Clofamazine is an anti-inflammatory agent and has a little bactericidal effect. This drug is the first choice for therapy in MB leprosy.[22] Adults aged or over 15 years received rifampin 600 mg/month, dapsone 100 mg/month and 100 mg/day, clofazimine 300 mg/month and 50 mg/day. MB leprosy therapy is taken for 12-18 months.[22,23] If there is intolerance to rifampin, then second-line therapy can be given, namely dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg and clofazimine 300 mg once a month taken in front of health workers. Dapsone 100 mg, ofloxacin 400 mg or minocycline 100 mg and clofazimine 50 mg once daily. Therapy is given at a dose of 24 months in 36 months.

If there is intolerance to rifampin and dapsone, clofazimine 300 mg, ofloxacin 400 mg, and minocycline 100 mg per month can be taken in front of health workers for the first 6 months, plus clofazimine 50 mg, ofloxacin 400 mg and minocycline 100 mg per day taken at home. In the next 18 months, clofazimine 300 mg and ofloxacin 400 mg or minocycline 100 mg once a month can be taken in front of health workers, and clofazimine 50 mg and ofloxacin 400 mg or minocycline 100 mg per day. Therapy was administered in total in 24 monthly doses over 36 months. In cases of intolerance to clofazimine, rifampin 600 mg, dapsone 100 mg, and ofloxacin 400 mg or minocycline 100 mg once a month can be taken in front of health workers, and dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg per day.[13,22]

4. Conclusion

The clinical manifestations of leprosy in this patient were multiple erythematous plaques, well-defined and accompanied by scales in several parts, namely the facial region et, truncus posterior et, inferior et bilateral superior extremities, and bilateral inferior. AFB examination on both ear lobes and lesions found negative IB and 0% IM. Histopathological examination with H&E and FF staining obtained results that support the diagnosis of type BL leprosy. The therapy for the patient was MDT-WHO, namely rifampin 600 mg per month, dapsone 100 mg per month, and clofazimine 300 mg once a month was taken in front of health workers. Clofazimine 50 mg and dapsone 100 mg were taken daily at home for 12 months.

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