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Case Report

Lucio Phenomenon: A Rare Type of Leprosy Reaction

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I N F O

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A B S T R A C T

Introduction: Leprosy is an infectious disease caused by Mycobacterium leprae (M. leprae), which affects the skin and peripheral nerves. Lucio phenomenon is a rare leprosy reaction characterized by severe necrotizing skin lesions. This case report aims to provide clinicians with more information regarding the rare Lucio phenomenon.

Case: A 53-year-old male patient presented with worsening lesions on both lower limbs. Physical examination revealed bilateral madarosis and saddle nose. Multiple erythematous lesions with deep ulceration, multiple necrotic tissues, and bilateral extremities deformities were found. There were amputations of the right hand's digits III and V and left hand's digits V. Decreased sensory function was found in the median, ulnar and posterior tibial nerves. Acid-fast bacilli (AFB) staining revealed bacterial index (BI) +3 and morphological index (MI) 10%. Histopathological examination showed foamy macrophages, leukocytoclastic vasculitis, lobular panniculitis, and diffuse multiple perivascular infiltrates. It also had extensive areas of necrosis with diffuse neutrophil infiltrate in the deep layer of the dermis and the globes in macrophages. The patient was diagnosed with the Lucio phenomenon and given treatment in the form of Multi-Drug Therapy (MDT) for its multibacillary leprosy, corticosteroids, antibiotics, and wound care. The patient died on the 18th day of treatment.

Conclusion: Early detection is necessary to start the treatment immediately and prevent disease worsening. Although MDT and corticosteroid treatment effectively ameliorates the lesions of the Lucio phenomenon, this patient had extensive skin and nerve involvement, secondary infection, and anemia. These resulted in a poor prognosis and increased morbidity.

Keywords: Leprosy Reaction, Lucio Phenomenon, Morbus Hansen

Introduction

Leprosy (Morbus Hansen) is a chronic granulomatous infectious disease that attacks the skin and peripheral nerves. Leprosy is a serious public health problem, especially in developing countries. The cause of leprosy is Mycobacterium leprae (M. leprae), an obligate intracellular acid-fast bacillus.[1,2]

According to the World Health Organization (WHO), there

were 202,256 new cases of leprosy registered globally in 2019.[3] Based on data from the Ministry of Health of the Republic of Indonesia, the incidence of new cases of leprosy in Indonesia in 2018 was 6.08 per 100,000 population, with a prevalence rate of 0.7 per 10,000 population.[4] Ridley and Jopling developed a leprosy classification system in 1966 based on clinical, immunological, and bacteriological severity, in order: Tuberculoid Tuberculoid (TT), Borderline Tuberculoid (BT), Borderline Borderline (BB), Borderline Lepromatous (BL), Lepromatous Lepromatous (LL). Conversely, the World Health Organization divides leprosy into two types based on the number of lesions: paucibasilar leprosy (lesions is fewer than 5) and multibasilar leprosy (lesions is greater than 5).[2,5,6]

The leprosy reaction is an acute immune-mediated inflammation. All leprosy patients are at risk for this reaction, both in patients with low and high leprosy bacilli counts. Multiple lesions along the peripheral nerves, involvement of the face area, and the existence of nerve thickening are all risk factors for the occurrence of leprosy reactions. Type 1 leprosy reaction (or reversal reaction) and type 2 leprosy reaction (or erythema nodosum leprosum) are the two forms of leprosy reactions.[5,7,8] Lucio phenomenon is a rare leprosy reaction characterised by severe necrotising skin lesions. It is considered a variant of type 2 leprosy reaction or type 3 leprosy reaction.[9] Lucio phenomenon is a common symptom in individuals with lepromatous spectrum leprosy, although it can also occur in borderline spectrum leprosy patients. The diagnosis and treatment of Lucio phenomenon are frequently delayed since it is quite uncommon and hard to recognise.[10] This is a case report regarding the Lucio phenomenon that occurred in a male patient.

Case

A 53-year-old male patient came with a chief complaint of sores on both lower limbs that were getting broader for one week prior to admission to the hospital. This complaint first appeared 3.5 years ago. The initial symptom was swollen red skin on the lower leg without pain. The lesions spread and progressively consolidated a few weeks later, yet the patient had not sought any treatment. The lesions then became darker and similar complaints appeared along with sores and blisters on both hands one year prior to hospital admission. The patient also complained of difficulty in picking up things and walking. Previous history of any similar disease was unknown, while any history of other autoimmune or systemic diseases, atopy, hypertension, diabetes mellitus, and drug or food allergy was denied. History of close contact with the patient's child, aged 10 years who lives in an orphanage. The patient's child complained of symptoms of the appearance of hypopigmented lesions that underwent hypoanesthesia. The patient's child was diagnosed with MH type PB and underwent treatment for approximately one year. There are no similar symptoms in the patient's child.

The physical examination reported moderate illness on its general appearance with full consciousness. The blood pressure was 110/79 mmHg, pulse rate was 110 beats/minute, respiratory rate was 20 times per minute, and temperature was 36.7°C. The patient weighed 45 kg with 160 cm height. Bilateral madarosis and a saddle nose were observed in the face region (Figure 1). Multiple erythematous lesions with deep ulceration, multiple tissue necrosis, and bilateral human abnormalities were seen in the upper limb region, with amputation of the right hand's digits III and V, and the left hand's digit V (Figure 2 A-C). Multiple well-defined erythematous lesions with profound ulcerations were detected in both lower extremities regions (Figure 2 D-F).

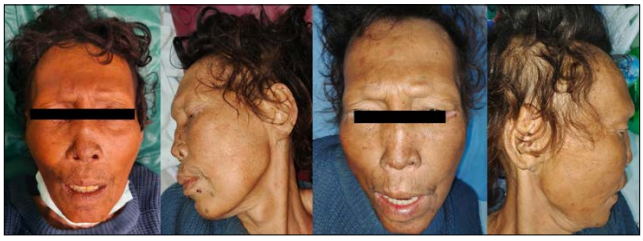

Figure 1.Facial Region; Bilateral Madarosis and Saddle Nose were Seen

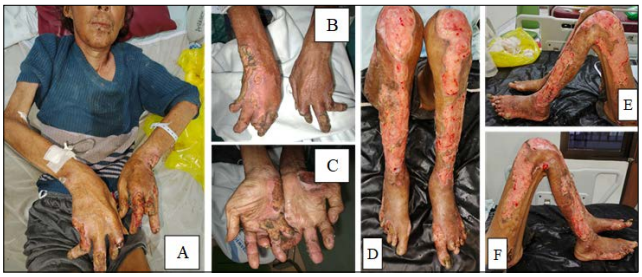

Figure 2.Bilateral Superior and Inferior Extremity Regions.A-C. Multiple erythematous lesions, deep ulcerations, multiple tissue necrosis, and bilateral manus deformities were seen, accompanied by amputation of digits III and V of the right hand, and amputation of the fifth digit of the left hand.D-F. Multiple well-defined erythematous lesions with deep ulceration of the bilateral lower extremities were seen

Neurological examination revealed reduced sensory function in the median, ulnar, and posterior tibial nerves. Examination of acid-fast bacilli (AFB) in the form of a skin slit smear (SSS) stained with Ziehl-Nielsen staining taken from both ear lobes of the patient showed a bacterial index (BI) +3 and a morphological index (MI) 10% (Figure 3). Routine haematology laboratory examinations showed a decrease in haemoglobin, hematocrit, and erythrocytes,

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with an increase in leukocytes. A decrease in albumin and creatinine levels, with electrolytes in the form of sodium, potassium, and calcium, were also observed in the patient.

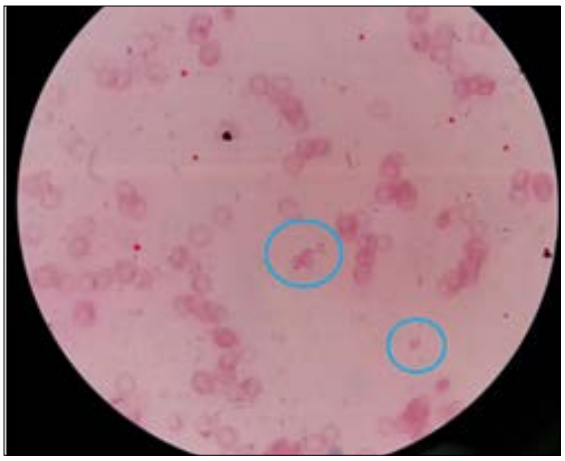

Figure 3.Examination of the Skin Slit Smear (SSS) obtained the Results of a Bacterial Index (BI) +3 / LPB and a Morphology Index (MI) of 10%

H&E staining from a lower leg ulcer revealed foamy macrophages leukocytoclastic vasculitis, lobular panniculitis, diffuse multiple perivascular infiltrates, and significant regions of necrosis in the deep dermis with diffuse neutrophil infiltrates (Figure 4 A-C). Numerous acid-fast bacilli (AFB) were detected in macrophages (globies) with IB +5 on fite faraco (FF) staining (Figure 5). The histopathological image was consistent with Lucio phenomenon description.

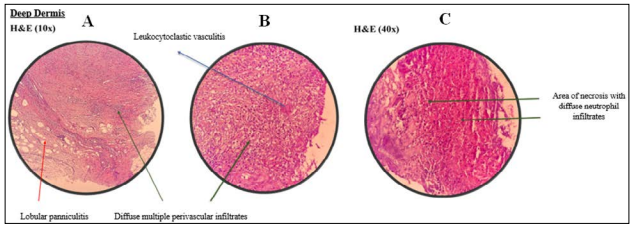

Figure 4.Histopathological Examination with Hematoxylin&Eosin (H&E) Staining from a Biopsy of the Lower Extremity Region. A-B.10x magnification;foamy macrophages were seen with leukocytoclasticvasculitis, lobular panniculitis, and diffuse multiple perivascularinfiltrates. C.40x magnification;large area of necrosis with a diffuse neutrophil infiltrate was identified

Based on the history, physical examination, and diagnostic investigations, the patient was diagnosed with Lucio phenomenon. This patient was given treatment with methylprednisolone 62.5 mg/day IV, injection of ceftriaxone 1gr/12 hours IV, Multi Drug Therapy (MDT) for multibacillary leprosy (MB) in the course of 12-18 months to cure the Lucio phenomenon reaction. Additionally, wound compress with 0.9% NaCl for 10-15 minutes accompanied by the use of gentamicin ointment 2 times per day were being done.

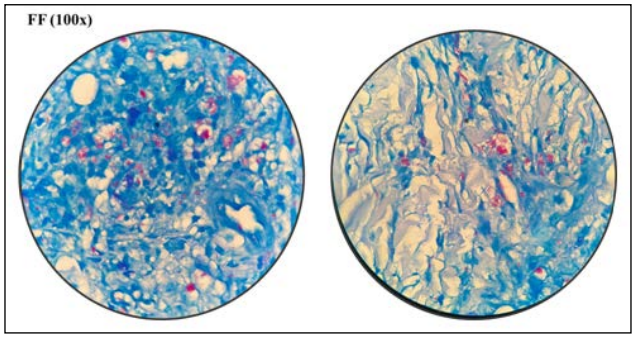

Figure 5.Histopathological Examination with Fite Faraco (FF) Staining. There were abundant acid fast bacilli (AFB) in macrophages (globi) with BI +5

The patient died on the 18th day of treatment, which is 6 days after undergoing treatment with the MDT regimen.

Discussion

The leprosy reaction is a severe immunological reaction that affects 20-50% of leprosy patients and is the major cause of disability among leprosy patients. The immune response to M. leprae triggers a cascade of humoral and cellular immunological responses, resulting in leprosy reactions. A type 1 and 2 of leprosy reactions are both possible outcomes of the immunological response to M. leprae.[2,5,11] Leprosy reactions are very rarely found in our dermatology and venerology polyclinic. Patients who come are usually new patients and routine controls only. The incidence of finding new MH patients at our dermatology and venerology polyclinic every month was around 3-5 patients with varying types between PB and MB.

The type 1 leprosy reaction is a delayed-type hypersensitivity reaction (type 4 hypersensitivity), which develops simultaneously with the cellular immune response to the antigenic determinants of M. leprae. Increased release of mycobacteria antigens in borderline spectrum leprosy (BT, BB, and BL) cause type 1 leprosy reactions, which are believed to be the result of worsening of preexisting or newly forming T cell responses. The most common histopathological findings in this reaction are periadnexal inflammatory infiltrate and lymphocytes in the granuloma, followed by papillary dermal oedema and intercellular oedema within the granuloma.[12-14]

Contrarily, type 2 leprosy reaction, known as erythema nodosum leprosum (ENL), is a systemic event that occurs in cases of borderline lepromatous and lepromatous spectrum leprosy. Type 2 leprosy reaction is a type 3 hypersensitivity reaction associated with the deposition of immune complexes produced by the binding of antigens from the destruction of bacilli with antibodies. This reaction is also associated with increased levels of proinflammatory cytokines, followed by neutrophilic infiltration which contributes to various clinical manifestations.[5,12,14] The most

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common histologic findings in this reaction are periadnexal inflammatory infiltrate, neutrophils in the granuloma, foamy macrophages followed by papillary dermal oedema, and neutrophilic panniculitis.[13]

The variant of type 2 leprosy reaction or type 3 leprosy reaction is called the Lucio phenomenon.[9] Lucio et al. in Ramal, C et al. described this leprosy which is known as "lazarine leprosy" in a study published in 1852. There is no localised skin penetration in this type. Reaction episodes appear as red spots that darken and ulcerate over time, producing atrophic and hypochromic scars with thin hyperpigmented borders. Lesions that spread upward are most usually found on the feet, legs, hands, forearms, and arms, with the face and chest being uncommon exceptions. Furthermore, in 1948, Latapi et al. in Ramal, C et al., added some characteristics to the description of Lucio et al. and called it the Lucio phenomenon.[15] This phenomenon is one of the clinical forms of lepromatous spectrum leprosy that occurs rarely in borderline spectrum leprosy. To date, the pathophysiology of Lucio phenomenon has remained unknown.[16] Nonetheless, the deposition of immunoglobulin G and C3 found in blood vessels and circulating immune complexes, supports an autoimmune mechanism as a possible aetiology. Direct damage and invasion by bacilli have also been proposed as possible causes of Lucio phenomenon. The diagnosis of Lucio phenomenon is based on the clinical manifestations and medical history.[17]

The clinical manifestations of Lucio phenomenon are skin lesions ranging from painful ecchymoses or macular purpura to blisters that rupture and develop into ulcers. These lesions are generally located in the lower extremities and develop distally to proximally. The upper extremities, trunk, and face may also be affected.[17] The lesions seen in this case included lesions that started in both lower limbs and progressed upwards. The lesions are multiple erythematous with deep ulceration, multiple necrotic tissue, and followed with deformities.

Diffuse infiltration of the skin in more advanced lesions gives the skin a thicker ichthyosis-like appearance. Systemic manifestations such as fever, chills, malaise, myalgia and arthralgia tend to occur after skin lesions. Peripheral nerve hypertrophy is a neurologic pathological feature of leprosy. The infection is usually centripetal, starting with the sensory nerve fibres and progressing to the motor fibres, thus explaining how sensory symptoms precede motor symptoms.[17]

Furthermore, the most common abnormalities found on laboratory examination are anaemia, hypocalcemia, hypoalbuminemia, leukocytosis, neutrophilia, and increased erythrocyte sedimentation rate.[17]

The patient had anaemia, hypoalbuminemia, hyponatremia, and hypocalcemia in this case. The histopathological findings may vary depending on the stage of the disease. Generally, necrotizing panvasculitis is identified; the epidermis shows foci of ischemic necrosis, often with ulceration and hyperplasia. The features of diffuse lepromatous leprosy can be seen in dermis, such as extensive infiltration by foamy macrophages Virchow cells with abundant AFB inside (globies) or outside the stroma associated with lymphocytes, around blood vessels, nerves, and adnexal structures including erector muscles. Blood vessels such as muscular arteries, arterioles, capillaries, venules, and skin veins (including the hypodermis) may also be involved in Lucio phenomenon; leukocytoclastic vasculitis in the venules generally may appear, which will show IgG, IgM, C3, C4, and fibrin after immunofluorescence staining. This is an acute reaction, in which the cellular immune response is not strong enough and the humoral response is exaggerated, thus the host cell develops immune complex disease.[18] Based on histopathological aspects, the appearance of frothy macrophages, leukocytoclastic vasculitis, lobular panniculitis, diffuse multiple perivascular infiltrates, and large areas of necrosis with diffuse neutrophilic infiltrate in the deep dermis, as well as the abundance of globi in the macrophages in this patient confirm the diagnosis of Lucio phenomenon.

According to WHO recommendations, treatment for Lucio phenomenon is similar to multibacillary leprosy treatment, particularly MDT which includes: rifampin 600 mg/month, clofazimine 300 mg/month, dapsone 100 mg/day, clofazimine 50 mg/day for 1 year, and prednisone 20-30 mg given daily until the acute phase is under control. Hospitalisation is recommended for patients with Lucio phenomenon.[18] In this patient, the treatment was given according to WHO recommendations, which are methylprednisolone and MDT for multibacillary leprosy in the course of 12-18 months, accompanied by ceftriaxone injection and wound care in the form of 0.9% NaCl compresses and gentamicin ointment.

The prognosis for leprosy patients who receive MDT early in the disease is usually excellent. However, patients who presented with extensive skin and nerve involvement, secondary infection, and anaemia, as in the case reported here, have a poor prognosis.[19] The patient, in this case, died on the 18th treatment day, which is 6 days after undergoing treatment with the MDT regimen.

Conclusion

Early detection of Lucio phenomenon is a key for immediate treatment in order to prevent the worsening of this disease. Although MDT treatment and corticosteroids according to WHO recommendations have been shown to be effective in improving the lesions of Lucio phenomenon, the patient, in this case, had extensive skin and nerve involvement,

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secondary infection, and anaemia which could result in poor prognosis.

Conflict of Interest: None

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