Morbus Hansen Multibacillary Type Mid Borderline: A Case Report
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ABSTRACT

Background: Morbus Hansen (MH) is a granulomatous infectious disease caused by an obligate intracellular pathogenic bacterium, Mycobacterium leprae (M. leprae). Cardinal signs of Hansen’s morbus (MH) include patches of numb skin, thickening of the peripheral nerves, and acid-fast bacteria (AFB) on a skin smear or biopsy. This case report aims to establish the diagnosis of mid borderline (BB) MH with clinical and histopathological examination. Case presentation: A 44-year-old woman presented with red patches on her face and body 1 month ago. Madarosis and multiple erythematous plaques confluent, poorly demarcated, raised edges, atrophic center with some smooth shiny and some rough surfaces found in the facial region and superior extremities et al. bilateral inferior with bilateral auricular infiltrates. A sensory examination of the lesion showed decreased sensitivity to pain and temperature. Skin-slit smear examination showed AFB with bacterial index (IB) +2 and morphological index (IM) 30%. On histopathological examination with hematoxylin and eosin staining, Grenz zone appeared, epithelioid granuloma affecting the epidermis, no lymphocytes, and no giant Langhans cells were found, and nerves were surrounded by lymphocytes and granulomas. On fite-faraco staining, BTA was obtained with IB +3 and IM 30%. The diagnosis of MH type BB was established, and the patient was given multidrug therapy (MDT) multibacillary (MB). Conclusion: Morbus Hansen type BB has a typical histopathological picture of granulomas composed of mature epithelioid cells, Grenz zone, AFB, enlarged and swollen nerves surrounded by lymphocytes or infiltrated with granulomas without damage. After 3 months of therapy, there was a decrease in IB and IM on AFB examination.

1. Introduction

Morbus Hansen (MH) or commonly called leprosy or leprosy, is a granulomatous infectious disease caused by an obligate intracellular pathogenic bacterium, Mycobacterium leprae (M. leprae), which was first discovered by a Norwegian doctor, Gerhard Armauer Hansen in 1873. mostly attacks the skin and peripheral nervous tissue. Distinctive destructive changes such as weakness of the affected limb, deformity, and disability are one of the main features of the disease that caused the stigma in ancient times.1,2 Risk factors for MH include living in an endemic area with poor conditions such as inadequate bedding, contaminated water, and insufficient food or other diseases that impair immune function.3

Lastoria et al. reported the prevalence of MH cases based on data from the World Health Organization (WHO) in 2015 at 0.29 per 10,000 population in the world.4,5 Singh et al. reported that the prevalence rate of leprosy in the Southeast Asia region in 2015 was 0.61 per 10,000 population, and Indonesia was a
contributor to 8% of MH cases worldwide in 2015. Based on data from the Ministry of Health of the Republic of Indonesia, there were 15,920 new cases of MH in 2017, with more male sufferers than women.

The diagnosis of MH can be established by history, physical examination, and laboratory and histopathological examination. Cardinal signs of MH include patches of numb skin, thickening of the peripheral nerves, and the presence of acid-fast bacteria on a skin smear or biopsy. The World Health Organization classifies MH into 2 groups, namely paucibacillary (PB) and multibacillary (MB), while based on the clinical, histopathological and immunological spectrum, Ridley-Jopling divides MH into 5 types, namely tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL) and lepromatous leprosy (LL). Morbus Hansen type BB is the most unstable form of MH and can develop into tuberculoid or lepromatous. Clinical manifestations of MH type BB are characterized by the presence of six or more skin lesions in the form of hypopigmented or erythematous plaques with raised margins that are less defined and atrophic in the middle or punched out and a slightly rough and shiny surface. Lesions accompanied by anesthesia were quite pronounced with the asymmetric distribution. Normal skin between BB-type MH lesions may give a “Swiss cheese” appearance. On the face may be found infiltrates and sometimes accompanied by nodules on the chin and ears. The involvement of several local asymmetrical peripheral nerves in the form of nerve enlargement accompanied by pain is common in BB type MH, but the loss of sensation in peripheral nerves is rare. On skin-slit smear examination with Ziehl Neelsen (ZN) staining, a number of M. leprae. The typical histopathological features of MH type BB are granulomas composed of mature epithelioid cells, no giant Langhans cells, Grenz zone, and BTA. Nerves are enlarged and swollen and surrounded by lymphocytes or infiltrated by granulomas but are not damaged. This study aims to describe cases of mid borderline type MH with atypical clinical symptoms accompanied by histopathological examination for diagnosis.

2. Case presentation

A 44-year-old woman came to the Dermatology and Venereology Clinic, Dr. Moewardi General Hospital with complaints of the appearance of red spots on the face and body. 1 month ago, the patient complained of the appearance of red spots on the right cheek, feeling numb/numb, no pain, no itching, and not accompanied by fever, but the patient did not check himself. One week before the examination, the patient felt a red patch on the right cheek getting thicker and increasing on the left cheek and forehead as well as both hands and feet. The patient then checked himself into the puskesmas and was referred to the Dermatology and Venereology Polyclinic, Dr. Moewardi General Hospital.

Based on the anamnesis, there were no similar complaints, a history of drug allergies, a history of food allergies, or previous atopy. The patient is a housewife. The patient lives at home and lives with her husband and two children. The patient denied any history of similar disease in the patient's family or people who lived around the patient. The patient denied any history of having lived outside the city or outside the island for a long time.

On physical examination, the patient appeared to be moderately ill, compos mentis, vital signs within normal limits, weight 57 kg, height 155 cm, and visual pain score analog scale. (VAS) 2-3. Dermatological status in the facial region appeared to be slightly madarosis, and multiple erythematous plaques were seen confluent, poorly demarcated, the edges were elevated, and the center was atrophic with a smooth, shiny surface and bilateral auricular infiltrates, bilateral superior and inferior extremity regions showed multiple erythematous plaques partially hyperpigmented well-demarcated, the edges are elevated, and the center is atrophic with a rough surface (Figure 1). Sensory examination revealed decreased sensitivity to pain and temperature in the lesion. On motor examination, there were no
From the anamnesis, physical examination, and supporting examination, our patient had a differential diagnosis of BB type MH, BL type MH, and tinea corporis. We performed simple laboratory examinations. Namely, skin scraping with KOH and skin-slit smear with ZN staining, and histopathological examination, in this case, to establish the diagnosis and rule out the differential diagnosis. Examination of skin scrapings with KOH gave negative results for fungi. On skin-slit smear examination with ZN staining, acid-fast bacteria (BTA) was found with a bacterial index (IB) +2 and morphological index (IM) of 30% (Figure 2).

Figure 1. Dermatological status check. (A-C). In the facial region, there is a slight madarosis (orange arrow), saddle nose (purple arrow), multiple erythematous plaques confluent, poorly demarcated, raised edges, and atrophic center with thin scales above (yellow arrows), and bilateral auricular infiltrates (red arrow). (D-K). In the bilateral superior and inferior extremity regions, multiple hyperpigmented partially hyperpigmented erythematous plaques are clearly demarcated, the edges are elevated, and the center is atrophic with thin scales on top (green arrows).

Figure 2. Acid-fast bacteria were painted positive with a bacterial index (+2) and a morphology index of 30% (Ziehl-Neelsen staining).
Histopathological examination was carried out by taking skin tissue using the Plong biopsy technique using a Plong biopsy tool number 4.0, and the tissue was taken perpendicularly to the subcutis depth of the skin on the right hand, then the tissue was immersed in a 10% buffered formalin solution. In the microscopic preparation of the skin, tissue was taken from the right cheek and then stained with hematoxylin and eosin (H&E) and Fite-Faraco (FF).

On macroscopic examination, the skin tissue with a diameter of 0.5 cm was yellowish brown. On microscopic examination using H&E staining (Figure 3), the epidermis shows a Grenz zone, the dermis shows an epithelioid granuloma that affects the epidermis, no lymphocytes, no giant Langhans cells, and the nerves appear surrounded by lymphocytes and granulomas. There were no signs of violence. The FF staining showed positive results for AFB with IB +3 and IM 30% (Figure 4), supporting the diagnosis of MH type BB.

Figure 3. (A) The epidermis shows the Grenz zone (blue arrows), and the dermis shows an epithelioid granuloma that affects the epidermis (red arrows) (H&E staining; 10x magnification). (B) Nerves surrounded by lymphocytes and granulomas (yellow arrow) are seen (H&E stain; 40x magnification). (C) Lymphocytes are present, and no giant Langhans cells (green arrows) are seen (H&E staining; 100x magnification).

Figure 4. (A-B) Acid-fast bacilli were stained positive with a bacterial index (+3) and a morphology index of 30% (FF staining; 100x magnification).

Based on the history, physical examination, simple laboratory examination, histopathological examination, and serological examination, the patient was diagnosed with MH MB type BB. The patient was referred back to the puskesmas for multidrug therapy (MDT) MB consisting of rifampin at a dose of 600 mg every month followed by 50 mg every day for as long as 12 months. Evaluation of therapy with clinical examination is scheduled once a month, and smear examination is scheduled every three months. In the third month after therapy, an AFB examination was performed, and the IB decreased to +1 and IM 10-15%. No new lesions were found, and no new sensory or motor impairment was found (Figures 5 and 6).
3. Discussion

Morbus Hansen (MH) or leprosy is a chronic granulomatous disease that mostly affects the skin and peripheral nervous tissue but can also affect various tissues and systems, including the eyes, upper respiratory tract, lymphoid tissue, testes, muscles, and bones.\textsuperscript{1,16} Mycobacterium leprae is thought to enter the human body through the skin and upper respiratory tract and then attack Schwann cells (SC) with a specific 21 kDa laminin-binding protein in addition to phenolic glycolipid-1 (PGL-1) which is a unique glycoconjugate on its surface, binding laminin-2 and causes demyelination due to direct bacterial ligation to the neuregulin receptor, activation of human epidermal growth factor-2 (HER-2) and extracellular signal-regulated kinases 1 or 2 (Erk1 or 2) and mitogen-activated protein kinase signaling and proliferation. (MAP kinase) as well as eliminating the conduction ability of peripheral nerves. Mycobacterium leprae attacks SC receptors, namely dystroglycan.
DG), and causes premature neurodegeneration. Macrophages are one of the most abundant host cells that come into contact with *M. leprae*. Mycobacterium leprae is phagocytosed by macrophages by intermediary complement receptor 1 (CR1) cluster of differentiation 35 (CD35), complement receptor 3 (CR3) cluster of differentiation 11b/18 (CD11b / CD18) and complement receptor 4 (CR4) cluster of differentiation 11c/18 (CD11c/18) and is regulated by protein kinases.\(^3\)

The incubation period for MH is difficult to determine because of the lack of tools to carry out adequate immunological examinations and the slow onset of the disease. The longest reported incubation period is 30 years or more, as is found in many war veterans exposed for a short time in endemic areas but living in non-endemic areas, but it is estimated to be around 3-10 years.\(^3\) Mathan et al. found that MH was most common in the age range of 21 to 40 years, and most of the sufferers were men.\(^17\) In this case, MH occurred in a 44-year-old woman. The cause of fewer MHs found in women is thought to be because women with MH do not understand the causes and symptoms of MH and have more limited access to health facilities than men. Female sufferers also experience rejection in the larger community than males.\(^1,18\) The age of the patient, in this case, was not included in the age group of most sufferers but did not rule out the possibility for patients with MH. Besides, the fear of seeking treatment which was more common in women was also found in this patient, so the patient did not immediately check his complaint.

Morbus Hansen type BB appears in patients with poor immunity and gives a clinical picture in the form of annular erythematous plaques, poorly demarcated with raised edges and atrophic and hypopigmented center of the lesion, giving a "punched out" with a rough and shiny surface. The distribution of BB-type MH lesions is asymmetrical. The clinical picture of MH type BB resembles MH type BL and tinea corporis. Neurological examination of the site of the affected skin often reveals decreased thermal sensitivity, touch and pain, and anhidrosis, especially in the center of the lesion. This neurological deficit is asymmetric. The clinical features of MH type BL are macules, papules, or plaques with numbers that are difficult to count but still appear healthy skin, smooth, shiny surface, indistinct borders, unclear anesthesia, and almost symmetrical distribution.\(^19-21\) The clinical picture of tinea corporis is a well-defined erythematous plaque with an active border and a healing center with scaling at the edges.\(^14\) Meanwhile, the clinical manifestation of psoriasis is a firmly bounded erythema plaque with thick, silvery-colored squalors on it.\(^15\) In this case the patient's fascial region appears slightly madarosis and appears to be a multi-bordered erythema plaque, less firmly bounded, the edge is elevated and the middle part is atrophied with a shiny smooth surface and infiltrates in the bilateral auricular region, the bilateral superior et inferior extremity region appears to be a partially bordered multiple hyperpigmentation erythema plaque, the edge is elevated and the middle part is atrophied with a rough surface. On sensory examination, a decrease in sensitivity to pain and temperature in the lesions was obtained. ria clinical manifestations for MH type BB.

The supporting examination carried out to establish the diagnosis, in this case, is a simple laboratory examination of skin-slit smear with ZN staining, skin scraping examination with KOH, and histopathological examination with H&E and FF staining. In BB-type MH, there are usually quite a lot of AFB germs, while in BL-type MH, there are usually a lot of AFB.\(^19\) In this case, a large number of AFB was obtained so that it supports the differential diagnosis of MH type BB and MH type BL. In the case of tinea corporis, the KOH examination will give a positive result for fungi, while in this case, the results are negative for fungi, so it is not in accordance with the differential diagnosis of tinea corporis.\(^14\)

The typical histopathological picture in MH type BB is characterized by granulomas composed of mature epithelioid cells and few macrophages, slight lymphocytic infiltration, no giant Langhans cells, Grenz zone, and BTA with IB 2+ to 3+. Nerves appear enlarged and swollen and surrounded by lymphocytes.
or infiltrated by granulomas but are not damaged. In MH type BL, a histopathological picture will be obtained in the form of a histopathological picture in the form of granulomas which are more dominated by more macrophages and fewer epithelioid cells, Grenz zone appears more clearly, and various lymphocytes and AFB with IB 3+ to 4+, nerves appear intact in the early phase. Psoriasis has histopathological features in the form of parakeratosis, acanthosis, and Munro microabscess. In this case, the histopathological picture was obtained in the form of granulomas dominated by epithelioid cells affecting the epidermis, slight lymphocytic infiltration and no giant Langhans cells, nerves surrounded by lymphocytes and granulomas, and Grenz zone. The histopathological picture, in this case, is in accordance with the histopathological picture of BB type MH so that the diagnosis of BB type MH can be established.

Therapy for MH type BB for adults recommended by WHO includes a combination of MB MDT consisting of rifampin at a dose of 600 mg every month, dapsone at a dose of 100 mg every month followed by 100 mg every day and clofazimine 300 mg every month followed by 50 mg every day for 12 months. In the third month after therapy, there was a decrease in the bacterial index and morphological index on AFB examination after therapy. No new lesions or a decrease in sensory and motor function were found.

4. Conclusion

Confirmation of the diagnosis of Morbus Hansen type BB with less typical symptoms is by AFB examination and histopathology. The results of histopathological examination, in this case, led to the diagnosis of MH type BB and the patient was given MDT MB therapy.

5. References

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