Severe Erythema Nodosum Leprosum in Lepromatous Leprosy Patient

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ABSTRACT

A case of a 58-year-old woman with lepromatous leprosy and severe ENL reaction is reported. The patient has symptoms of pustules for 1 year and the nodules were getting worse in the last week, accompanied by fever, joint pain, nausea, and vomiting. Physical examination revealed madarosis, infiltrates of both ears, and multiple painful erythematous nodules on the extremities and trunk. Slit skin smear examination showed bacterial index +3 and morphological index of 15%. Histopathological examination revealed neutrophil infiltration and vasculitis in the upper dermis. The patient was diagnosed with lepromatous leprosy and severe ENL reaction. The patient received multidrug therapy and methylprednisolone (62.5 mg/day), which was gradually reduced. The ENL reaction is caused by the deposition of *M. leprae* antigens and antibodies in small blood vessels, resulting in vasculitis and the release of enzymes that damage tissues. ENL reactions are commonly found in multibacillary MH and occur before, during, and after treatment. This reaction is mediated by cytokines produced by T-helper-2 (Th2). ENL reactions can cause disability.

Keywords: Erythema nodosum leprosum, leprosy, multi-drug therapy

ABSTRAK

Dilaporkan sebuah kasus pada wanita berusia 58 tahun dengan kusta lepromatosa dan reaksi ENL parah. Pasien memiliki gejala bintil-bintil selama 1 tahun, memburuk dalam 1 minggu terakhir disertai demam, nyeri sendi, mual dan muntah. Pemeriksaan fisik menunjukkan madarosis, infiltrat pada kedua telinga, dan beberapa bintil eritematosa yang nyeri pada ekstremitas dan batang tubuh. Pemeriksaan apusan kulit celah menunjukkan indeks bakteri +3 dan indeks morfologi 15%. Pemeriksaan histopatologi menunjukkan infiltrasi neutrofil dan vaskulitis dermis bagian atas. Pasien didiagnosis kusta lepromatosa dan reaksi ENL parah. Pasien menerima terapi *multidrug* dan *methylprednisolone* 62,5 mg/hari yang secara bertahap dikurangi. Reaksi ENL disebabkan oleh pengendapan antigen dan antibodi *M. leprae* di dinding pembuluh darah kecil, mengakibatkan vaskulitis dan pelepasan enzim yang merusak jaringan. Reaksi ENL umumnya ditemukan pada MH multibasiler dan terjadi sebelum, selama, dan setelah pengobatan. Reaksi ini dimediasi oleh sitokin yang diproduksi oleh *T-helper-2* (Th2). Reaksi ENL dapat menyebabkan kecacatan. **Adelia Wuri Pramudita, Harijono Kariosentono, Annisa Marsha Evanti, Aiman Hilmi Asaduddin. Eritema Nodosum Leprosum Parah pada Pasien Kusta Lepromatosa.**

Kata Kunci: Eritema nodosum leprosum, kusta, terapi multi-obat.

INTRODUCTION

Morbus Hansen (MH) or leprosy is a granulomatous chronic infectious disease caused by *Mycobacterium leprae* (*M. leprae*).[1] Leprosy initially attacks skin tissue and peripheral nerves, further impacting oral mucosa, upper airway, reticuloendothelial system, eyes, muscles, bones, and testicles but not the central nervous system.[2] The World Health Organization (WHO) in 2020 reported 127,558 new leprosy cases from 129 countries. In Indonesia, new cases of leprosy were recorded as many as 11,173 cases.[3,4]

Leprosy reactions occurred in 30%–50% of leprosy patients and may appear before, during, and after leprosy treatment. Erythema Nodosum Leprosum (ENL) or type 2 reactions cause inflammation in various organs, such as neuritis, lymphadenitis, arthritis, nephritis, and vasculitis.[4] ENL reactions are generally accompanied by fever, arthralgia, and malaise,[3] thus can be misdiagnosed with other diseases.

Leprosy reaction treatment aims to relieve inflammation and pain, prevent recurrent reaction episodes, and prevent nerve damage. Very mild reactions can be treated with non-steroidal anti-inflammatory drugs (NSAIDs), while more severe leprosy reactions are treated with corticosteroids. Prompt and proper management may reduce the risk of

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disability complications in MH patients with ENL reactions.[5,6]

A case of severe erythema nodosum leprosum with an unspecified complaint of joint nodule was reported.

CASE

A 58-year-old woman with complaints of red nodules and spots on the body, arms, and legs. The nodules started on both lower limbs 1 week ago, then spread to both upper limbs, upper and lower arms, back, and stomach. The nodule was painful when pressed. The patient also complained of fever, joint pain, nausea, and vomiting. The nodules on both legs have occurred since the last year, which sometimes get better spontaneously. She noticed that her eyebrows and eyelashes had fallen out since the last 8 months, accompanied by swelling and darker discoloration of both earlobes. Since last week, the nodules have become more widespread, accompanied by a high fever and severe pain. Then, she was taken to the emergency room of Dr. Moewardi Hospital.

The vital sign of the patient was within the normal limit. Dermatological examination can be seen in **Figure 1**. Anesthesia was found in the second to fourth left toe, the distal part of the left foot, the right big toe, and the medial side of the right instep. Peripheral nerve examination showed bilateral enlargement of ulnar, common peroneal, and posterior tibialis nerves with a rubbery consistency. All enlarged nerves were accompanied by tenderness.

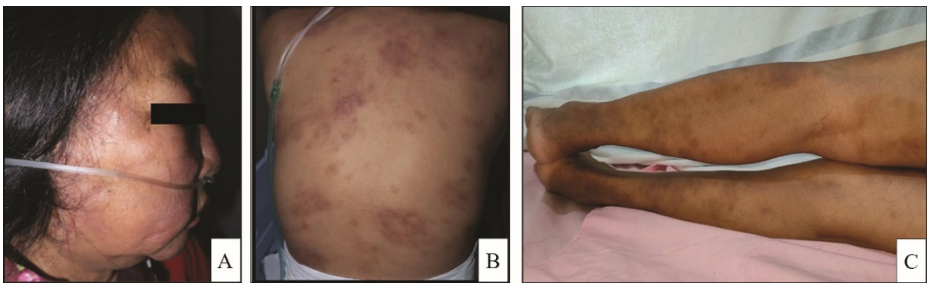

Figure 1. A–C. Dermatologic examination of the facial region showed madarosis, bilateral auricular region showed multiple infiltrates, violaceous, diffuse, generalized areas appeared patches to dim to hyperpigmented erythematous plaques, multiple discrete, circumscriptive to diffuse, partly confluent, accompanied by erythematous subcutaneous nodules, multiple, discrete, rubbery consistency with tenderness.

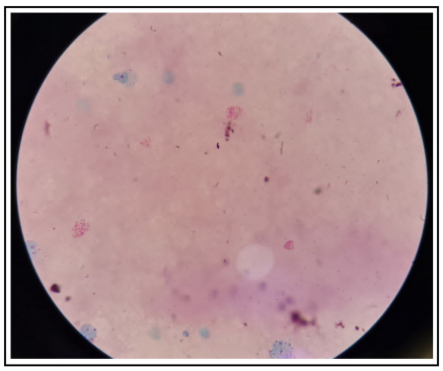

Figure 2. Bacterioscopy examination of thepatient's skin lesions.

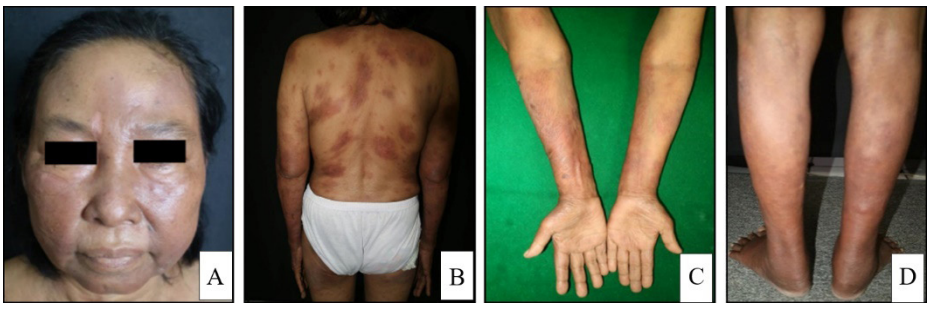

Figure 3. A–D. In the 1st week control after hospitalization, lumps in extremities and body had diminished, leaving multiple erythematous plaques with minimal pain.

Laboratory examination showed anemia (hemoglobin 9.0 g/dL), leukocytosis 14,900 uL, thrombocytosis 662,000 g/dL, hypoalbuminemia 3.1 g/dL, hyponatremia 128 mmol/L, and hypochloridemia mia 92 mmol/L. Bacterioscopy examination obtained a bacterial index of +3 with a morphological index of 15% (**Figure 2**). The patient was diagnosed with MH-type lepromatous leprosy (LL) without treatment, recurrent ENL reactions, anemia, and grade 1 leprosy defects.

The patient underwent hospitalization with the management of multidrug therapy (MDT) MB (rifampicin 600 mg/month, dapsone 100 mg/day, and clofazimine 300 mg/month, followed by 50 mg/day). MDT MB treatment was planned for a minimum of 12 months. Other treatments included intravenous paracetamol 1g/8 hours for fever, intravenous methylprednisolone 62.5 mg, intravenous ranitidine 50 mg/12 hours, ketorolac 30 mg/8 hours, desoximethasone ointment 0.25% 2 times daily on erythematous skin lesion area, and urea cream 2 times daily after bath on skin without lesions.

On the eighth day of treatment, the bumps improved, pain decreased, and no new lumps appeared. Methylprednisolone was reduced to oral 1x32 mg for 7 days, then 1x24 mg orally for 14 days. Topical drugs were continued. After one week, lumps had diminished with minimal pain **(Figure 3. A–D).**

DISCUSSION

Erythema nodosum leprosum (ENL) is an immunological reaction in not adequately treated MH cases. ENL affects approximately 50% lepromatous leprosy (LL) and 10% borderline leprosy (BL) patients. The incidence per person-years at risk (PYAR) of ENL was estimated between 1 and 8 per 100.[7] The ENL reaction is associated with changes in cytokine activity. Increased *M. leprae* amount in MB-type MH lesions indicates the inability of

elimination macrophages due to the presence of transforming growth factor (TGF)-β that inhibits antimicrobial activity of macrophages.[8] This cytokine suppresses the response of T-cells and inhibits IFN-γ, IL-2, and macrophage activity that causes infection progressiveness.[9]

In the ENL reaction, there was an increase in antigens from a large number of killed *M. leprae* that reacted with the antibodies, as well as a decrease in suppressor T-cell function and an increase in tumor necrosis factor (TNF)-α levels.[10] An increase in cytokine mRNA produced by T-helper-2 (Th2) was found in skin lesions of MH patients of MB type. In contrast, T-helper 1 (Th1), which produces the cytokines IL-2, IL-15, IFN-γ, and TNF-α, is related to tuberculoid-type leprosy. This suggests different cytokine profiles are related to the leprosy spectrum.[10,11]

Natural immune cells play a role in MH pathogenesis by excessively releasing reactive oxygen species (ROS). ROS will react with cell membrane lipids, forming malondialdehyde (MDA), which damages cell membranes due to impaired osmosis balance and water ingress into cells, further causing cell swelling and apoptosis.[12] *M. leprae* fragments emerge from cells and trigger an antibody-antigen response. Acute symptoms present in ENL are thought to signal an excessive improvement in natural immune function (TNF-α, TGF-β, and anti-PGL-1 IgM antibodies).[13]

Differential diagnosis of ENL is reversal reaction (type 1 reaction). The type 1 reaction is a delayed hypersensitivity reaction. Type 1 reactions occur in the borderline spectrum of the disease except for very rare reports in lepromatous leprosy. However, ENL acute can occur due to other common causes such as drugs, intestinal infection, tuberculosis, *Streptococcus* infection, and sarcoidosis.[13]

The treatments for mild ENL reactions are rest and anti-inflammatory drugs. Lepromatous leprosy is treated according to WHO standards using a multidrug regimen that includes dapsone, rifampicin, and clofazimine for a duration of 24 months and should be continued in case of ENL.[14] In severe ENL cases, corticosteroids, thalidomide, clofazimine, cyclosporine, and minocycline may be considered.[15] The patients received MDT MB therapy, methylprednisolone, paracetamol, ranitidine, ketorolac in case of pain, desoxymethasone ointment, and urea cream. Corticosteroids inhibit the early and slow phases of inflammatory processes, decrease neutrophil chemotaxis, and inhibit prostaglandin synthesis. Corticosteroids also suppress cellular immunity through T-cell depletion; thus, there is a change in the ratio of T-cells to the helper and suppressor. As the ENL reaction improves, the dose of corticosteroids can be lowered slowly and then stopped properly.[16] The gradual dose reduction of corticosteroids aims to prevent recurrence of reactions and reduce the side effects.[17]

SUMMARY

A case of a 58-year-old woman with lepromatous leprosy and severe ENL reaction was reported. Early diagnosis and accurate management can improve results and prevent complications.

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