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Case Report
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# Overlapping Primary and Secondary Syphilis in a Bisexual Patient with Human Immunodeficiency Virus

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**ABSTRACT**

**Background:** Syphilis and HIV are diseases that can be transmitted through sexual contact. Bisexual groups have a higher potential for HIV and syphilis transmission. In syphilis patients who have been infected with HIV, secondary syphilis often occurs along with primary syphilis, which can be found 2-3 times more often than in those who are not infected by HIV. **Case:** A 24-year-old male with HIV who is a bisexual man, complained chancre on his scrotum and on the tip of the penis that was painless and also has condyloma lata around the anus. Dermatological examination revealed multiple papules, patches, and plaques. The serological results for VDRL and TPHA were reactive. Histopathology examination of skin plaque suggests secondary syphilis. The Patient was diagnosed with overlapping primary-secondary syphilis and given therapy with single-dose intramuscular injection of benzathine penicillin G. **Discussion:** Bisexual groups have a higher potential for HIV and syphilis transmission. In HIV patients, primary and secondary syphilis often overlap. This was due to changes in the immune system causing the spread of Treponema pallidum more quickly and slowing the healing of primary lesions. **Conclusion:** Overlapping of primary and secondary syphilis in bisexual patients with HIV is common; in addition, the appearance of skin lesions in secondary syphilis can resemble other diseases, so confirmation by histopathology examination needs to be done.

**Keywords:** Bisexual, Human Immunodeficiency Virus, Overlapping, Primary Syphilis, Secondary Syphilis.

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## BACKGROUND

Syphilis is a sexually transmitted infection that is chronically progressive and caused by *Treponema pallidum*.[1,2] The natural history of syphilis consists of primary syphilis, secondary syphilis, latent syphilis, and tertiary syphilis.[1,2,3] Syphilis and HIV (Human Immunodeficiency Virus) are diseases that can be transmitted through sexual contact, so it is very likely that someone will suffer from both at the same time.[4,5] In syphilis patients who have been infected with HIV, secondary syphilis often occurs along with primary syphilis, which can be found 2-3 times more often than in those who are not infected by HIV.[1,2]

Based on the Integrated Biological and Behavioral Survey (Survey Terpadu Biologi dan Perilaku/STBP) in 2011 in Indonesia, the prevalence of syphilis in the HIV-infected female sex worker population was 16.7%, compared to 9.47% in those who were not infected with HIV. The prevalence of syphilis in the men who have sex with men (MSM) and HIV-positive population is 23.8%, while in those who are HIV-negative, it is 16.67%.[4] However, there is no clear data on the prevalence of syphilis in the bisexual population with or without HIV infection.

Bisexuality is a person's attraction to both men and women simultaneously to achieve sexual satisfaction. Bisexual groups have a higher potential for HIV transmission and syphilis when compared to MSM and heterosexual groups.[5] Based on Liao *et al.*, this could be due to an increase in HIV and syphilis transmission from bisexual groups to women.[6] Bisexual behavior is still a matter of debate, both in legal, social, religious, and cultural aspects.[7] Health aspects consider bisexual behavior to play an important role in the transmission

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of HIV and sexually transmitted infections, including syphilis.[5] Data from the Centers for Disease Control (CDC) in 2013 showed an increase in cases of primary and secondary syphilis in the bisexual group reaching 75%.[8]

We report a case of overlapping primary and secondary syphilis in a 24-year-old bisexual male patient with HIV. Patient has comprehended, agreed to, and signed the informed consent for this case. The purpose of this case report is to provide clinicians with insight into the overlapping primary and secondary syphilis that is more common in HIV patients. In addition, the appearance of skin lesions in secondary syphilis can resemble other diseases; especially in HIV patients, the possibility of misdiagnosis is higher, so it is hoped that this case report can increase the accuracy of establishing a proper diagnosis and management.

**CASE**

A 24-year-old male patient came to the Dermatology and Venereology clinic at Dr. Saiful Anwar General Hospital Malang (RSSA) with a chief complaint of sores on the tip of the penis and scrotum. Initially appeared some sores in the scrotum 5 weeks ago. The wound also appeared on the tip of the penis since a week ago. The wound was not accompanied by pain, and there was no previous history of trauma. In addition, the patient also complained that there had been several lumps around the anus since a month ago. The lump feels like it surrounds the anus and slowly expands; sometimes it hurts when defecating with a 3/10 VAS and occasionally itches with a 2/10 VAS.

Based on his social history, the patient works as an employee on a construction project and lives with his parents The patient is not married, but he has had sex since he was 23 years old. The last time he has sex was about a year ago. He has both male and female sexual partners and has had multiple partners. Female sexual partners are his close friends, ladies escort and commercial sex workers. The male sexual partner is also his close friend. He has sex with women orally and genitally. While the way to have sex with men is oral and anogenital, in which the patient acts as top and bottom. During intercourse, the patient sometimes uses a condom, and the patient does not know whether his sexual partner is or has ever had a sexually transmitted infection or HIV (Human Immunodeficiency Virus). The patient denied any history of blood transfusions or tattoos. In addition, the patient also denied that there was a history of previous sexually transmitted infections and that he had never had an HIV test before.

Physical examination of the patient's general state showed the patient appeared mildly ill with compos mentis consciousness. The vital signs showed normal results. Examination of the patient's nutritional status revealed a BMI of 16.89, which is included in the thin category.

Examination of the dermatological status of the facial region (Figure 1) showed hyperpigmented papules that were multiple, sharply marginated, and varied in shape and size. On the tongue, there was a whitish plaque with sharply marginated and irregular edges. The posterior trunk region (Figure 2) revealed hyperpigmented patches and papules that were sharply marginated and variable in shape and size. The right upper limb region (Figure 3) and the right lower limb region (Figure 4) showed patches, hyperpigmented plaques and papules, sharply marginated, irregular edges, multiple, varied in shape and size with some erythematous base erosion, multiple, sharply marginated, irregular edges, and varied shapes and sizes.

The venereological status examination (Figure 5) of the pubic region, body part of the penis, external urethral meatus, and perineum were within normal limits, and the prepuce was circumcised. On the glans penis, there was a shallow ulcer with an erythematous base, solitary, 0.5 cm x 0.3 cm in size, sharply marginated, indurated, and painless. On the scrotum, there was a shallow ulcer with an erythematous base, multiple sharply marginated, indurated margins, some covered with yellow crusts, and no pain. Perianal papules appear skin-colored, slightly erythematous, multiple, well-defined, variable in shape and size, and with a negative acetowhite test.

Dark Field Microscope (DFM) on superficial ulcers of the glans penis and scrotum, revealed no spirochaete *Treponema pallidum*. The Gram stain examination with 1000x magnification on the whitish plaque of the tongue, no budding yeast or pseudo-hyphae were seen (Figure 6).

Histopathology examination with a punch biopsy of a plaque lesion on right thigh with Hematoxylin-Eosin (H&E) staining (Figure 7) showed excised skin tissue with lichenoid reaction and vasculopathy. The epidermis shows hyperkeratosis and parakeratosis. Acanthosis is seen, and the rete ridges are irregularly elongated. The dermis shows an infiltrate of lymphocytes and histiocytes, some of which form aggregates (both superficial and perivascular and between fibro-collagenous connective tissue). Lichenoid reactions and vasculopathy may be features of secondary syphilis.

Rapid test Anti-HIV was reactive, with CD4 at 149 cells/uL. The Venereal Disease Research Laboratory (VDRL) examination was reactive with a titer of 1:16, and the Treponema Pallidum Hemagglutination Assay (TPHA) was reactive. Complete blood counts showed eosinophilia at 6.7%, and monocytosis at 7.6%. Other laboratory findings and Chest X-rays were within normal limits.

The patient was diagnosed with overlapping primary and secondary syphilis and HIV. The patient was prescribed with an injection of benzathine penicillin 2.4 million IU intramuscularly in a single dose, normal saline compress 0.9% for 10 minutes 3 times a day, then applied gentamicin ointment twice a day to skin erosions and ulcers. There was no Jarisch-Herxheimer reaction after injection of Benzathine penicillin. The patient was then consulted by the Internal Medicine Department and prescribed Cotrimoxazole 960 mg and antiretroviral FDC Tenofovir/Lamivudine/Efavirenz 1x1 tablets. Patients were advised to do a follow-through and re-examination of VDRL at 3, 6, 9, 12, and 24 months after injection of benzathine penicillin and given education not to have sex during treatment.

The third-month evaluation (Figure 8) revealed several thickened, blackened skin lesions, and some erosions and black crusts were seen in the plaque lesion of the patient's hamstring (A). The patient complained of itching with a VAS of 3/10. There are no visible genital ulcers or lumps in the anus. Serological examination revealed a VDRL titer of 1:16 and a CD4 cell count of 149 cells/uL. The patient was planned to continue to have control and re-examination of VDRL at 6, 9, 12, and 24 months after injection.

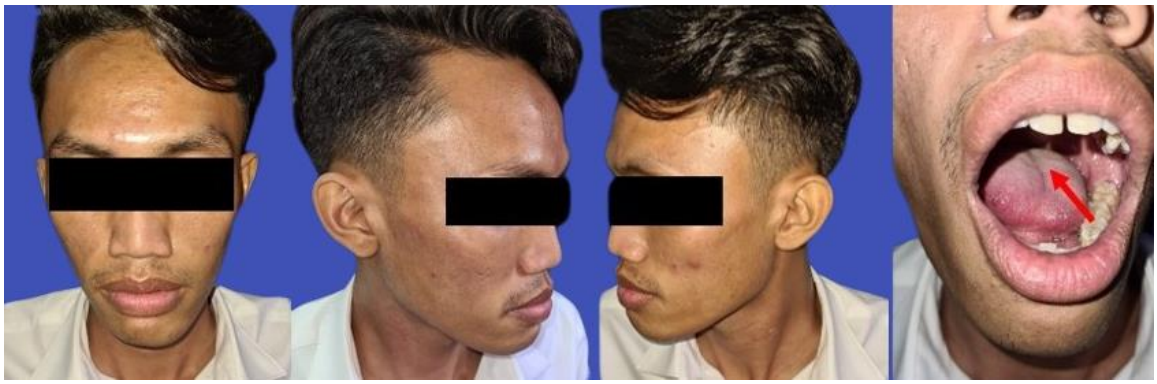

**Figure 1.** Hyperpigmented papules of multiple, sharply marginated, variable shapes and sizes on the face region. The tongue looks whitish plaque with sharply marginated, irregular edges edges on the tongue (red arrow).

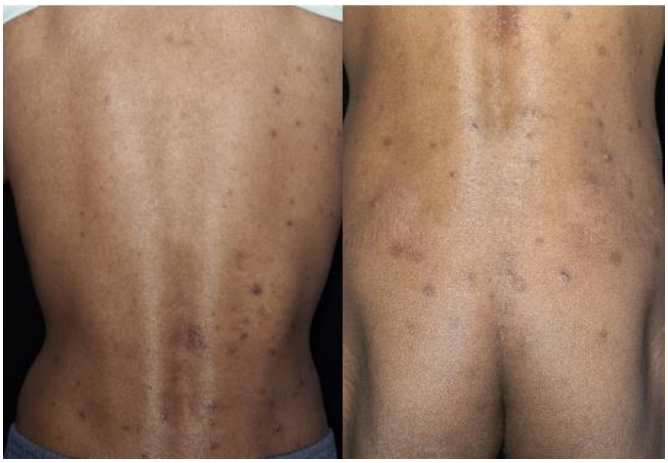

**Figure 2.** Hyperpigmented patches and papules, sharply marginated and variable in shapes and sizes, on the posterior trunk region.

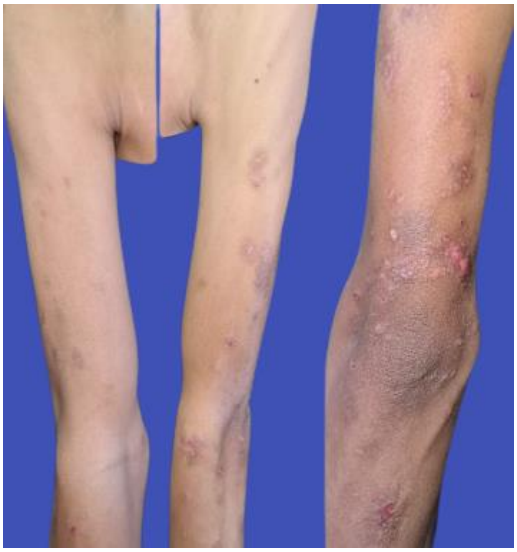

**Figure 3.** Patches, hyperpigmented plaques and papules, sharply marginated with irregular edges, multiple, varied in shape and size with some erythematous base erosion, multiple, sharply marginated irregular edges, and varied shapes and sizes on the superior extremities.

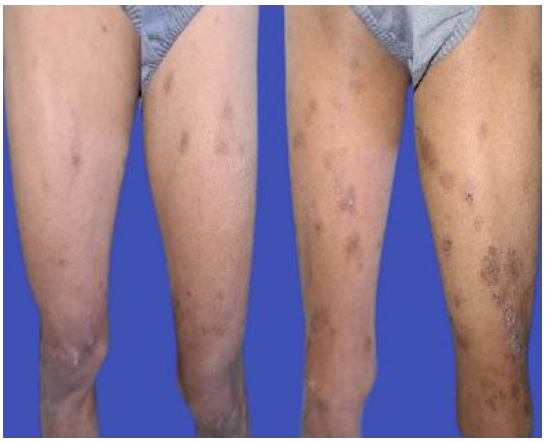

**Figure 4.** Plaques and papules with sharply marginated, irregular edges, multiple, variable in shape and size with some erythematous base erosion, multiple, sharply marginated irregular edges, varying shapes and sizes on the lower extremities.

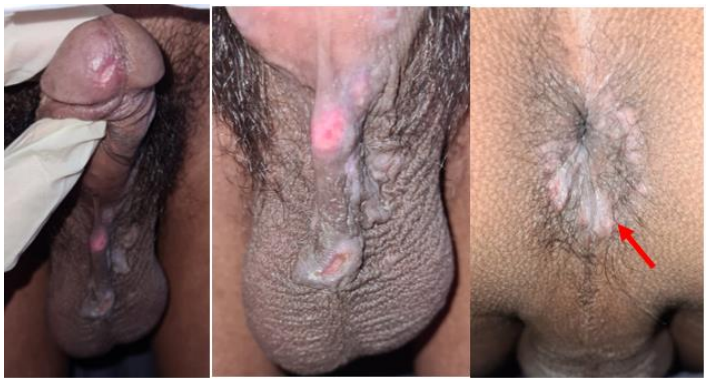

**Figure 5.** Examination of venereological status: A shallow ulcer, erythematous base, solitary, 0.5 cm x 0.3 cm in size, sharply marginated, indurated edges, and no pain on the glans penis. Multiple shallow ulcers with an erythematous base, sharply marginated, indurated margins, some covered with yellow crusts, and no pain on the scrotum. Multiple skin-colored papules with slightly erythematous, sharply marginated, variable shape and size on the perianal with a negative acetowhite test (red arrow).

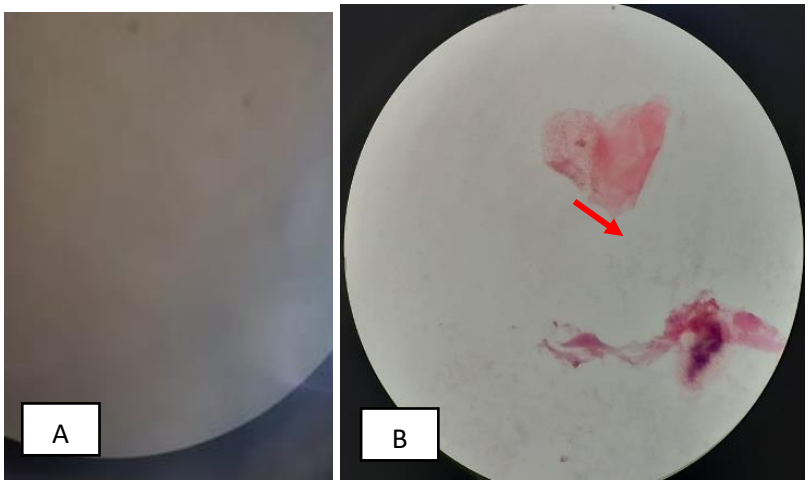


**Figure 6.** Investigations: Dark Field Microscope (DFM) on superficial ulcers of the glans penis and scrotum, no spirochaete *Treponema pallidum* were seen (A). A gram stain examination with 1000x magnification on the whitish plaque of the tongue, found no budding yeast or pseudo-hyphae (→) (B).

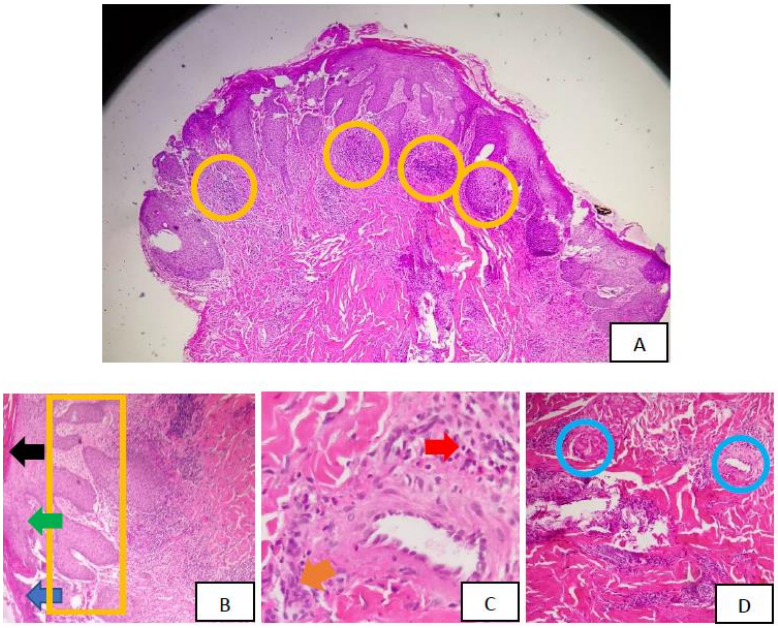


**Figure 7.** Histopathology examination with H&E staining. A. Enlargement x40, a lichenoid reaction is seen, which is characterized by a lymphocytic infiltrate that obscures the dermo-epidermal junction (yellow circle). B. Enlargement x40, the epidermis shows hyperkeratosis (→) and parakeratosis (→). Acanthosis (→) is seen, irregularly elongated rete ridges (yellow box). C. Enlargement x400, dermis visible infiltrate of lymphocytes (→) and histiocytes (→). D. Enlargement x100, some form aggregates (both superficial and perivascular and between fibro-collagenous connective tissue). Vasculopathy (blue circle) is seen.

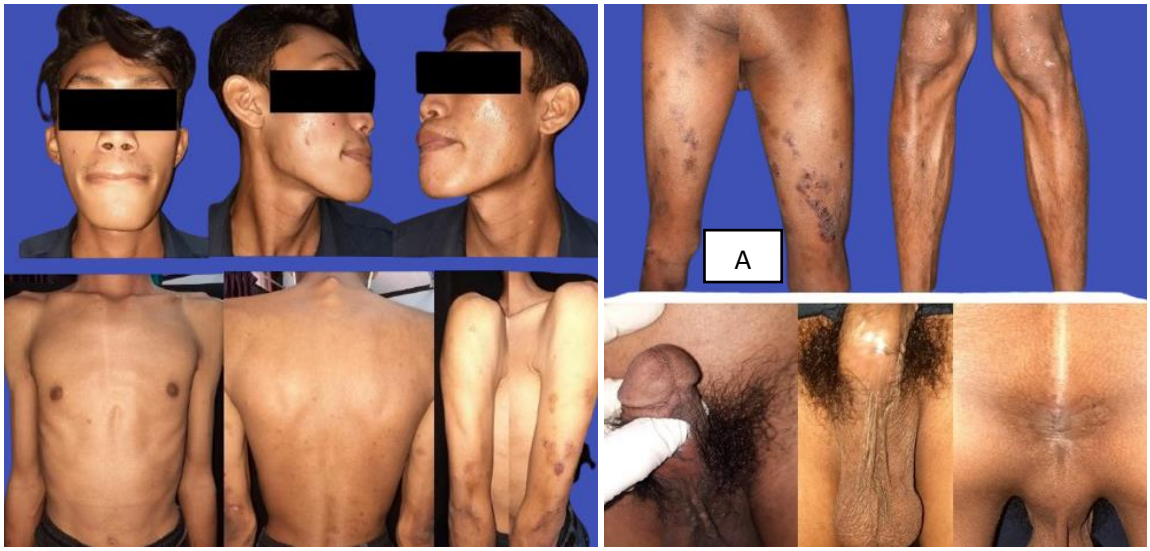


**Figure 8.** Third-month evaluation. Several thickened, blackened skin lesions were seen, and several erosions and black crusts were seen in the plaque lesion of the patient's hamstring (A). There were no visible genital ulcers or visible lumps in the anal.

## DISCUSSION

Syphilis is defined as a sexually transmitted infection that is a chronic, progressive, systemic infection that in the course of the disease, can affect almost all body structures with clear clinical manifestations, but there is a latent period that can be asymptomatic.[1]

The incidence of syphilis has increased over the past two decades, especially in the United States, Europe, Canada, Australia, and China.[8-16] Data from the Centers for Disease Control (CDC) in 2013 showed an increase in primary and secondary syphilis cases in the bisexual group, reaching 75%.[7] In 2011, The integrated Biological and Behavioral Survey (IBBS) in Indonesia reported that the prevalence of syphilis was still quite high. In the transgender population, the prevalence of syphilis is 25%, FSW (female direct sex workers) 10%, and MSM (men who have sex with men) is 9%.[4] Syphilis prevalence is positively correlated with HIV prevalence. In 2011, The integrated Biological and Behavioral Survey (IBBS) in Indonesia reported that the prevalence of syphilis in the HIV-infected FSW population was 16.7%, compared to 9.47% in those who were not infected with HIV. The prevalence of syphilis in the HIV-positive MSM population was 23.8% while in those who are HIV-negative, it was 16.67%.[4] The patient in this case report is male, 24-year-old. The patient was bisexual and was diagnosed with syphilis and HIV.

Syphilis is caused by *Treponema pallidum*. This bacterium is spiral-shaped, Gram negative with an average length of 11 μm and a diameter of 0.09 – 0.18 μm. *Treponema pallidum* has 3 types of movement, namely rapid rotation along the long axis of the helix, cell flexion and can move forward like a corkscrew movement. These bacteria cannot be cultured in vitro and can be seen using a darkfield microscope.[17,18]

Syphilis is most often acquired through sexual contact when a person comes in contact with infectious syphilis lesions, namely in primary and secondary syphilis. The infectious lesions of syphilis include the chancre, condyloma lata, and mucous patches. They can affect any part of the body but are usually around the genitals, anus, or mouth. Direct contact with infectious lesions during oral, vaginal, or anal sex or during other sexual activities may result in inoculation and infection. Syphilis can also be transmitted through non-sexual contact, including blood transfusion, accidental inoculation (eg., laboratory workers or health care workers), tattoos, or congenital syphilis.[2] As a result of anamnesis in this patient, syphilis is suspected to have been acquired through sexual contact, both genito-genital and anogenital.

*Treponema pallidum* can invade the circulation and penetrate body barriers, such as the blood-brain barrier to then infect many tissues and organs of the body. Untreated syphilis can progress to several stages of disease, namely primary, secondary, latent, and tertiary syphilis stages.[2] Primary syphilis is characterized by the appearance of a solitary and indurated ulcer or chancre at the site of contact with infection within 10-90 days after suspected coitus.[2] In two-thirds of patients infected by HIV, the ulcers may be multiple, non-indurated, and irregularly circumscribed.[1]

Bilateral inguinal lymph node enlargement without pain is common in the majority of patients. These ulcers are often found on the genitals, perineum, and anus.[2] In men, they are often found on the glans penis or around the coronary sulcus and scrotum.[1] Ulcers can heal spontaneously without treatment within 3-6 weeks, and if treated, they can heal within 1-2 weeks.[2] Without treatment, pathogens can invade endothelial cells and produce hematogenous spread, resulting in systemic infection.[1] In case reports, the patient has ulcers or chancres on his glans penis and scrotum. The characteristics of the lesion are the same as in theory, namely that the ulcer on the glans penis is oval in shape, the edges are indurated, the base is clean without exudate, and it is painless. Because the patient is also infected with HIV, multiple ulcers on the scrotum can be found with irregular shapes and edges that are still indurated, clean with no exudate, and have a painless base. Inguinal lymph node enlargement was not found in the patient in this case report.

Secondary syphilis results from the multiplication and spread of Treponema to the body and generally occurs approximately 3-12 weeks after the chancre or within 6 months after contact.[1,2,18] Lesions can be Roseola syphilitica, Biett collarette, Crown of Venus or corona veneris, Clavi syphilitica, Alopecia syphilitica, and Plaques fauchée en prairie. These lesions may be accompanied by painless submandibular or cervical lymphadenopathy.[19] Condyloma lata is a grayish-white papule or plaque that is well-defined, flat, moist and has a macerated surface. Condyloma lata appears in areas close to the primary chancre, generally in the perineum or around the anus; this is due to the direct spread of Treponema from the primary lesion. In addition, condyloma lata can be found in other moist areas such as the armpits, between the toes, under the breast folds, and the umbilicus.[2]

Patients with syphilis who are HIV-infected often develop secondary syphilis along with primary syphilis, which can be found 2-3 times more often than those who are not infected with HIV.[1,2] In HIV patients, primary and secondary syphilis often overlap. Immunological changes in HIV patients can cause the spread of *Treponema* more quickly, resulting in a more rapid progression from primary syphilis to secondary syphilis. Furthermore, these immunological changes may result in delayed healing of the primary lesion.[2]

The patient in this case report also had manifestations of secondary syphilis in the form of condyloma lata on his anus. According to the theory that condyloma lata often appears in areas close to the primary chancre, likely on the glans penis and scrotum. Because the patient is also infected with HIV, the symptoms of secondary syphilis occur simultaneously with those of primary syphilis.

Syphilis laboratory examination consists of the detection of *T. pallidum* and syphilis serological and histopathology tests.[1,2] Detection of *T. pallidum*, one of which can use a dark field examination (DFE) with specimens for cases of primary syphilis from ulcer or chancre lesions, secondary syphilis from condyloma lata lesions and mucus from rhinitis in congenital syphilis.[2] In this way, *T. pallidum* appears as a glowing white spiral body on a black background.[1] DFE examination is able to confirm the diagnosis of syphilis directly in primary, secondary, and early congenital syphilis.[1]

Syphilis serological tests are divided into two types, namely non-treponemal tests and treponemal tests.[1,2] The most commonly performed non-treponemal test was the Venereal Disease Research Laboratory (VDRL) test.[2] This test can be used to diagnose and monitor the response to therapy.[2] The most commonly performed treponemal test was the T. pallidum hemagglutination assay (TPHA).[2] A reactive treponemal test result can exclude a false positive reaction to a non-treponemal test, so reactive non-treponemal and treponemal tests confirm the diagnosis of syphilis.[2] The interpretation of non-treponemal and treponemal serological tests for HIV patients was the same as for HIV-uninfected patients.[20]

Histopathology examinations are not always performed to diagnose syphilis, except in doubtful cases.[2] Histopathologic features of secondary syphilis may vary. There is a lichenoid infiltrate consisting of many plasma cells, lymphocites and histiocytes.[21] The dermis is found to have edema of the papillary dermis and a perivascular and/or periadnexa infiltrate of lymphocytes and/or histiocytes. In one-third of cases, *T. pallidum* can be found, usually in the epidermis and dermis, with Warthin–Starry staining.[2]

In this case report, DFE using a specimen from the ulcer or chancre did not reveal *T. pallidum*. The VDRL serology test was reactive with a titer of 1:16, and TPHA was reactive. The results of a reactive VDRL and TPHA examination were sufficient to confirm the diagnosis of syphilis in this patient; however, this patient's histopathology examination was continued since there were manifestations of skin lesions that led to suspicion of malignant syphilis. Histopathology examination of the patient in the case report showed secondary syphilis with lichenoid reaction and vasculopathy. Reaction vasculopathy was found in the histopathology picture of malignant syphilis. However,

the diagnosis of malignant syphilis in the patient in this case report could be ruled out because it did not meet the other criteria for the diagnosis of malignant syphilis.

Benzathine penicillin G is the first-line treatment for all stages of syphilis. The dose and duration of treatment depend on the stage or clinical manifestation of syphilis. There was no difference in the dose and route of administration in both non-HIV and HIV patients.[2] Benzathine penicillin G 2.4 million units intramuscularly in a single dose is the first-line treatment for primary and secondary syphilis.[2] However, the use of benzathine penicillin G cannot prevent the progression of neurosyphilis in patients with HIV. Some suggest that the minimal treatment of primary or secondary syphilis infection with neurologic involvement in patients with HIV is 2.4 million units of benzathine penicillin G, given three times intramuscularly at one-week intervals.[22] After penicillin administration, it is important to observe the Jarisch-Herxheimer reaction.[1,2] Because the diagnosis was established as overlapping primary-secondary syphilis and no neurological disorders were found, the patient in this case report received a single injection of 2.4 million units of benzathine penicillin G intramuscularly. In addition, no Jarisch-Herxheimer reaction was found in this case report.

Clinical and quantitative serological evalution of primary and secondary syphilis patients with HIV coinfection was performed at 3, 6, 9, 12, and 24 months after treatment.[1,2] Treatment was successful if there was a fourfold decrease in VDRL/RPR titer at 6 and 12 months for, either primary or secondary syphilis with or without HIV.[1] In secondary syphilis, generally, the VDRL/RPR test will become non-reactive 12-24 months after therapy.[2] In this case report, the patient was evaluated at month 1 and 3 due to HIV coinfection. Until the 3rd month evaluation, there were no decrease in non-treponemal titers; this is in accordance with the theory that in secondary syphilis, a fourfold decrease in titers can occur at 6 - 12 months. However, clinically, the patient's ulcer or hancre and condyloma lata had disappeared during the first month of evaluation. The patient will be followed up with a VDRL titer and clinical evaluation at 6, 9, 12, and 24 months.

In conclusion, syphilis is a chronic and progressive sexually transmitted infection caused by *Treponema pallidum*. Syphilis has a course of disease consisting of primary syphilis, secondary syphilis, latent syphilis, and tertiary syphilis. Syphilis and HIV are diseases that can be transmitted through sexual contact, so it is very likely that someone will suffer from both at the same time. Syphilis patients who have been infected with HIV often have secondary syphilis simultaneously with primary syphilis, which can be found 2-3 times more often than those who are not infected with HIV. This is due to immunological changes in HIV patients that can cause the spread of *Treponema* more quickly, resulting in the development of primary syphilis into secondary syphilis more quickly and causing delayed healing of the primary lesion. This case report confirms that the clinical manifestations of syphilis in HIV patients can occur at several stages of the disease course and are often atypical, so that in this case the diagnosis can be made with supporting examinations such as a laboratory examination consisting of the detection of *T. pallidum*, and syphilis serological and histopathology tests.

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