

## Secondary syphilis mimicking mid-borderline leprosy in HIV-positive patient



Rheza Rahmadika Putra<sup>1</sup>, Usman Hadi<sup>2\*</sup>

### ABSTRACT

**Background:** Syphilis increases the risk of HIV transmission. Coinfection of both infectious diseases potentially changes the presentation of mucocutaneous lesions and accelerates disease progression, complicating the diagnosis and treatment with standard regimens. In the case study, we present a case of secondary syphilis in an HIV-positive patient with clinical manifestations resembling mid-borderline leprosy.

**Case presentation:** A 23-year-old male patient was referred to the emergency care unit of Dr. Soetomo General Hospital with red spots on the palms of the hands and soles of the feet for the past four months. The skin manifestation first appeared as a single spot, grew over time with itch and pain. The patient had lost 15 kg of body weight in the last three months which was confirmed as HIV-positive. He was also treated for leprosy based on the skin manifestations ever since. There was no history of direct contact with leprosy patients. The patient admitted that he had sex with men in the last 3-4 years. The laboratory examination showed negative results for *Mycobacterium leprae* through skin biopsy and negative for IgM and IgG of anti-phenolic glycolipid-1 (PGL-1). The patient however was positive for syphilis due to high titers of venereal disease research laboratory/rapid plasma regain (VDRL/RPR) and treponema pallidum hemagglutination (TPHA), supported by histological findings. The patient's condition improved after receiving penicillin benzathine G, the definitive treatment for syphilis.

**Conclusion:** Secondary syphilis is a great imitator to mid-borderline leprosy, especially in HIV patients. To avoid misdiagnosis and mistreatment, a careful physical and laboratory examination, including serology and histopathology, should be carried out.

**Keywords:** Secondary syphilis, mid-borderline leprosy, HIV, *Mycobacterium leprae*, coinfection.

**Cite This Article:** Putra, R.R., Hadi, U. 2022. Secondary syphilis mimicking mid-borderline leprosy in HIV-positive patient. *Bali Medical Journal* 11(3): 1789-1794. DOI: 10.15562/bmj.v11i3.3688

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Hospital, Surabaya, 60132, Indonesia;

<sup>2</sup>Division of Infectious Disease and Tropical Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Airlangga - Dr. Soetomo Hospital, Surabaya, 60132, Indonesia;

\*Corresponding author:

Usman Hadi;  
Division of Infectious Disease and Tropical Medicine, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Hospital, Surabaya, 60132, Indonesia;  
[usman.hadi2@fk.unair.ac.id](mailto:usman.hadi2@fk.unair.ac.id)

Received: 2022-09-14

Accepted: 2022-10-15

Published: 2022-11-29

### INTRODUCTION

Syphilis is a chronic sexually transmitted infection caused by *Treponema pallidum* through sexual intercourse, blood transfusion or transplacental transmission.<sup>1,2</sup> Syphilis is the second most common sexually transmitted infection and could increase the risk of transmitting human immunodeficiency virus (HIV) up to 3-5 times.<sup>3</sup> In 2012, there were 18 million total cases of syphilis globally with an average incidence of 1.5 cases per 1000 women and 1.5 cases per 1000 men.<sup>1</sup> In Indonesia, the prevalence of syphilis coinfection with HIV was 23.8% in men who have sex with men (MSM) and 16.7% in female sex workers.<sup>3</sup>

Syphilis has varied clinical manifestations, serological and histopathological findings.<sup>4</sup> Coinfection of syphilis and HIV can alter the clinical course of the disease, notably

mucocutaneous lesions, hasten disease development, complicate the diagnosis and raise the likelihood of additional organ problems and treatment failure with standard regimens.<sup>5,6</sup> In this article, we report a case of secondary syphilis in an HIV-positive patient with clinical features imitated mid-borderline leprosy.

### CASE PRESENTATION

A 23-year-old man, unmarried, a student, was referred from Siti Khodijah Sepanjang Hospital to the Emergency Care Unit of Dr. Soetomo Hospital with red spots on his palms and soles for four months ago, previously diagnosed with HIV-positive. At first, there was only one spot, but over time it grew without itch and became numb. Then skin of palms and soles were peeled off since two months ago. The patient also complained of an itchy right head wound in the last two weeks. In

addition, there were spots on the lower abdomen and genitals due to itching and scratching since the last one year and have improved. In the last five months, the patient also complained of the patient's hair starting to fall out. Redness on the face, joint pain and swelling on certain parts of the body were denied.

The patient complained of thrush, white tongue and painful swallowing since last month. He complained of fever in the last three days, accompanied by nausea and vomiting. Cough with white phlegm has occurred in the last three weeks without any night sweats. The patient had decreased appetite and lost 15 kg of body weight in the last three months. Since then, the patient was diagnosed with leprosy and treated based on the skin manifestations at Siti Khodijah Sepanjang Hospital. The patient had no history of direct contact with any leprosy

patient. History of red spots, drug allergy, food, asthma or frequent sneezing in the morning were denied. The patient had sex with men since past 3-4 years. History of blood transfusion, sharing needles and tattoos were denied.

The physical examination revealed that the patient's general condition was weak, alert with Glasgow Coma Scale (GCS) 15, blood pressure 120/80 mmHg, heart rate 70x/min, respiratory rate 16 x/min, axillary temperature 36.9°C and SpO<sub>2</sub> 98%. The patient had BMI 15.57. On examination of the head and neck, white plaques were found on the tongue and in the mouth. On thoracic examination, the chest movement was found symmetrical, no retractions and the heart and lungs were within normal limits. The normal bowel sound was found in abdomen. On the extremities, they were warm, dry red and no edema. Localized status examination revealed well-defined erythematous macules that mainly affected the right palmar, plantar, head and frontal areas (Figure 1A to D). Mild hypoesthesia was found in skin lesions and peripheral nerve examination was within normal limits. There was no muscle weakness and lymphadenopathy.

The results of the laboratory examination showed hemoglobin 10.4 g/dL, hematocrit 30%, MCV 75 fL, MCH 26 pg, MCHC 34.7 g/dL, leukocytes 9.930/mm<sup>3</sup>, neutrophils 80.7%, lymphocyte 10.1%, monocyte 9.1%, eosinophil 0%, basophil 0.1%, platelets 312,000/mm<sup>3</sup>, erythrocyte sedimentation rate (ESR) 50 mm at the first hour and 107 mm at the second hour, blood urea nitrogen (BUN) 13 mg/dL, serum creatinine 0.67 mg/dL, serum glutamic oxaloacetic transaminase (SGOT) 28 U/L, serum glutamic pyruvic transaminase (SGPT) 31 U/L, albumin 3.5 g/dL, glucose 71 mg/dL, potassium 4.3 mmol/L, sodium 133 mmol/L, chloride 100 mmol/L, HBsAg non-reactive, anti-HCV non-reactive but the three tests to diagnose HIV, antibody test, antigen/antibody test, and nucleic acid tests (NATs) were reactive. The anteroposterior chest x-ray examination revealed sufficient inspiration, the heart and lungs were within normal limits.

Based on the medical record, the patient was diagnosed with HIV stage 3, oral candidiasis, mid-borderline

leprosy and suspected secondary syphilis. We continued with bacterial index (BI) and morphological index (MI) examination, venereal disease research laboratory (VDRL), *Treponema pallidum* hemagglutination (TPHA), viral load, CD4 counts, sputum culture/sensitivity, GeneXpert sputum for tuberculosis, skin biopsy and dark field microscopy (DFM) examination. The patient kept receiving antifungal therapy and multidrug therapy (MDT) for leprosy while waiting for the results of laboratory tests.

On the second day of treatment, the patient complained of skin redness, painful swallowing, nausea and vomiting. The fever and cough begun to subside. Laboratory test revealed CD4 count of 14 cells/ $\mu$ L and viral load of 1,582,851 copies/mL. The GeneXpert was negative. The patient received additional treatment of fixed-dose combination (FDC) antiretroviral therapy (tenofovir, lamivudine and efavirenz) and cotrimoxazole 960 mg orally once a day.

The sixth day of treatment, complaints of skin redness remained the same. There were no complaints of nausea, vomiting, fever, cough and painful swallowing. The results of the sputum culture/sensitivity examination showed *Streptococcus viridans*. Examination of the BI and MI were negative and examination of the ear lobes lesions did not result any positive of acid-fast bacilli like *Mycobacterium leprae*. The level of IgM and IgG of anti-phenolic glycolipid-1 (PGL-1) was 80 U/mL (positive if >605 U/mL) and 0 U/mL (positive if > 630 U/mL), respectively.

A skin biopsy was performed for the skin lesions and the histology results revealed hyperkeratosis and acanthosis with elongated rete ridges in the epidermis; while in the dermis, there was proliferation of capillary blood vessels and lymphocyte infiltration without the presence of granulomas, foamy macrophages and acid-fast bacilli (Figure 2A to D). Dark field microscopy (DFM) negative for *T. pallidum*, but the VDRL/RPR and TPHA were reactive by the titers 1:256 and 1:2560, respectively. The patient was diagnosed as probable secondary syphilis based on histopathological, serological, and clinical manifestations. The patient received injection of 2.4 million units benzathine penicillin G intramuscularly



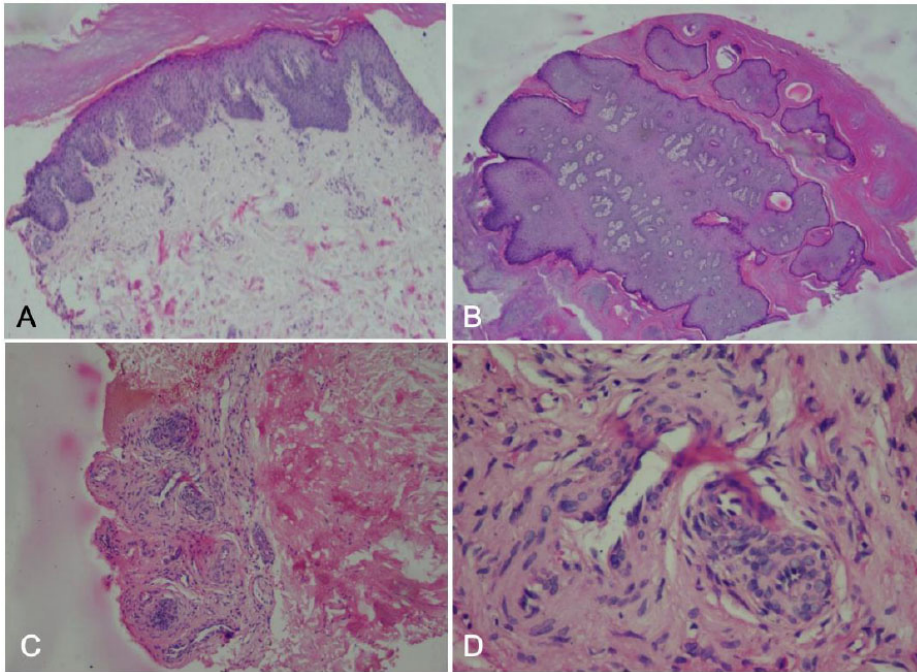
**Figure 1.** (A) An erythematous macule with irregular edges and erosions in the frontal area. (B) The hair loss (alopecia) in “moth-eaten” pattern with the thinning eyebrows. (C) Multiple erythematous macules with clear edges in the palmar area. (D) Multiple erythematous macules with desquamated edges in the plantar area.

once as definitive treatment of syphilis, while MDT for leprosy was discontinued due to the mismatched diagnosis with the existing result examination.

At the time of polyclinic control 3 months after hospital admission, the evaluation of laboratory results following the definitive therapy improved with reactive VDRL 1:64 and reactive TPHA 1:1280. Complaints of itching in the facial area, red spots on the palms and soles were no longer found (Figure 3A and B).

## DISCUSSION

HIV is an RNA virus causing acquired immunodeficiency syndrome (AIDS).



**Figure 2.** (A, B) Hyperkeratosis, irregular acanthosis and elongated rete ridges in upper dermis. (C, D) Capillary blood vessels proliferation with lymphocyte infiltration in dermis. Granulomas, foamy macrophages and acid-fast bacilli (AFB) are not detected.



**Figure 3.** Three months after treatment, a marked improvement was noted in the palmar area (A) and the plantar area (B).

The virus is equipped with an external protein gp120 that helps bind CCR5 and CXCR4 co-receptors, transmembrane protein gp41 and reverse transcriptase enzymes. The virus is capable of reducing the level of CD4 T-lymphocytes.<sup>7,8</sup> The transmission of HIV commonly occurs in homosexual men, injection drug users, blood transfusion recipients, female sexual partners with HIV-infected men and newborns with HIV-infected mothers.<sup>9</sup> The diagnosis of HIV is established using two methods which are serological examination (rapid immunoassay test and

enzyme immunoassay) and virological examination (RNA of HIV). An HIV test result is positive if: 1) three serological tests using three different methods or reagents show reactive results; 2) quantitative or qualitative virological examination detected HIV.<sup>10</sup> In addition, World Health Organization (WHO) divides HIV in adults into four stages based on clinical manifestation (lymphadenopathy, weight loss and opportunistic infections) and laboratory results.<sup>11,12</sup>

The treatment of HIV starts with post-diagnosis counseling, laboratory

and tuberculosis examination, followed by anti-retroviral (ARV) side effects screening.<sup>10</sup> The ARV is initiated in HIV patients without tuberculosis infection regardless of CD4 count.<sup>13</sup> First-line ARVs are given in combination of two nucleoside reverse-transcriptase inhibitors (NRTI), added with a non-nucleoside reverse-transcriptase inhibitor (NNRTI) or protease inhibitor (PI).<sup>11</sup> The treatment of FDC once a day consisting of tenofovir disoproxil fumarate, lamivudine and efavirenz is a combination that shows good therapeutic and virological response, rarely causes severe side effects and is the main choice of ARV in Indonesia. In addition, several studies have shown that prophylactic administration of cotrimoxazole (TMP-SMX) in patients with low CD4 count can reduce the risk of opportunistic infections and mortality.<sup>10,13</sup>

In this case, the patient was diagnosed with HIV stage III due to weight loss of 15 kg (>10%) in 3 months, oral candidiasis in the last one month, history of sexual intercourse with men, chronic respiratory and mucocutaneous infections, reactive results of the three methods of HIV examination, had a CD4 count of 14 cells/ $\mu$ L and a viral load of 1,582,851 copies/mL. Fixed dose combination of ARV therapy (tenofovir disoproxil fumarate, lamivudine and efavirenz) was given because there was no pulmonary tuberculosis comorbidity (GeneXpert negative) and other laboratory results were normal. The patient also received cotrimoxazole 960 mg as prophylactic therapy due to low level of the patient's CD4 count.

Syphilis is a chronic systemic infection caused by *T. pallidum*, often sexually transmitted and characterized by active episodes interspersed with latent periods.<sup>2,14</sup> The bacterium is an obligate parasite for humans, spiral-shaped, gram-negative with a length ranged 6-20  $\mu$ m, a diameter ranged 0.09-0.18  $\mu$ m and can replicate twice in 30 hours. It lives on mucous membranes such as oral cavity and intestinal tract as well as skin membranes. Sexual transmission of syphilis is caused by inoculation of abrasions due to sexual trauma which causes a local response resulting in erosion and ulceration. This is followed by spreading bacteria to regional lymph nodes and blood circulation to

**Table 1. The differences between secondary syphilis and borderline leprosy.**<sup>16,20</sup>

|                         | Secondary syphilis   | Leprosy type <i>Borderline I</i>   |
|-------------------------|--|--|
| Etiology                | <i>Treponema pallidum</i>  | <i>Mycobacterium leprae</i>  |
| Onset                   | 6-8 weeks after primary infection  | 3-5 after physical contact   |
| Transmission            | Sexual, related to HIV   | Contact with the leprosy patients  |
| Distribution            | Men (men who have sex with men)  | Men > women  |
| Organ target            | Skin, joints, lymph nodes, systemic  | Skin, nerves   |
| Typical skin lesions    | erythematous macules or papules over palms and soles, hyperkeratosis, Biett collarette   | Erythematous macules, hypopigmentation, symmetrical or asymmetrical                                  |
| Other manifestations    | Systemic symptoms (fever, malaise, arthralgia, sore throat, lymphadenopathy); <i>moth-eaten alopecia</i>   | Peripheral nerve thickening (auricularis magnus, ulnar) with hypoesthesia; madarosis, facies leonina |
| Skin reaction           | <i>Jarisch-Herxheimer</i> (after treatment)  | Type 1 reaction, sometimes erythema nodosum leprosum (ENL)   |
| Bacterial examination   | Darkfield microscopy, PCR  | Bacterial index, morphological index, AFB from ear lobes   |
| Serological examination | VDRL/RPR, TPHA   | IgM & IgG of anti PGL-1  |
| Histological result     | Infiltration of plasma cells in the epidermis; vascular dilatation, irregular acanthosis; elongation of rete ridges; vacuolar and lichenoid pattern with infiltration of lymphocytes, histocytes and plasma cells or keratinocyte apoptosis. | Mixture of epithelioid granulomas and foamy macrophages  |

other body parts. There are several factors that make syphilis contribute to the HIV transmission process: (1) damage to the epithelial barrier as an entry point, (2) an increase in macrophages and T cells which are HIV receptors, (3) excess cytokine production by macrophages stimulated by *Treponema* lipoprotein will increase HIV replication, (4) the induction capability on HIV-1 gene expression from monocytes and macrophages and (5) its lipoprotein induces CCR5 from monocytes.<sup>5,15,16</sup>

Patients with HIV infection experience dysregulation of immune response which causes a decrease in the number of T-helper cells, lymphopenia, reduced interleukin-1 (IL-2) production, decreased natural killer (NK) cell activity, weakened delayed-type hypersensitivity (DTH) reactions and impaired production of specific antibodies.<sup>5</sup> In syphilis, *T. pallidum* lipoprotein will activate nonspecific immune effector cells (monocytes, macrophages and endothelial cells) at the beginning of chancre formation. In addition, delayed-type hypersensitivity (DTH) acts as a major immune mechanism for bacterial destruction and healing of syphilitic lesions.<sup>15</sup> In syphilis with HIV infection, there is an increase in the production of proinflammatory cytokines (IL-5, IL-6, IL-8, IL-12, MIP-1 $\alpha$ , MIP-1 $\beta$ ) accompanied by an increase

in the regulatory T cells (Treg) response through the production of transforming growth factor(TGF)- $\beta$  and IL-10. which increased 10 times compared to non-HIV patients. The immune response (DTH) becomes not optimal due to decreased CD4 T-cells and increased HIV viral load during infection.<sup>17</sup> In the context of clinical manifestation, the slow healing of primary syphilis will trigger the acceleration of secondary syphilis lesions and viral multiplication in various tissues, causing persistent genital ulceration and rapid progression of neurosyphilis.<sup>15</sup>

Based on the duration, syphilis is divided into early syphilis (less than two years, including primary, secondary and early latent syphilis) and late syphilis (more than two years, including latent syphilis and tertiary syphilis). Primary lesions usually occur 2-6 weeks after sexual contact in form of painless ulcers with circular indurated edges or atypical primary lesions with regional lymphadenopathy and resolve in 4-6 weeks without treatment. Secondary syphilis occurs 6-8 weeks after primary infection with bacterial dissemination through lymphatics to the bloodstream and organs so that the clinical manifestations are more diverse (fever, malaise, arthralgia, sore throat, dizziness and generalized painless lymphadenopathy) and difficult

to diagnose. Skin lesions that manifest as great imitators in secondary syphilis with the most common characteristic of a palmoplantar syphilitic eruption with erythematous macules or papules with hyperkeratosis, Biett collarette appearance (papules with an outer white ring), nodular or ulcerative lesions. Besides the manifestation of skin, moth-eaten alopecia and mucosal patches are common. In late-phase syphilis, a gumma is found with infiltrative granulomatous lesions or destructive ulcers with scars healing appearance, followed by neurosyphilis (asymptomatic, meningovascular, tabes dorsalis and general paresis) and cardiovascular syphilis.<sup>2,14,16</sup>

Syphilis is confirmed through laboratory or histopathological examination, in addition to clinical manifestations. Dark-field microscopy and polymerase chain reaction (PCR) was used to detect *T. pallidum* in early syphilis. Serological analysis is a general examination consisting of nontreponemal tests (VDRL, RPR, toluidine red unheated serum test (TRUST)) and treponemal-specific tests (fluorescent treponemal antibody absorption (FTA-ABS), TPHA, *Treponema pallidum* particle agglutination assay (TPPA), enzyme immunoassay (EIA)). In primary syphilis, VDRL and RPR are 62-78% sensitive for diagnosis,

while PCR is the preferred method. In secondary syphilis with various clinical manifestations, the diagnosis is made when a positive result of darkfield microscopy and a reactive result of treponemal or nontreponemal test is obtained. False positive or false negative laboratory results must be matched to the clinical condition when examined. In early syphilis, the treatment will result in a seronegative conversion, indicating that syphilis has been cured without any risk of recurrence. However, in latent and late syphilis, the laboratory results remain the same.<sup>2,3,16</sup>

Histopathological examination of secondary syphilis usually comes from biopsy of skin or mucosal lesions. Histological features may include a predominance of plasma cellular infiltrate in epidermis; endothelial swelling and dilatation of blood vessels; irregular acanthosis indicating irregular epidermal hyperplasia; elongation of rete ridges; vacuolar pattern of inflammation (damage to basal cells in the lichenoid reaction and intracellular vacuolar edema); lichenoid pattern of inflammation (infiltration of lymphocytes, histiocytes and plasma cells); and keratinocyte apoptosis.<sup>2,18</sup>

Leprosy is a chronic dermatologic infection caused by *Mycobacterium leprae*. The diagnosis of leprosy is established by finding cardinal symptoms of leprosy in the form of erythematous or hyperpigmented macular skin lesions with sensory loss (hypoesthesia), thickening peripheral nerves (auricularis magnus and ulnar nerves) and the discovery of *acid-fast bacilli* (AFB) (e.g., *Mycobacterium* species) on examination of skin or nerve tissue. In addition, the diagnosis is also supported by the results of BI and MI which range 1+ to 6+ as well as anti-PGL-1 antibody correlated with the number of bacteria and functioned as a predictor of neurological disorders. The clinical manifestations develop along a horizontal spectrum with two poles (tuberculoid and lepromatous) and three intermediate forms (borderline-tuberculoid, borderline-borderline, and borderline-lepromatous).<sup>19,20</sup>

Secondary syphilis in HIV patients resembles leprosy, especially the borderline type due to chronic skin manifestations with polymorphic lesions.<sup>2</sup> The differences

between secondary syphilis and borderline leprosy are shown in [Table 1](#).

In this case, the patient complained of a syphilitic eruption accompanied by multiple erythematous macules with scales in the palmoplantar area, moth-eaten alopecia with the thinning eyebrows, history of MSM homosexuality. These findings were supported by reactive VDRL 1:256, reactive TPHA 1:2560 and histopathological results in the form of hyperkeratosis, acanthosis with elongated rete ridges in the epidermis and proliferation of capillaries and lymphocyte infiltration in the dermis which support the diagnosis of secondary syphilis with HIV infection although *T. pallidum* bacteria were not found in DFM.

Hypopigmented macules with hypoesthesia and peripheral nerve enlargement were not found. The examinations of BI and MI result negative, also for the skin biopsy, AFB presence through GeneXpert, IgM and IgG of anti-PGL-1 which support the exclusion for leprosy as the diagnosis. Consequently, MDT was discontinued.

Management of syphilis in patients with HIV depends on the stage and the presence or absence of neurosyphilis. In early syphilis, the Centers for Disease Control and Prevention (CDC) recommends 2.4 million units benzathine penicillin G in a single intramuscular dose which is more effective than divided into 3 doses. Alternatively, patients can be treated with 750,000 units procaine penicillin intramuscularly for 10 days. In late-latent syphilis, 2.4 million units benzathine penicillin G can be administered intramuscular once a week for 3 weeks or 750,000 units procaine penicillin every day for 17 days. Late-latent syphilis with abnormal cerebrospinal fluid is treated as neurosyphilis. In neurosyphilis, treatment is recommended with 18-24 million units aqueous crystalline penicillin G per day intravenously, divided in 3-4 million units every 4 hours or continuous infusion for 10-14 days or 2.4 million units aqueous penicillin procaine G intramuscularly with oral probenecid 500 mg every 6 hours for 10-14 days.<sup>14,21,22</sup>

Syphilis patients with HIV who receive adequate therapy should be evaluated clinically and serologically every 3

months during the first year and every 6 months in the second year. The TPHA and RPR test was performed at 3 months after treatment for primary or secondary syphilis to evaluate the success of therapy and detect reinfection. The treatment is considered successful if the RPR titers fell 4 times compared to the previous one and were considered reinfection with a planned repeat therapy at an increase in the RPR titers after a 24-month evaluation. In addition, patients diagnosed with HIV should be screened for syphilis, and vice versa.<sup>3,5</sup>

In this study, the patient received a single dose of 2.4 million units of intramuscular penicillin benzathine G after being diagnosed with probable secondary syphilis. The evaluation was carried out 3 months after therapy, clinical complaints of secondary syphilis improved followed by a decrease in VDRL titers.

## CONCLUSION

The symptoms of secondary syphilis can resemble mid-borderline leprosy coinfecting with HIV and this could increase the error rate in diagnosis and treatment. In addition to thorough physical examination, the serological and histopathological examinations are necessary in ensuring the diagnosis. An appropriate diagnosis and definitive treatment will lead to a better outcome.

## PATIENT CONSENT

The patient provided informed consent to include the case as case report.

## ACKNOWLEDGMENTS

The authors would like to thank to the patient and Dr. Soetomo Hospital.

## DISCLOSURE OF CONFLICTS OF INTEREST

No conflict of interest.

## FUNDING

None.

## AUTHOR CONTRIBUTION

Both authors contributed significantly to the case-report.

## REFERENCES

- World Health Organization. WHO Guidelines for The Treatment of *Treponema pallidum* (syphilis). In: Research TDoRHa, editor. Geneva, Switzerland: World Health Organization Press; 2016. p. 1-60.
- Li X, Yang LG, Li J, Zhao XY, Wei CB, Li YY, et al. Syphilis in HIV/AIDS Patients [Internet]. Mucocutaneous Manifestations of HIV/AIDS. Springer Singapore; 2020. p. 105–24. Available from: [http://dx.doi.org/10.1007/978-981-15-5467-4\\_4](http://dx.doi.org/10.1007/978-981-15-5467-4_4)
- Health Mo. Syphilis management guidelines for syphilis control in primary health care. Directorate General of Disease Control and Environmental Health; 2013.
- Fernandez-Nieto D, Ortega-Quijano D, Jimenez-Cauhe J, Fernandez-Gonzalez P, Moreno-Moreno E, Bea-Ardebol S. Secondary syphilis mimicking tuberculoid leprosy in an HIV-positive individual: a case report. *Int J STD & AIDS* [Internet]. 2019;30(12):1235–8. Available from: <http://dx.doi.org/10.1177/0956462419869136>
- Gustina F, Legiawati L, Rihatmadja R, Daili SF. Syphilis in Human Immunodeficiency Virus infection. *Media Dermato-Venereologica Indones*. 2011;36:33-41.
- Tambe S, Zambare U, Nayak C. Nodulo-ulcerative and erythrodermic secondary syphilis in human immunodeficiency virus-infected individuals. *Int J STD & AIDS* [Internet]. 2019;30(5):505–8. Available from: <http://dx.doi.org/10.1177/0956462418815310>
- Macdonald G. Harrison's Internal Medicine, 17th edition. - by Fauci AS, Kasper DL, Longo L, Braunwald E, Hauser SL, Jameson JL, Loscalzo J. *Intern Med J* [Internet]. 2008;38(12):932. Available from: <http://dx.doi.org/10.1111/j.1445-5994.2008.01837.x>
- Harnanti DV, Hidayati AN, Miftahussurur M. Concomitant Sexually Transmitted Diseases In Patients With Diagnosed Hiv/Aids: A Retrospective Study. *African J Infect Dis* [Internet]. 2018;12(1S):83–9. Available from: <http://dx.doi.org/10.21010/ajid.v12i1s.12>
- Maskoep WI, Nasronudin N, Khairunisa S, Sudjarwo SA. The Influence of Anti-Hiv-1 Specific IgY In Inhibiting HIV-1 Infection in Binding Phase with Syncytium Examination of CD4 Receptor Density Using the Flowcytometry Method. *Folia Medica Indones* [Internet]. 2021;56(4):290. Available from: <http://dx.doi.org/10.20473/fmi.v56i4.24636>
- Health Mo. National Guidelines for HIV Management Medical Services. Jakarta: Ministry of Health Republic of Indonesia; 2019.
- Farrar J, Hotez PJ, Junghanss T, Kang G, Lalloo D, White NJ. Preface to the Twenty-Third Edition [Internet]. *Manson's Tropical Infectious Diseases*. Elsevier; 2014. p. xi. Available from: <http://dx.doi.org/10.1016/b978-0-7020-5101-2.00094-7>
- World Health Organization. WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children. Geneva: World Health Organization; 2007.
- Juanita L, Hadi U, Arfijanto V. Association Between Neopterin Levels and Outcome in 30 Day HIV/AIDS Naive Patients. *Biomol Heal Sci J* [Internet]. 2019;2(2):102. Available from: <http://dx.doi.org/10.20473/bhsj.v2i2.14965>
- Çakmak SK, Tamer E, Karadağ AS, Waugh M. Syphilis: A great imitator. *Clin Dermatol* [Internet]. 2019;37(3):182–91. Available from: <http://dx.doi.org/10.1016/j.clindermatol.2019.01.007>
- Carlson JA, Dabiri G, Cribier B, Sell S. The immunopathobiology of syphilis: the manifestations and course of syphilis are determined by the level of delayed-type hypersensitivity. *Am J Dermatopathol* [Internet]. 2011;33(5):433–60. Available from: <https://pubmed.ncbi.nlm.nih.gov/21694502>
- Lukehart SA. Syphilis. In: Jameson JL, Kasper, D.L., Longo, D.L., Fauci, A.S., Hauser, S.L., Loscalzo, J., ed. *Harrison's Principles of Internal Medicine* 20th Edition. New York: McGraw Hill Education; 2018: 1279–85.
- Kenyon C, Osbak KK, Crucitti T, Kestens L. The immunological response to syphilis differs by HIV status; a prospective observational cohort study. *BMC Infect Dis* [Internet]. 2017 Jan 31;17(1):111. Available from: <https://pubmed.ncbi.nlm.nih.gov/28143443>
- Liu XK, Li J. Histologic Features of Secondary Syphilis. *Dermatology* [Internet]. 2019;236(2):145–50. Available from: <http://dx.doi.org/10.1159/000502641>
- Avelar Pires CA, Soares JCM, Lopes dos Santos MA, Cordeiro HP, Campos Lodi VJ, Couto Rocha RP do, et al. Leprosy in a Patient Coinfected with HIV and Syphilis. *Am J Infect Dis* [Internet]. 2019;15(2):72–7. Available from: <http://dx.doi.org/10.3844/ajidsp.2019.72.77>
- Walker SL, Withington, S.G., Lockwood, D.N. Leprosy. In: Farrar J, Hotez, P.J., Junghanss, T., Kang, G., Lalloo, D., White, N.J., ed. *Manson's Tropical Diseases*. United Kingdom: Elsevier Saunders; 2014: 506–18.
- Wardiana M, Prakoeswa CRS, Sawitri R, Astari L, Prasetyo B, Budiono HAN. Dealing with tests and treatments for HIV, syphilis, and hepatitis B infection to prevent mother-to-child transmission (MTCT) from a tertiary hospital in Indonesia. *Bali Med J*. 2022;11:334–40.
- Costa-Silva M, Azevedo C, Azevedo F, Lisboa C. Early syphilis treatment in HIV-infected patients: single dose vs. three doses of benzathine penicillin G. *J Eur Acad Dermatology Venereol* [Internet]. 2016;30(10):1805–9. Available from: <http://dx.doi.org/10.1111/jdv.13766>
- Muliawan P, Sawitri AAS. Prevalence of HIV Infection Among Tuberculosis Patients in Bali, Indonesia. *Bali Med J* [Internet]. 2016;5(1):75. Available from: <http://dx.doi.org/10.15562/bmj.v5i1.272>



This work is licensed under a Creative Commons Attribution