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Case Report

Lucio phenomenon with secondary pseudomonas aeruginosa infection: A rare case report

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Abstract Lucio phenomenon (LP) is a rare type of leprosy reaction. Lesions may begin as erythematous patches then progress to necrosis and leave fibrotic tissue. Secondary bacterial infection is common in patients with LP The organism that is commonly found is *Pseudomonas aeruginosa* which also found in this case. A 57-year-old woman came with complaints of black and painful wounds on hands and feet since 8 weeks ago. Bilateral madarosis, saddle nose, and infiltration on auricularis region dextra-et-sinistra were found in facial examination. Multiple ulcers with a firmly bordered, irregular edge, erythem base, partially accompanied by necrotic tissue, slough, blood, pus and granulation were found in extremities examination. The chosen management are multibacillary multi-drug-therapy (MB MDT), methylprednisolone, and amikacin. The wounds were treated with NaCl and mupirocin ointment. The main risk factor of LP is neglected leprosy infection. Secondary infection on LP is common. Management of LP with secondary infection consists of MB MDT and antibiotic base on the underlying bacterial infection. Lucio phenomenon is a rare severe type reaction of leprosy and associated with disability. Lucio phenomenon can occur before, during and after a complete MDT regimen. Systemic antibiotics are usually needed to treat LP with secondary infection.

Key words
Lucio phenomenon; Leprosy; Pseudomonas aeruginosa.

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*.[1] Lucio phenomenon is a type III leprosy reaction which is suspected to be related to a new species of *Mycobacterium*, namely *M. lepromatosis*.[2,3] The World Health Organization (WHO) in 2021 reported that in 2019 there were 202,256 new cases of leprosy globally.[4] The Data and Information Center for the Directorate General of Disease Prevention and Control of Indonesia in 2019 reported the prevalence rate of leprosy were 0.7 cases/10,000 population.[5] Marissa, *et al.* in 2020 reported 6 new LP cases in Jakarta.[6] Lucio phenomenon generally occurs in leprosy patient who do not receive treatment or inadequate therapy.[7] Clinical features of LP are erythematous spots in various shapes and sizes that are painful. In 24-48 hours infiltration will appear, then on the third or fourth day, the lesions will become darker followed by vesicles or bullae that cause necrosis.[6] Secondary bacterial infection often occurs in patients with LP. Organisms that are commonly found are S*taphylococcus aureus*, *Pseudomonas aeruginosa* and *Proteus mirabilis*.[3] Supporting examinations to establish the diagnosis of LP include acid-fast-bacteria (AFB) examination, histopathological examination with Hematoxylin Eosin (HE) and Fite-Faraco (FF) staining and immunopathological examination.[8,9] Treatment of LP includes MDT therapy according to the

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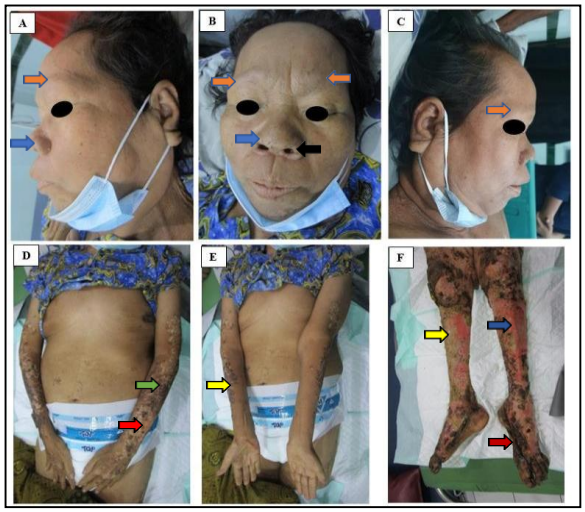

Figure 1. (A-C) The facial region shows madarosis (orange arrow), the nasal cavum appears saddle nose (blue arrow) accompanied by blackish erosion and crusts (black arrow). (D-E) Bilateral superior extremity region shows multiple ulcers with an erythematous base with irregular borders (red arrows), partially covered with crusts (green arrows). (F) Bilateral lower extremity region showing multiple ulcers on an erythematous base with irregular borders well defined (blue arrows), accompanied by slough, blood, pus (yellow arrows) and necrotic tissue (red arrows).

type of leprosy, high-dose corticosteroids (1mg/kg/day), and systemic antibiotics.[10,11] This case report aims to increase knowledge about the diagnosis and management of LP with secondary *Pseudomonas aeruginosa* infection so as to reduce disease morbidity and mortality

Case Report

A 57-years-old female patient came to the Dermatovenereology Department of Dr. Moewardi General Regional Hospital (RSDM) Surakarta with the main complaint of wounds on hands and feet. Eight weeks before examination, the patient complained of numbness and pain in her feet. The patient then went to general practitioner and was given Amoxicillin 3x500mg, Allopurinol 1x300mg, Mefenamic Acid 3x500mg and Piroxicam 1x10mg. The patient's complaints were reduced. Two weeks later the patient complained of red bumps and spots appearing on her hands, feet and both ears which were getting wider and accompanied by blisters that burst into open wounds. The patient then went back to the general practitioner and was given 1x4 mg of methylprednisolone, 3x0.5mg of dexamethasone, 1x10mg of loratadine and concoction ointment. Two weeks before entering the hospital, complaints did not improve and the patient felt increasingly weak, then the patient was referred to RSUD Dr. Moewardi. The patient admitted that she had a history of diabetes mellitus for 3 years and did not routinely take medication. There was no history of leprosy and lived in an endemic area previously, history of trauma and hypertension was denied.

On physical examination, the general condition of the patient appeared to be in moderate pain. Vital signs within normal limits, namely BP 120/74 mmHg, HR 98x/minute, RR 24x/minute, temperature 36.8^{o}C and pain scale 3. Bilateral madarosis, saddle nose, and infiltration on auricularis region dextra et sinistra were found in facial examination. Multiple ulcers with a firmly bordered, irregular edge, erythem base, partially accompanied by necrotic tissue, slough, blood, pus and granulation were found in extremities examination **(Figure 1).** On examination of nerve function, motoric function of the common peroneal nerve bilaterally and sensoric function of the ulnar nerve bilaterally, bilateral median nerve and bilateral posterior tibial nerve were found decreased. Based on the results of the history and physical examination of the patient, our differential diagnosis was LP and necrotizing Erythema Nodosum Leprosum (ENL) in lepromatous leproy (LL)-type leprosy.

Laboratory examination with Ziehl Nielsen staining showed positive results with the finding of AFB with a bacterial index (IB) +3 and a morphological index (IM) of 5%. On laboratory blood tests, there was a decrease in hemoglobin,

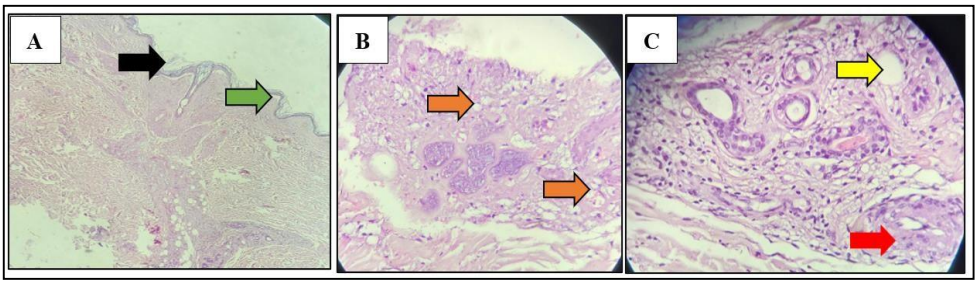

Figure 2 Histopathological examination with HE staining. (A) 4x magnification shows hyperkeratosis (black arrow), Grenz zone (green arrow). (B) 10x magnification shows adipose tissue/nodular/lobar paniculitis (orange arrow). (C) 40x magnification shows small blood vessels filled with erythrocytes (red arrows) and foam cells were also found (yellow arrows).

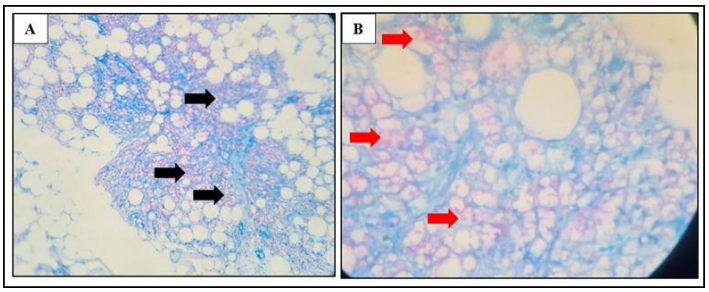

Figure 3 (A-B) Histopathological examination with FF staining showed positive results in which many AFB was found. Partially intact and partially fragmented, stained red in the dermis layer (black arrow) and in the endothelial layer of blood vessels which partially invaded the blood vessels (red arrows).

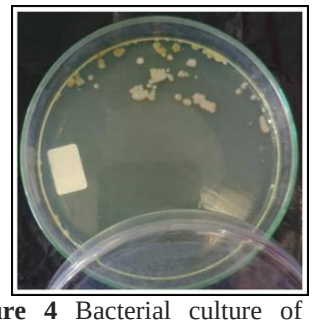

Figure 4 Bacterial culture of pus in nutrient agar media. Fluorescent, round, smooth colonies were seen. These results indicate the presence of Pseudomonas aeruginosa

increase in leukocytes, increase in neutrophils and decrease in lymphocytes level. Anti-PGL-1 ELISA examination showed IgM >6300u/ml (normal value 605 u/ml), IgG 417 u/ml (normal value 630 u/ml). The MH PCR examination showed a positive result. The results of histopathological examination of the biopsy performed on the ulcer in the dextral gluteus region with HE staining showed a microscopic picture of the epidermis with basket-wave-type hyperkeratosis, atrophy and flattening of the rete ridges. Foamy cells in the lower dermis, vasculitis and perivascular infiltrate were also found **(Figure 2).** The results with FF staining showed that many AFB were intact and some were granular and fragmental stained red (IB +5) in the globi and some invaded the blood vessels **(Figure 3).** The results of the pus culture found *Pseudomonas aeruginosa* bacteria sensitive to amikacin and meropenem, as shown in **Figure 4.**

Based on the history, physical examination and supporting examinations, the patient was diagnosed with LP. The patient was hospitalized and was given soft diet therapy 1700 kcal, Asering infusion 20 drops/minute, MB MDT (rifampin 600mg/month, dapsone 100mg/day, clofazimine 50mg/day and 300mg/month), methylprednisolone tablets 48mg/day, ranitidine injection 50mg/12 hours, meloxicam tablet 15mg/day, vitamin B 1x1 tablet. The patient was given systemic antibiotics according to the results of the pus culture, namely intravenous amikacin 500mg/24 hours for 7 days. Wound care was done with 0.9% NaCl and mupirocin ointment twice-a-day. After receiving therapy and care for eight days in the inpatient unit, the patient was allowed to continue therapy on an outpatient basis and the lesions were repaired in the first month after therapy. The results of a re-examination of the ear serum were a decrease in IB +1 and IM 0%.

Discussion

Leprosy is a chronic granulomatous infection caused by *M. leprae* which attacks the peripheral nerves, skin, oral mucosa, upper respiratory tract, reticuloendothelial system, eyes, muscles, bones and testes. Leprosy reaction is an immunological reaction which has a significant impact on the course of the disease and is associated with disability. This reaction was first discovered in Mexico in 1853 by Lucio and Alvarado then in 1948 by Latapi and Zamora.[12,13] The most common leprosy reactions are reversal reaction (type 1 reaction) and ENL (type 2 reaction), while LP is a severe type reaction that is rarely found and occurs in patients with diffuse non-nodular lepromatous leprosy who have not received or have not completed therapy. Lucio phenomenon is also called "pretty leprosy" or lepra bonita because it gives a clinical picture of the skin that is not typical and does not cause complaints to patients, so that diffuse lepromatous leprosy is often not diagnosed.[14] Lucio phenomenon is a rare skin disorder. Blok *et al.*'s 2020 study in the Netherlands stated that the prevalence of leprosy occurred in more than 200,000 new cases per year in the world's population.[15] Pinheiro *et al.*'s 2020 study in Brazil stated that the prevalence of new cases of leprosy from 2014 to 2018 was 13.64% per 100,000 per year.[16] Research by Kariosentono *et al.* in 2020 in Surakarta stated that the prevalence of leprosy in 2018 was 6.08 per 100,000 cases with an average of 0.7 per 10,000 population. Cipto Mangunkusumo Hospital in Jakarta in the 2013-2017 period reported 6 cases of the LP with male and female incidence, namely 5:1.[6]

The clinical manifestations of LP are often atypical so that the disease is often ignored. The initial clinical features of LP include infiltrates on the face and hands that resemble myxedema and give the impression of healthy skin, at a later stage teleangiectasias appear on the body and face, the earlobes appear edematous, erythema and shiny, and generalized infiltrates which give the impression of skin that looks smooth. Lucio phenomenon is also known for the term leonina facies which is characterized by a symmetrical centrofacial distribution of lesions and loss of eyelashes and eyebrows (madarosis). Involvement of the nasal mucosa also causing septal damage and deformity of the nasal skeleton (saddle nose).[18] Lucio phenomenon often occurs in 3-4 years after disease onset. Clinical manifestations of LP begin with erythematous patches on the extremities that expand and followed by infiltration within 24-48 hours. On the third or fourth day, the lesions turn into dark purpura with necrosis in the center. After a few days, a dark red scar will appear and peel off leaving a white atrophic scar.[19] In this patient case, madarosis was found, there was an infiltrate in the ear, there was peripheral neuropathy (gloves and stockings anesthesia). The patient complained of reddish spots appearing on both fingers and both feet which were getting wider accompanied by blisters in several parts which then broke into ulcers with extensive necrotic tissue.

Based on history and physical examination, this patient was diagnosed with LP in diffuse lepromatous leprosy and necrotizing ENL. Clinical manifestations of necrotizing ENL include lesions that look like papules, nodules or well-defined plaques accompanied by painful vasculonecrotic lesions.[20] In this patient, the lesions are diffuse and there is no clinical picture of nodules or plaques that are well defined so that the differential diagnosis of necrotizing ENL in LL leprosy can be removed.

Microscopic examination (AFB examination) of serum samples taken from ears, skin lesions or nasal mucosa stained with Ziehl-Neelsen stain can help determine the type of leprosy and

assess treatment results. In both types of *Mycobacterium*, both *M. leprae* and *M. lepromatosus* will give image of red bacilli on a blue background.[21,22] In LP cases, the number of AFB is very large and it is easy to find in the infiltrates of skin lesions and other body parts. In this case, many AFBs were found on microscopic examination of both earlobes and the interpretation of the results of IB +3 showed that AFB were still found in large numbers and IM 5% indicated that leprosy in patients was still infectious because they had not received treatment.

Histopathological examination can assist in establishing the diagnosis of LP. In LP, the histopathological picture of the epidermis appears normal with the basal layer having reduced melanin, while the dermis shows dilated blood vessels, endothelial proliferation, perivascular or perineural infiltrates by macrophages and lymphocytes to form vasculitis and necrosis. The histopathological picture of the necrotizing ENL shows different abnormalities because it is located in the hypodermis layer which is accompanied by panvasculitis and paniculilis as well as a wider picture of necrosis.[23] In this case, the histopathological picture of the skin biopsy taken from the ulcer of the right gluteus region showed vasculitis and invasion of AFB in the blood vessel endothelium with a picture that matched LP so that from the histopathological picture a diagnosis of necrotizing ENL could also be ruled out.

Examination of bacterial culture and antibiotic sensitivity in LP ulcers is important to determine additional antibiotic therapy as a management of secondary infections and prevent sepsis. Saha *et al.*'s 2019 study in India showed that LP was generally accompanied by secondary *P. aeruginosa* infection, so systemic antibiotics were needed to reduce sepsis complications.[24] In this patient, pus culture and antibiotic sensitivity were examined for indications of pus present in an ulcer covered with extensive necrotic tissue. *Pseudomonas aeruginosa* is sensitive to the antibiotics piperacillin plus tazobactam (91.6%), cefoprazone plus sulbactam (83.3%), amikacin (83.3%) and imipenem (83.3%).[24] The results of pus culture and antibiotic sensitivity in this patient showed a *P. aeruginosa* organism that sensitive to the antibiotic amikacin. *Pseudomonas aeruginosa* is a gram-negative bacterium that is often found as a cause of opportunistic infections, but can also appear in immunocompetent patients. The clinical manifestations of P. aeruginosa infection range from localized skin infection to life-threatening disease.[25]

In the management of LP, an MDT regimen of leprosy type MB is given to eradicate AFB and then the response to therapy is evaluated after 4-6 weeks of therapy. Lucio phenomenon's patients can also be given systemic corticosteroid therapy equivalent to prednisone 60-80mg/24 hours. Systemic antibiotics need to be given in the management of LP with secondary infection because LP ulcers can expand and there is necrotic tissue that can cause sepsis. Amikacin is one of the antibiotics that can be given to patients with LP with secondary infection of P. aeruginosa. Amikacin is a broad-spectrum antibiotic drug that belongs to the aminoglycoside group. Amikacin is generally used in severe gram-negative bacterial infections. Mechanism of action of Amikacin is by binding to the bacterial 30 S ribosomal subunit, resulting in inhibition of protein synthesis.[26] In this patient, MB MDT as recommended by WHO was given as soon as possible. Corticosteroid tablets in the form of methylprednisolone 48mg/24 hours were also given and then tapered off slowly according to clinical improvement. This patient was also given intravenous amikacin 500mg/24 hours.

Necrotomy is needed in the management of ulcers with extensive necrotic tissue as a wound bed preparation aimed at wound healing and removing components that interfere with the healing process. This patient also underwent necrotomization, especially in the bilateral lower extremities and was given systemic antibiotics to prevent complications.

The wound care technique for LP ulcers is generally not much different from other ulcer treatments which is by compressing the ulcer with 0.9% NaCl and then applying topical antibiotics such as mupirocin ointment.[27] Wound care was performed with 0.9% NaCl compresses and then smeared with mupirocin ointment twice-a-day. Mupirocin is an antibiotic agent previously known as pesudomonic acid A which is the main fermentative product of *Pseudomonas* fluorescence. Mupirocin is effective against both gram-positive and gram-negative bacteria. Mupirocin inhibits protein ribonucleic acid (RNA) and bacterial cell wall synthesis. This inhibition occurs at a specific target of mupirosine, namely on isoleucyl-transRNA synthetase. Cellular levels of isoleucyl RNA will cause inhibition of bacterial synthesis, so that bacteria cannot grow and develop.[28] At the evaluation of the first month after therapy, improvements were found in the lesions and SSS examination, namely a decrease in IB from +3 to +1 and IM 5% to 0, therapy was continued until complete remission.

Conclusions

A case of LP in a 57 year old woman has been reported. The diagnosis is based on anamnesis, physical examination and histopathological examination. Therapeutic option for this patient is MB MDT, methylprednisolone, and intravenous amikacin. The wounds were treated with NaCl and mupirocin ointment. At the evaluation of the first month after therapy, improvements were found in the lesions and AFB examination and the therapy was continued until complete remission. Early detection and appropriate investigations are necessary to establish the diagnosis and prevent worsening of LP. Timely diagnosis will provide the optimal therapeutic prognosis.

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