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Case Report

Case Report: Secondary Syphilis And Human Immunodeficiency Virus Coinfection

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ABSTRACT

Introduction: Syphilis is a sexually transmitted infection that is chronically progressive, with a broad spectrum of active clinical and asymptomatic periods. A total of 80.6% of men with syphilis were Men Who Sex with Men (MSM), 47% of the population was coinfected with Human Immunodeficiency Virus (HIV).

Case Presentation: Male, 23-yo, MSM, unmarried, HIV, complaining of red bumps and spots on the palms, soles, and upper arms since 4 days ago. One week earlier, he complained of sores in the genitals, which recurred 1 year ago and healed on their own. Dermatological examination revealed multiple erythematous patches and papules. The corpus penis, glans penis, and scrotum showed erosions and multiple ulcers with an erythematous-based, covered with yellowish crusts. VDRL and TPHA were reactive. The patient was diagnosed with secondary syphilis and treated with an intramuscular injection of benzathine penicillin 2.4 million IU once. A 1-month evaluation showed significant lesion improvement, VDRL titer 1:64. Evaluation of the 3rd and 6th months revealed a VDRL titer of 1:4.

Conclusion: The clinical manifestations of syphilis patients with HIV coinfection are generally more atypical, aggressive, and overlap caused by changes in the immune system in HIV infection. Unsafe sexual behavior in MSM increases the transmission of syphilis infection. Diagnosis and therapy are generally the same. Men Who Sex with Men is a factor that allows the transmission of syphilis in HIV patients. Administration of benzathine penicillin injection once gave lesion improvement and significantly reduced VDRL.

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INTRODUCTION

Syphilis is a chronic progressive sexually transmitted infection with a broad spectrum of clinically active and asymptomatic periods caused by *Treponema pallidum* [1]. In 2015, the European Center of Disease Prevention and Control (ECDC) received 28,000 new case reports, an increase of 49% since 2010. Syphilis cases are mostly found in patients 15-49-yo, dominated by men who have sex with men (MSM) [2,3]. A total of 80.6% of men with syphilis were MSM, 47% were co-infected with HIV [4].

Unsafe sexual behavior increases the transmission of infection [4]. HIV-coinfection also increases the incidence of neurosyphilis [5]. HIV-coinfection in syphilis causes increased disease progression, less effective treatment outcomes, overlapping symptoms, multiple chancre lesions, and impaired serological response in the form of high titers, false negatives, and delayed seroactivity [6].

This case report describes secondary syphilis in a 23-year-old MSM man who has HIV and presents cases of patients who have overlapping symptoms. To establish a diagnosis and treatment requires special learning. This case report aimed to provide an understanding of syphilis with HIV coinfection, so that appropriate management can be implemented.

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CASE PRESENTATION

A 23-year-old man with BMI of 18,28 was consulted from the Internal Medicine Polyclinic RSUD Dr. Saiful Anwar (RSSA) Malang complained about the appearance of red spots on the palms of his hands and feet 4 days before. Small nodules appeared on the palms followed by red spots and spread to the upper arms. Two days later, red spots and nodules also appeared on the soles, accompanied by itching (VAS 7/10). The patient also complained of red scaly patches above the eyebrows, cheeks, nose folds, and lips 2 months before, accompanied by itching (VAS 4/10). History of fever(-), nausea and vomiting (-). Thrush (+) on the tongue since 4 days before. Swallowing pain (-), drooling eyes and blurred vision (-), headache (-), convulsions (-).

The patient also complained of sores on the genitals 1 week before, pain when exposed to friction (VAS 2/10), and itching (VAS 3/10). Lump in the groin (-). Elasticity in the genitals or a history of swelling before the wound appears (-). Discharge from the genitals(-), pain when urinating (-), lumps or warts on the genitals or around the anus (-).

There was a history of recurrent lacerations in the genitals since 1 year ago. In December 2020, the patient complained of coughing up phlegm for 2 months and weight loss (10 kg). The patient was diagnosed with HIV and received FDC antiretroviral Dolutegravir/ Lamivudine/ Tenofovir 1x1 tablet since 1st March 2021, Fluconazole 1x150 mg, and 1x1 Fe tablet from the Internal Medicine Department.

The patient has never received treatment. History of drug allergy (-). The patient was unmarried. The patient was MSM. The patient had changed partners 6 times. His last sexual intercourse was 1 year ago, anogenitally without a condom and alternated top and bottom positions. The patient did not know whether his partner was infected with HIV. He denied similar complaints to sexual partners.

Dermatological examination of the tongue showed multiple whitish plaques, well-defined, irregular edges, varied in shape and size, easy to collect, blood (-). The facial region showed multiple erythematous patches, indistinct borders, irregular edges, varying in shape and size with yellowish-white scales on top. Paper oil test(+). The regions of superior extremities, palmar and dorsal manus, and plantar and dorsal pedis showed multiple erythematous patches and papules, well-defined, irregular edges, variable in shape and size, minimal scale (Fig.1). The corpus penis, glans penis, and scrotum showed erosions and superficial ulcers (erythematous bases), well-defined, irregular edges, varying in shape and size, covered with yellowish crusts. The erosions and ulcers are mostly dry and there is no tenderness (Fig.2).

Gram examination of the penis did not show PMN cells, bacteria, and school of fish images. A Darkfield Microscope examination was not performed. Examination of 10% KOH on the scales did not reveal hyphae or spores. Gram examination of the tongue revealed budding yeast.

CBC showed Hb 9.6 mg/dL, lymphopenia 12.7%, and monocytosis 15.1%. Rapid test AntiHIV was reactive with CD4 14 cells/uL. Reactive VDRL (1:32) and TPHA (>1:5120). Nonreactive HBsAg and nonreactive Anti-HCV examination. Examination of IgM Anti-CMV negative, IgG Anti-CMV positive 317.2, IgM and IgG anti-toxoplasma negative. Examination of the expert sputum gene did not detect *Mycobacterium tuberculosis*. CXR examination showed rough bronchovascular pattern that indicated upper respiratory infection.



Fig. 1. **Initial Dermatological Examination**. Multiple erythematous papules and plaques, well demarcated, varying in shape and sizes (→) were seen on (A) superior extremity; (B) palmar and dorsum manus; and (C) plantar and dorsum pedis

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Fig.2. Venereological examination. (A) Initial examination. Erosions and superficial ulcerations with multiple erythematous bases were seen, well demarcated, some covered with yellowish crusts. **(B) 6th month examination.** No erosions and ulcers were seen

The patient was diagnosed with secondary syphilis, seborrheic dermatitis, oral candidiasis, HIV stage 4, underweight, and anemia. The patient was injected with benzathine penicillin 2.4 million IU intramuscularly once, desonide 0.05% cream 2x/day on the face, and nystatin drop 4x400,000 IU. There was no Jarisch-Herxheimer reaction. Therapy from the Internal Medicine Department was continued. Patients were planned for VDRL examination at 1, 3, 6, 9, 12, and 24 months after injection and educated to have no sex during treatment.

In the first month, there was a significant improvement in the lesions. There were no genital sores or new lesions. It was not itchy. The VDRL titer was 1:64. At the 3rd month there were no new lesions, the old lesions had improved, and the VDRL titer was 1:4. At the 6th month (Fig. 3) there were no new lesions and the VDRL titer remained 1:4.

DISCUSSION

Syphilis is caused by *Treponema pallidum*. These bacteria can be seen using a darkfield or phase contrast microscope [7]. A total of 80.6% of men with syphilis were MSM, and 47% were coinfected with HIV due to unsafe sexual behavior and recreational drug use[8,9]. In Indonesia, the prevalence of syphilis in 2011 was still high, 9% of cases were MSM. The patient was 23 years old, an MSM with HIV since December 2020, and undergoing ARV since 1st March 2021.

Primary syphilis is characterized by a primary chancre. Secondary syphilis occurs 3-12 weeks after primary infection, mucocutaneous lesions, organ involvement, and systemic symptoms. Early latent syphilis occurs <1 year after contact and may develop recurrent secondary syphilis. Advanced latent syphilis occurs >1 year. Symptoms of tertiary syphilis include mild late-phase symptoms (16%), cardiovascular symptoms (10%), and neurosyphilis (5%-10%). The most common neurosyphilis is ocular syphilis [10].

The initial lesion is a 5-1.5 cm papule that appears at the site of venereal contact, 10-90 days after exposure. Within a week it turns into a chancre that is caused by infiltration of host lymphocytes and macrophages. Bilateral regional lymphadenopathy is common. Syphilis of the anus and rectum is common in MSM men. Chancre lesions will heal on their own without treatment within 3-6 weeks [11].

Secondary syphilis, systemic disease with vasculitis and is referred to as "the great imitator"occurs after a few weeks/months or may occur at the same time as the primary lesion[1,11,12]. In the secondary phase, spirochete proliferation increase resulting in systemic infection [13]. Secondary lesions begin with copper-red macular lesions and then develop into skin lesions, symmetrical, brownish-red discrete maculopapular rashes on the trunk, extremities, soles of the feet and hands, and *roseola syphilitica*, measuring 0.5-2 cm and covered by a *Biett collarette*, may smooth, follicular, or pustular lesions [11].

Symmetrical lesions are found in 40%-70% of cases on the palms or soles. Plantar lesions may resemble clavi syphilitici. In certain cases, lesions of the Crown of Venus/*corona veneris* are found. Lesions can also be nickels and dimes [13]. The mucosal lesions in secondary syphilis may be ulcerated, painless pseudomembranous lesions such as mucosal patches, keratoses, or plaques, may be accompanied by painless submandibular/cervical lymphadenopathy [14,15]. Confluent patch lesions on the tongue are referred to as *fauchee en prairie* plaques [16]. Secondary lesions are generally accompanied by *condyloma lata* [11]. The patient's manifestations resembled secondary syphilis due to the presence of symmetrical brownish red maculopapular lesions on the trunk, extremities, palms, and soles, chancre lesions on the genitals, and a history of repeated genital sores. Secondary syphilis may coexist with the development of chancre lesions, and it is common in HIV-coinfected patients.

Treponemal and nontreponemal tests after clinical manifestations appear for at least three weeks [4]. The most common nontreponemal tests are VDRL and Rapid Plasma Reagin (RPR) which begin to be reactive 4-5 weeks after infection, and sensitivity is 100% at 12

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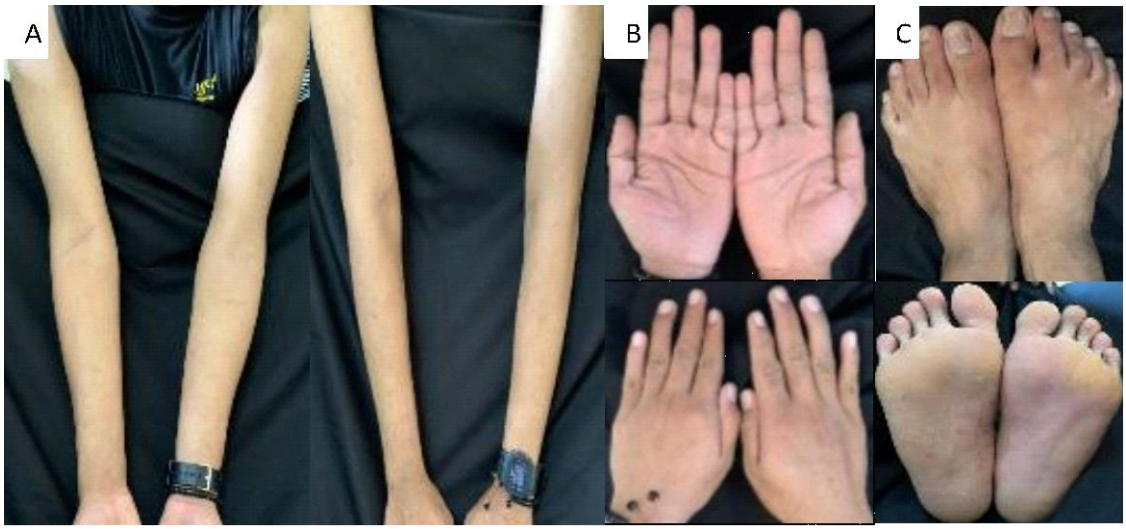


Fig. 3. **6th month dermatological examination.** Multiple well-defined hyperpigmented patches were seen on (A) superior extremity; (B) palmar and dorsum manus; and (C) plantar and dorsum pedis

weeks, dropping to nonreactive in 25-30% of latent syphilis. The results of the VDRL titer examination should be carried out on the day of starting therapy [17].

The treponemal tests consist of TPPA test, MHA-TP, FTA-ABS, TPHA, and the enzyme immunoassay treponemes. This test has a higher sensitivity and specificity[1]. Darkfield microscopy from chancre lesions or condyloma lesions is recommended. Sensitivity is 74-79% and decreases over time due to dead *Treponema* bacteria [18].

In this case, the patient's VDRL (1:32) and TPHA (>1:5,120) examinations were reactive. It was sufficient to diagnose a patient with syphilis. Darkfield microscopy was not performed because there was no serous exudate sample. Syphilis infection was more common in HIV-coinfection, especially in the MSM group. Research by Novak et al. showed that of the 6,888 participants, 57% were MSM men. This is the majority population with syphilis (82.8% of participants with syphilis) [19]. In patients with HIV, CD4 T cells are decreased, leading to reduced immunity [5]. ARV is said to compensate for risk and reduce the fear of transmitting HIV infection [5,20].

Syphilis can open a portal through disruption of the mucosa so that cells become susceptible to HIV. CD4 cells recruited to the site of infection will be easily infected by HIV. Stimulation of macrophages by the Treponema lipoprotein increased the expression of HIV-1 and CCR5 genes. Peripheral blood mononuclear cells exacerbate T. pallidum infection-causing simultaneous transmission of HIV and T. pallidum [5].

Chancres in coinfected patients are generally multiple, deeper, wider, more atypical and aggressive. HIV-coinfection also increases the incidence of neurosyphilis [1]. HIV infection can complicate the serological diagnosis of syphilis and its monitoring [4]. seronegative results in a patient clinically suspected of syphilis, biopsy, darkfield microscopy, or T. pallidum PCR may be performed [1].

In this case, there was co-infection of secondary syphilis and HIV without neurological disorders. The patient's social history, such as MSM, multiple sex partners, and sexual intercourse without using a condom are factors that allow the transmission of syphilis transmission in HIV patients. The patient was also diagnosed with seborrheic dermatitis and oral candidiasis, clinical manifestations of HIV acquired from stage 2.

A single dose of 2.4 million units of benzathine penicillin is the first line of treatment. Ceftriaxone 1 gram IV/IM daily for 10 days for patients allergic to Penicillin. Tetracycline 500 mg 4x/day or doxycycline 100 mg 2x/day for 14 days are alternative treatments [11]. Minimal therapy for primary or secondary syphilis infection with neurologic involvement in HIV coinfected patients is 2.4 million units of benzathine penicillin given three times, with each dose spaced one week apart [4].

Effective treatment will be characterized by the disappearance of the lesions in a matter of days. RPR examination will show negative results after 1-2 years or longer in cases of secondary syphilis [11]. Follow-up in HIV coinfected syphilis patients was performed at 3, 6, 9, 12, and 24 months post-treatment. Treatment success was characterized by a fourfold decrease in titers on the VDRL and RPR tests. In secondary syphilis, the VDRL and RPR tests generally become nonreactive 12-24 months after therapy [1].

Patients were evaluated at 1, 3, and 6 months post-treatment, and continued at months 9, 12, and 24.

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Evaluation 1 month after treatment showed significant improvement of body lesions, genital lesions had disappeared, and no lesions were found. new. Serological examination revealed a VDRL titer of 1:64. The TPHA titer examination does not need to be carried out for monitoring, while there is an increase in the VDRL titer. The increase in the VDRL titer was not significant, so there was no need for repeat therapy. However, the patient needs further monitoring to see the effectiveness of secondary syphilis treatment. Evaluation at 3 months showed an eightfold decrease in VDRL titer, which was 1:4 and at 6 months it remained 1:4, without any new lesions.

CONCLUSION

An unmarried man, 23 years old, MSM, diagnosed with secondary syphilis and HIV. Clinical manifestations are generally more atypical and aggressive, and overlap between primary, secondary, latent, and tertiary syphilis. Diagnosis and therapy are generally the same. In this case, the patient received a one-time injection of benzathine penicillin. Evaluation at 1, 3, and 6 months revealed a significant improvement in the lesion and a decrease in VDRL titer.

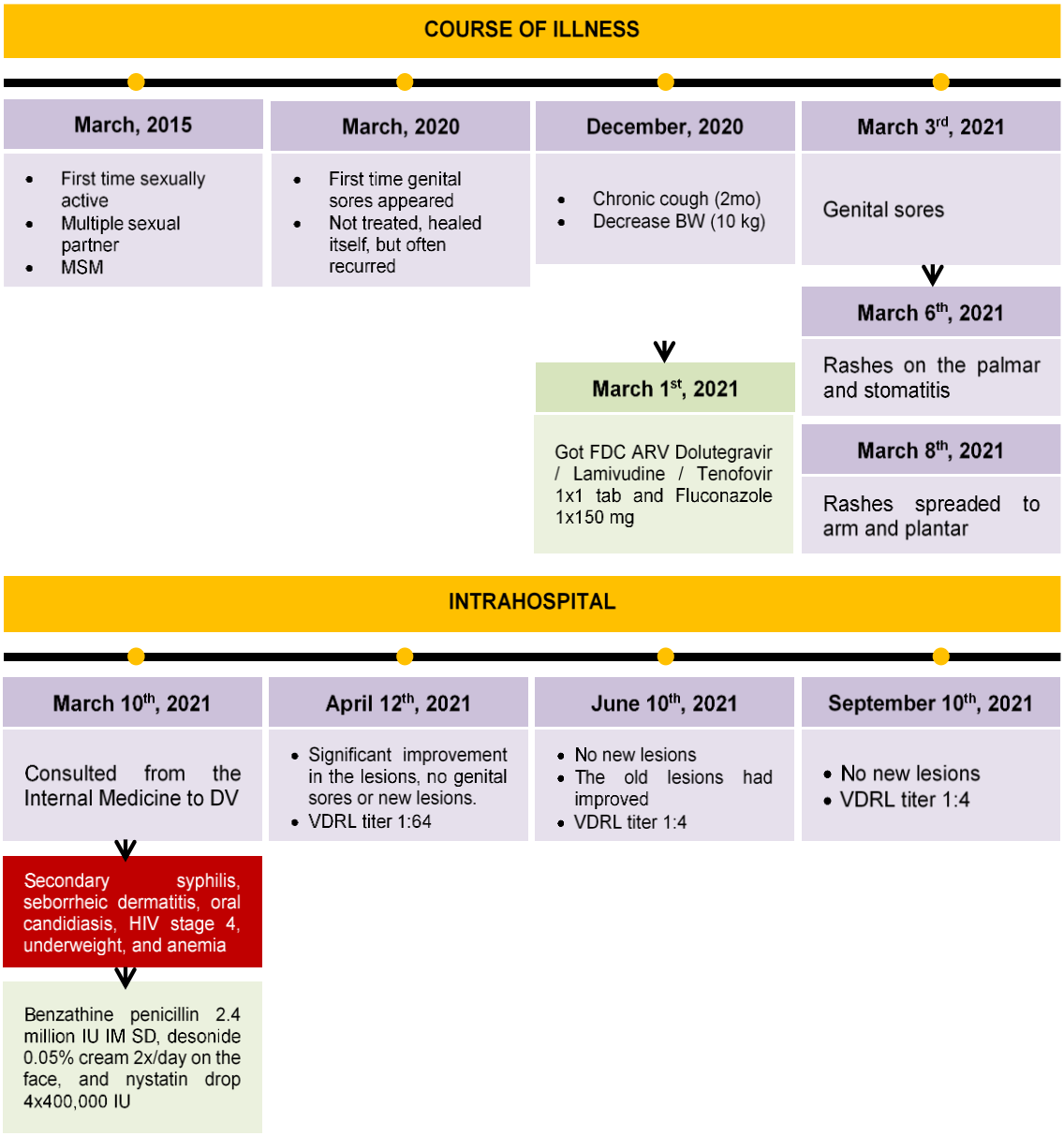


Fig. 4. Timeline of Patient's Disease and Medication

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CONFLICT OF INTEREST

The authors state that they have no conflicts of interest.

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