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Research Report

LEPROSY AND HUMAN IMMUNODEFICIENCY VIRUS COINFECTION: A RARE CASE

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ABSTRACT

Leprosy, or Morbus Hansen, is a chronic infectious disease which caused by Mycobacterium leprae. It is associated with inflammation that may damage the skin and peripheral nerves. Leprosy remains an important public health problem in Southeast Asia, America, and Africa. It has been speculated that, as with tuberculosis, Human Immunodeficiency Virus (HIV) infection may exacerbate leprosy lesions and/or lead to increase susceptibility to leprosy. We are reported the case of leprosy and HIV coinfection and reveals its clinical manifestation. A 34-year-old female came to outpatient clinic complaining of redness plaque on her face of 2-months duration. It was also accompanied with thick sensation without itchy or burning sensation. We found thick erythematous plaque with sharp margin and hypoesthesia on her face and body. There were no madarosis, saddle nose, lagophthalmos and sign of neuritis. The slit-skin smear revealed BI 1+ globi and MI 2%. From laboratory examination we found IgM anti PGL-1 titer was 1265 u/mL and IgG anti PGL-1 was 834 u/mL. The similar lesion of leprosy was found on her both of ear lobe and legs by using histological examination. The detection of HIV antibody was positive with CD4 count on 325 cells/ μ L. We treat her with multidrug treatment (MDT) for multibacillary leprosy along with anti-retroviral therapy or ART consist of Tenofovir, Lamivudine, and Efavirenz. After 6-months follow-up we are observed no progression of the lesions though the slit-skin smear become negative. M. leprae does not seem to accelerate the decline of immune function when associated with HIV infection. HIV infection does not seem to affect the clinical classification and progression of leprosy. The treatment of the HIV-leprosy coinfecting patient consists of the combination of ARTs and anti-leprosy agents. Those treatment gives the good result in the bacteriological state of the patient.

Keywords: leprosy, Hansen disease, HIV Co-infection, leprosy-HIV, MH.

ABSTRAK

Kusta, atau Morbus Hansen, merupakan penyakit inflamasi kronik yang disebabkan oleh Mycobacterium leprae, terkait dengan inflamasi yang merusak kulit dan saraf perifer. Kusta tetap menjadi masalah kesehatan masyarakat di Asia Tenggara, Amerika, dan Afrika. Koinfeksi dengan HIV memiliki pengaruh besar terhadap perkembangan penyakit, terutama penyakit mikobakterial. Telah diduga sebelumnya, seperti halnya tuberkulosis, infeksi Human Immunodeficiency Virus (HIV) menyebabkan eksaserbasi lesi kusta dan/atau meningkatkan kerentanan terhadap kusta. Kami melaporkan kasus koinfeksi kusta dan HIV dan menunjukkan manifestasi klinisnya. Seorang wanita 34 tahun datang ke klinik rawat jalan mengeluhkan bercak kemerahan sejak 2 bulan. Hal ini disertai pula dengan sensasi tebal tetapi tanpa gatal atau rasa terbakar. Tidak disertai demam atau benjolan. Dari pemeriksaan ditemukan plak eritematosa berbatas jelas dan hipoestesia pada wajah dan badan. Tidak ditemukan madarosis, hidung pelana, lagofthalmos, atau tanda neuritis. Pemeriksaan basil tahan asam menunjukkan BI 1+ globi dan MI 2%. Pemeriksaan laboratorium darah menunjukkan dalam batas normal, titer Ig M anti PGL-1 1265 u/mL dan IgG anti PGL-1 834 u/mL. Kedua pemeriksaan histologis dari cuping telinga dan tungkai menunjukkan gambaran menyerupai kusta. Deteksi antibody HIV positif dengan hitung CD4 325 cells/ μ L. Pasien diterapi dengan multidrug treatment (MDT) untuk leprosy tipe multibasiler dan anti-retroviral therapy atau ART yang terdiri dari Tenofovir, Lamivudine, and Efavirenz. Setelah 6 bulan terapi dapat kami amati bahwa tidak ditemukan perkembangan bermakna dari lesi meskipun pemeriksaan basil tahan asam menjadi negatif. Kasus ini merupakan koinfeksi kusta-HIV. M. lepra tampaknya tidak

mempercepat penurunan fungsi imun terkait infeksi HIV. Infeksi HIV juga tidak mempengaruhi klasifikasi klinis dan perkembangan kusta. Terapi pasien koinfeksi kusta-HIV terdiri dari kombinasi ART dan agen anti-kusta MDT. Terapi tersebut memberikan perbaikan hasil bakteriologis yang cukup baik untuk pasien.

Kata kunci: kusta, penyakit Hansen, koinfeksi HIV, kusta-HIV, MDT

INTRODUCTION

Leprosy, or Hansen disease (HD), is a chronic infectious disease which caused by *Mycobacterium leprae* which is associated with inflammation that may damage the skin and peripheral nerves.¹ Despite the claim by the World Health Organization (WHO) that it would no longer be a public health problem after the year 2000, leprosy is far from being eliminated, with more than 200,000 new cases being reported yearly during the past 5 years. Leprosy remains an important public health problem in Southeast Asia, America and Africa.^{2,3}

Human Immunodeficiency Virus (HIV) infection prevalence rates are high in many countries where leprosy is still endemic.^{2,4,5} In 2008, 121 countries were reported a total of 249,007 new leprosy cases to WHO. Most endemic countries for leprosy also have a high HIV prevalence, increasing the possibility of HIV-leprosy coinfection. Although the number of coinfecting patients has not been estimated yet, the increasing geographic overlap of these two diseases will result in increasing number of person being dually infected.⁶

Meanwhile, there are few number of case reports of leprosy that have association with HIV infection.^{4,6} A few studies have tried to evaluate reasons for this rare co-existence. Tissue cell-mediated immune response against *M. leprae* is known to be preserved even though the peripheral blood lymphocyte count was reduced in concurrent leprosy and HIV-infected patients.⁶ Thus probably, there are less reports of leprosy in association with HIV.

The present case of leprosy in an HIV-infected person is herewith reported for its rarity. This case report is aimed to describe the different manifestation of leprosy and HIV coinfection. The understanding about the existence of coinfection should be remember and it bring also the obligation to follow standardized guideline treatment.

CASE

A 34-year-old female came to the dermatology outpatient clinic of Dr. Soetomo General Hospital Surabaya on December 13th 2017. She came with chief complaint of redness plaque on her face. She is complained about it since about 2 months before admission. Firstly, she got this lesion on her face with small size, by the time then this lesion became larger. This symptom was also accompanied with thick sensation over the red area but without itchy or burning sensation. She had no fever before. She went to several general practitioners and was diagnosed with atopic dermatitis. She got some medications but there were no significant differences before and after taking those

treatments. After several weeks back then, there were some erythematous and blackish macule that was spread on her extremities. Because of feeling afraid of this condition, she sought any help to dermatology and venereology outpatient clinic of Dr. Soetomo General Hospital and was diagnosed as leprosy.

About one month after she got treatment from there, she had a chronic diarrhea and had a low fluid intake until she became severe dehydration. Because of this condition she was hospitalized in other hospital and did some general examination which is one of those examination panel was HIV rapid testing. Those laboratory data revealed that she got HIV infection. She was started on antiretroviral therapy (ART) one month later.

The patient was married with a man since about 10 years ago. She is refused to have a sexual intercourse before she was married. She is claimed that her husband was the one and only sexual partner of her. Her husband was a worker on the building construction project. The history of sexual activity of her husband was unknown. The patient is denied of the same disease before and her husband was not having the same symptoms. There was no history of consuming drugs before the lesions appeared, drug hypersensitivity, blood transfusion, injection drug user, or drug abuser. History of fever, headache, malaise, and weight loss were denied.

The physical examination of general state was all within normal limit. Blood pressure was 100/70 mmHg, pulse rate was 84 times per minute, respiratory rate was 18 times per minute and body temperature was 36,4⁰ C. From head and neck, there were no signs of anemia, cyanosis, icterus, or dyspneu. From thorax examination, heart and lungs were normal. From abdomen, liver and spleen were not palpable. From her upper and lower extremities there were no edema and warm on palpation. There was no enlargement of the cervical, axillar, inguinal and genital lymph nodes.

Dermatological examination on her right face especially on the periorbital region discovered the thick erythematous plaques with sharp margin, some are covered with white fine scales and hypoaesthetic (Fig. 1 A). No madarosis of the eyebrows or eyelashes was observed. There were no saddle nose or diffuse infiltrate on the face, and lagophthalmos. There was also multiple erythematous macule that sharply marginated accompanied with erythematous papules that varied in size about 0,5-1 cm on her trunk, upper, and lower extremities (Fig. 1 B-E). There was no thickened peripheral nerves on the left and right ulnar nerves and did not accompanied with tenderness on palpation. In addition, peripheral neurological symptoms, including motoric, sensory and autonomic nerve disturbance were not detected based on a neurological assessment that included light



Figure 1. The Clinical Manifestation of the Patient on The First Examination on Right Facial Region, There Was Erythematous Plaque with Sharp Margin (Picture A); The Other Manifestation of The Patient on The Trunk and Extremities Region, There Were Multiple Erythematous and Hyperpigmented Macules that Varied in Size (Picture B-E)

touch, pin-prick test, thermal sensory test, manual muscle strength test and monofilament test.

We found that acid-fast bacilli was detected by the slit – skin smear test of the ear lobes and lesion (Bacterial Index: 1+ globi; Morphological Index: 2%). The laboratory examination on December 13th 2017 was revealed: haemoglobin was 14,0 g/dL, white blood count 8.090/mm³, thrombocyte 302.000/L, and hematocrite 41,2%. Detection of HIV antibody (3 methods) on January 2018 was positive with CD4 count on 525 cells/ μ L. Serologic test by detecting antiphennolic glycolipid I (anti PGL-1) antibody was positive by the score of IgM = 1265 (cutt off = 605 u/mL) and IgG = 834 (cutt off = 630 u/mL).

Histological examination of the ear lobe skin was revealed atrophy and short-flattening of rete ridge on the upper epidermis, there were some group of hystiocyte or foam cell on superficial to deep dermis. No specific microorganisms were identified by Fite – Faraco staining. The conclusion of that biopsy was borderline leprosy. The picture of this examination can be clearly seen on the Figure 2A.

Because of our suspicion on several diagnosis of the lesions on her trunk and extremities, we did the biopsy examination on that location too. The skin biopsy on extremity was revealed atropy and short-flatening of rete ridges on epidermis, some epithelioid cells which form granuloma, some lymphocyte and eosinophil infiltration on the dermis. There was no bacteria were observed on Fite–Faraco staining. The conclusion was similar to the lesion of borderline tuberculoid leprosy. In those two examination we did not see any differences in the manifestation of the disease according to the histologic examination. The picture of this examination can also be clearly seen on the Figure 2B.

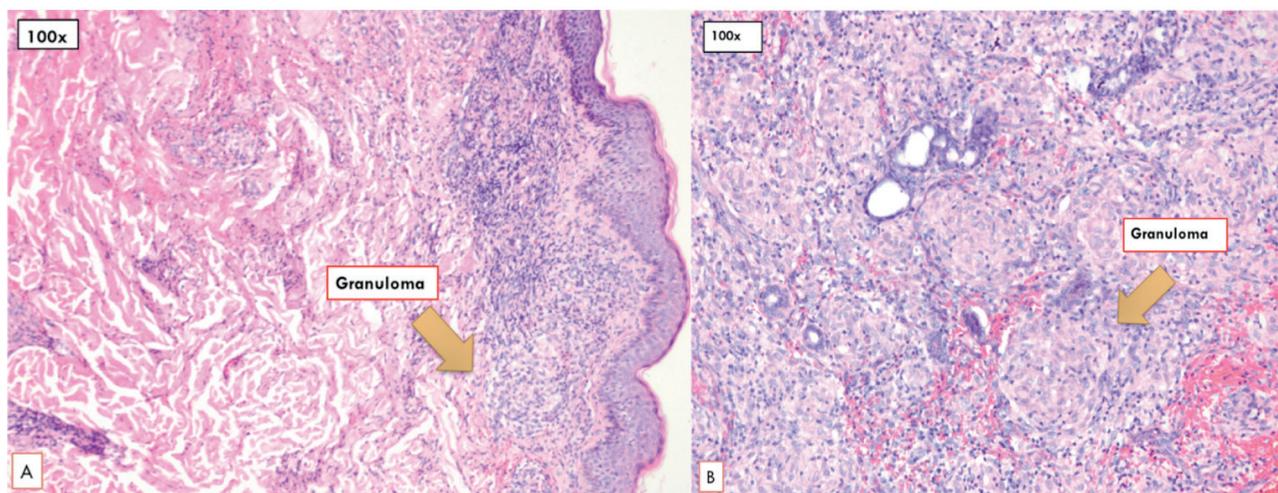


Figure 2. The Histologic Examination of Ear Lobe (Picture A) Revealed Atrophy of Epidermis with Short-Flattening of Rete Ridges, We Found Group of Histiocyte Or Foam Cell On Superficial To Deep Dermis and Datia Langhans Cell, There Were No Bacteria Observed and The Conclusion Was Borderline Leprosy; The Other Histologic Examination On The Extremity (Picture B) Revealed A Slight Different That We Found Epithelioid Cells That Form Granuloma and Some Lymphocyte and Eosinophil Infiltration, We Conclude The Result As Borderline Tuberculoid Leprosy



Figure 3. The Skin Lesion on Her Face at The First Come (Picture A), 3rd Month of MDT (Picture B); and after 6th Month of MDT (Picture C). We Found No Progression of The Lesions.

Based on these findings, from physical and laboratory examination, the diagnosis of multibacillary, borderline lepromatous (BL) leprosy with HIV coinfection was established. There was no sign of the leprosy reaction at this time. The patient were observed for the period of time to observe the amendment of her condition.

According to the World Health Organization (WHO) classification, she was classified as having Multibacillary Leprosy and got Multidrug Treatment of Leprosy (MDT). Those regimen consisted of Rifampicin 600 mg monthly, Clofazimine 300 mg once a month and 50 mg daily, and Dapsone 100 mg daily for 12 months which is the WHO recommended for multibacillary leprosy. She was also initiated on first-line antiretroviral therapy (ART) regimen including Tenofovir, Lamivudine, and Efavirenz.

Six months since initiating MDT for leprosy, the patient remained stable without new lesions or neurological deficits. However, there were no progression of the lesions even though she has been treated for 6 months. The progression of the disease was clearly described in Table 1 and the lesions can be seen on Figure 3 to 5

DISCUSSION

Leprosy is one of a deliberately progressive infectious disease caused by *Mycobacterium leprae*. It is a disease which primarily affects the skin and peripheral nerve, and in highly bacillated state, any internal organ except central nervous system can be affected too. The damage to peripheral nerves results in sensory and motor impairment which characterized by dreadful abnormalities and debilities.⁷⁻⁹

Talhari *et al.* were proposed the classification for leprosy associated with HIV infection. This classification recognizes true leprosy-HIV coinfection, opportunistic leprosy disease, and leprosy related to ART.⁸ Recently, it was suggested that even though leprosy-HIV coinfection does not manifest homogenously across affected populations, immunological features seem to be shared by certain subgroups. In this context, a clinical classification of *M. leprae* and HIV/



Figure 4. The Skin Lesion on Her Forearms at The First Come (Picture A), 3rd Month of MDT (Picture B); and After 6th Month of MDT (Picture C). We Still Found No Progression of The Lesions.

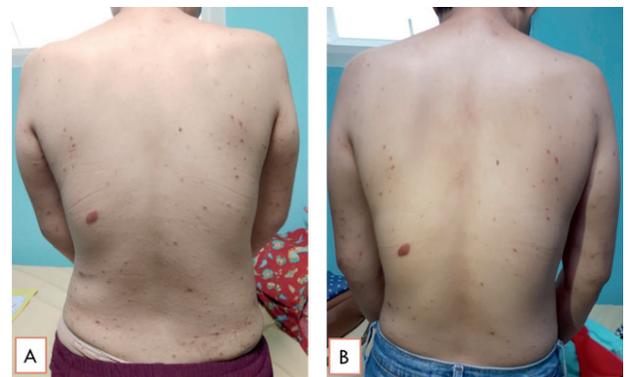


Figure 5. The Lesions on Her Back Were The Same between Her First Come (Picture A) and After 6th Month of MDT (Picture B)

Table 1. Progression of The Disease

	Dec 13, 2017	Jan 2, 2018	Feb 14, 2018	April 30, 2018
SUBJECTIVE				
1. Redness	+	+	+	+
OBJECTIVE				
1. Erythematous plaque	+	+	+	+
2. Scale	+	+	-	-
3. Patches on extremities	+	+	+	+
ASSESSMENT				
Borderline lepromatous leprosy + HIV	+	+	+	+
PLANNING OF DIAGNOSIS				
1. Slit skin smear	+	-	-	-
2. Punch biopsy	+	-	-	-
3. HIV antibody test	+	-	-	-
PLANNING OF THERAPY				
1. MDT-MB	+	+	+	+
2. HAART	+	+	+	+
3. Thiamin tablet	+	+	+	+
4. Vitamin B complex tablet	+	+	+	+
5. Urea 10%	+	+	+	+

AIDS-coinfected patients including in the following criterias.² The first criteria are *M. leprae*-HIV true coinfection. This group consists of HIV positive individuals who do not fulfill AIDS criteria and are not under HAART. The patients have similarity to immunocompetent subjects.² The next criteria are opportunistic leprosy disease. This criteria consist of AIDS patients who do not

receive HAART, presenting usually with multibacillary leprosy. This group would include individuals manifesting leprosy as an opportunistic mycobacteriosis, as expected in immunosuppressed individuals.² The last criteria are HAART-related leprosy. This criteria include AIDS patients presenting all clinical forms of leprosy related or not to IRIS. Combined HAART and MDT may cause upgrading shift within the leprosy clinical spectrum, as may be revealed by long-term follow-up.²

According to those criterias, we could define the leprosy and HIV in this case as *M. leprae*-HIV true coinfection. This case illustrates clinical manifestations of leprosy that was not worsen by HIV infection, although it slowly progressed during the follow-up.

It is a well-known fact that in tuberculosis (TB) and HIV coinfectd patients, TB and HIV infection itself contributes to the progression of each other.¹⁰⁻¹² Active TB infection in HIV-infected patients is associated with increased immunodeficiency and mortality in those patients.¹³⁻¹⁵ It has been hypothesized that HIV infection may exacerbate leprosy lesions and/or lead to increased susceptibility to leprosy. This condition was thought to be like in TB and HIV infection. However, there is less evidence to support this hypothesis. In the contrary, there were several studies that have found that in leprosy and HIV coinfectd patients, each disease progresses independently.^{6,16}

A few studies were performed to evaluate the reasons for this rare co-existence. Tissue cell-mediated immune response against *M. leprae* is known to be preserved even though the peripheral blood lymphocyte count was reduced in concurrent leprosy and HIV-infected patients.⁶ The deficiency in cell-mediated immunity (CMI) is specific to the *M. leprae* antigens and has nothing to do with the decreased peripheral CD4 count of HIV.¹⁷ Thus probably, there are less reports of leprosy in association with HIV.

Mycobacterium leprae does not seem to accelerate the decline of immune function when associated with HIV infection. This condition was different with the fact which often happens in tuberculosis coinfection.^{18,19} Reactional states may occur more frequently in individuals with HIV coinfection. However, there are still many conflicting data regarding increased reaction frequency in this group.¹⁶

As noted in this patient, HIV infection did not seem to affect the clinical classification and progression of leprosy. As we found in a study by Pereira *et al.* that the clinical, immunologic, histopathology, and virology features among 22 HIV-leprosy coinfectd Brazilian patients indicate that each disease is progressed as in single infection.²⁰ Despite overall HIV-associated immunosuppression, cell-mediated immune responses to *M. leprae* are well preserved at the site of the disease.^{20,21} Based on our experience as we found in our patient, the disease was progressed slowly, and the lesions did not alter morphologically over a period of 6 months follow up. This suggests that the pathogenesis of leprosy in this patient was unaffected by her immunodeficiency. This finding was similar to the result of the study that was mentioned above.²⁰

Initiation of HAART has been associated with Immune Reconstitution and Inflammatory Syndrome (IRIS) in various situations. IRIS in leprosy may trigger potential adverse effects, such as leprosy acute inflammatory episodes.^{7,10,22} This usually leads to a worsening of the initial lesion characterized by erythema and tenderness in the setting of rising CD4 count and falling viral load. These reactions are more common in patients with low CD4 counts especially during the initial 3 months of initiation of ART. Typically, as the immune system further recovers, the lesions become tuberculoid or paucibacillary as opposed to lepromatous.

In our patient, there was no change in the appearance of the skin lesions after starting HAART with no evident virological suppression and immune reconstitution with the latter. More so, there were no neurological deficits noted even after 6-months therapy of MDT and HAART.

The follow-up of this case after 6 months of MDT for leprosy combined with HAART was revealed negativity of skin slit smear. Although it has no significant different in the clinical manifestation, but the progression in skin slit smear indicates the cure of leprosy in this patient. Moreover, we still continue the MDT regimen for 12 months for multibacillary leprosy based on the WHO's recommended treatment regimens for multibacillary leprosy.

The therapy for leprosy with HIV coinfection is still the same with leprosy without coinfection. HIV infection might affect the efficacy of multidrug therapy for leprosy. The HIV positive patients are potentially taking longer to be treated or experiencing a higher relapse rate of leprosy. But some published data were suggested that leprosy-HIV coinfectd patients respond equally well to multidrug therapy without the need for prolonged treatment.¹⁶ Relapses are rare after multidrug therapy. It counts about 1 per 1000 person-years for tuberculoid patients and 0-20.4 per 1000 person-years for multibacillary patients.^{16,23}

CONCLUSION

Based on the available data, we can conclude that leprosy and HIV coinfection has three different criteria. One of them is the true coinfection, such in this case, is the diseases that progress independently. In general, the therapy for this patient is the same as the disease was separately. Those treatment includes standard WHO-MDT in conjunction with HAART according to the patient's clinical state. The influence of HIV infection on cell-mediated immune responses to *M. leprae* in the HIV- infected patient needs more exploration. Leprosy and HIV coinfection is an evolving situation with ongoing discoveries and further research needs.

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