

Secondary Syphilis with Human immunodeficiency Virus (HIV) Coinfection: A Case Report

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Abstract

Syphilis is a sexually transmitted disease caused by spirochete microorganism *Treponema pallidum*, the infection spreads in four stages: primary, secondary, latent, and tertiary. It can impact almost all organ systems in the body, even years or even decades after the initial infection. Syphilis is an infection that could be transmitted sexually with almost 21.000 new cases in Indonesia. The CDC also estimates that 44% of men who have sex with men and bisexual men who test positive for syphilis will also have HIV. The infection has also re-emerged in developed countries in homosexual population with high number of cases co-infected with HIV. Syphilis is also very common among people with multiple sexual partners, Significant risk factors include HIV infection, this coinfection is common, and the two diseases affect each other in several ways. HIV and syphilis each facilitate infection by the other, and aggravate one another's clinical course. A 34-year-old male was referred from public health center with red rashes found on the palm and soles bilaterally since 1 month before visit. Dermatological examination of the palms and soles showed multiple violaceous macules with clear boundaries, with varying sizes between 0.5cm-1cm, no alopecia, no abnormalities were found in oral mucosa, The result of VDRL examination the titer was 1:64, and TPHA result was Positive. Rapid HIV test showed positive result. Patient was prescribed Benzathine Peniciline injection intra muscular 2.4 million IU, the patient experienced clinical improvement and decreased VDRL and TPHA titers after a two month of evaluation. Co-infection of syphilis and HIV, HIV and syphilis each facilitate infection by the other, and aggravate one another's clinical course. The majority of persons with HIV infection respond appropriately to the recommended benzathine penicillin G treatment regimen for primary and secondary syphilis.

Keywords: Sexually Transmitted Disease; Secondary syphilis; Benzathine penicillin; Coinfeksi HIV

1. Introduction

Syphilis remains a global public health problem; the World Health Organization (WHO) estimates an incidence of 12 million new cases each year, with more than 90% of the cases occurring in the developing world⁷. Syphilis is an infection that could be transmitted sexually and caused by certain bacteria called *Treponema pallidum*. Based on clinical examination alone, syphilis is hard to diagnose thus this disease has other name such as "great imitator" and "mimicker"⁷. The particular manifestations of *Treponema pallidum* infection depend upon time, site, and the immune status of the infected individual. Time (duration of infection) relates to the designation of the stages of syphilis as primary, secondary, and tertiary disease. *Treponema* is a genus of spiral-shaped bacteria with outer membrane that contain phospholipid membrane^{1,18}. The infection has also re-emerged in developed countries in homosexual

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population with high number of cases co-infected with HIV⁴. Syphilis is also very common among people with multiple sexual partners. Syphilis is also linked with other sexually transmitted disease such as Human Immunodeficiency Virus (HIV).⁶

Center for Disease Control and Prevention reported more than 80 thousand new cases of syphilis, syphilis is also very common among sex worker with incidence of active syphilis among them was 10.8% in 2018, almost quarter of those cases were primary and secondary syphilis³. Sexually transmitted infections (STIs) continue to be a significant cause of morbidity and public health risk, particularly in men who have sex with men (MSM)². Men aged between 20-29 is the highest demographical group for syphilis. Syphilis is also linked with other sexual transmitted disease such as Human Immunodeficiency Virus or HIV³. Both syphilis and HIV infections are part of sexually transmitted diseases. Sexual contact is one of the mode of transmissions for both infections, thus co-infection is perhaps common. The majority of persons with HIV infection respond appropriately to the recommended Benzathine penicillin G, 2.4 million units IM in a single dose regimen for primary and secondary syphilis⁸.

2. Case study

A 34 year-old male was referred from public health center to a dermatologist with red rashes found on the palm and soles bilaterally. The complaint had been persistent since 1 month before examination. One months before the visit he complained a painless lesion in the genital area. But the lesion was gone quickly without treatment. The rashes were not itchy, and tended to be stable. The patient has never complained symptoms before, the patient had sexual activity with man and another man.

The vital sign on the patient was normal. There are no sign of anemia, icterus, cyanosis, and dyspnea. Chest physical examinations were clear. No abnormality was found in the rest of examination. A dermatological examination not showed painless ulcer (chancre) in the genitalia. No alopecia, papular macular rash, condyloma lata, lymphadenopathy, nickles and dimes, rupioid, corona veneris, and hyperkeratotic lesion were found in the rest of the examination. No palpable lymph nodes were found.

Dermatological examination of the palms and soles showed multiple red macules with clear boundaries, with varying sizes between diameter 0.5cm -1cm and multiple red macules in face, no abnormalities were found in the oral mucosa. The result of VDRL examination is 1:64, and TPHA result was Positive, Rapid HIV test showed positive result Since 2017 from Menur hospital. The patient was diagnosed with secondary syphilis with HIV co-infection, for the secondary syphilis patient was prescribed by single dose of Benzathine Penicillin injection 2.4 million IU IM from the dermatologist.

Serologic evaluation (VDRL and TPHA) was planned on the 3, 6, 12, and 24 months after treatment. Two months after treatment, rashes on the soles and palms had vanished. VDRL titer after treatment 1:8 and TPHA Positive. Improvement in clinical and serologic examination showed a good response to therapy.



Figure 1 (a,b) Physical examination of plantar pedis region and plantar manus Multiple erythematous and hyperpigmented macules with distinct borders in varied sizes (Before Treatment, with a single dose of Benzathine Penicillin G 2,4 million IU IM)

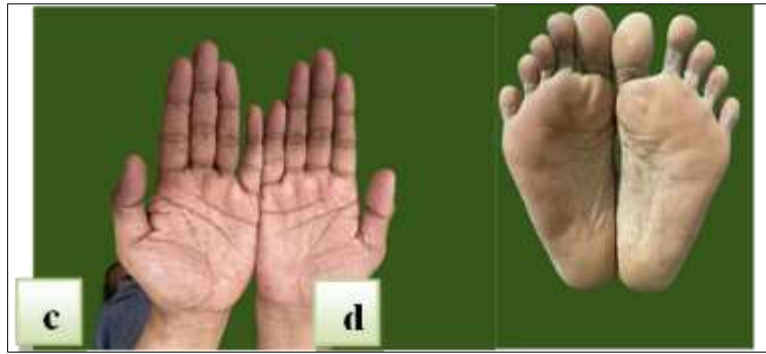


Figure 1 (c.d). Physical examination of plantar pedis region and plantar manus Showed a vanished rash after a two month of treatment. (After Treatment a single dose injection of Benzathine Penicillin G 2,4 million IU IM)

3. Results and discussion

Syphilis treatment rates in Indonesia are significantly impacted by stigma, according to Kementerian Kesehatan Republic Indonesia. The country's syphilis incidence continued to rise. About 12.000 cases of syphilis were reported in 2016. There will be 21.000 cases of syphilis in 2022¹⁰. Syphilis is a worldwide illness the frequency of syphilis grew steadily after 2000. In the United States, the syphilis incidence in 2000 was 11.2 per 100,000 individuals^{5,9}. North America and Western Europe has occurred almost exclusively in men, many of whom have sex with men and/or are co-infected with human immunodeficiency virus (HIV)⁶.

The risk of contracting syphilis is multifactorial. Intercourse in the anal region without protection is one of the common risk factors for syphilis. Numerous infections have also been connected to sexual interactions including group sex. Numerous studies have shown that coinfection with HIV is also quite prevalent, and that patients who are HIV positive have more severe clinical symptoms¹¹. The CDC also estimates that 44% of men who have sex with men and bisexual men who test positive for syphilis will also have HIV. The infection has also re-emerged in developed countries in homosexual population with high number of cases co-infected with HIV. There are three different types of syphilis infection: primary, secondary, and tertiary. initial Primary syphilis This stage is also referred to as the "chancre phase"; a solid, circular, painless ulcer at the site of an infectious organism's entry is called a chancre.

The location of *T pallidum* spirochete inoculation, generally on the genitalia, a chancre begins as a papule, usually single. In Women the chancre can show up on the cervix ,and since it painless, the patient is probably not even aware that it exists¹.Secondary Syphilis stage usually starting two to eight weeks following the main chancre's removal, symptoms can affect any system or portion of the body and manifest in a variety of systemic ways. A diffuse and extensive maculopapular rash that includes the palms of the hands and the soles of the feet, as well as oral lesions in the mouth, are the characteristic cutaneous manifestations of secondary syphilis¹⁹.Tertiary syphilis stage is a late symptomatic disease that can manifest months, years, or even decades after the initial infection as cardiovascular syphilis (aortic aneurysm, aortic valvulopathy), neurosyphilis (meningitis, hemiplegia, stroke, aphasia, seizures, spinal neuroarthropathy, tabes dorsalis, syphilitic paresis), or gummatous syphilis (infiltration of any organ and its subsequent destruction)¹.

The manifestations of secondary syphilis could also varies in clinical manifestation with findings such as, mucous patches, palmar or truncal rash, papulosquamous rash, condyloma lata, or alopecia.¹ At this point patient has positive serologic test but no clinical manifestasions. The manifestation of tertiary syphilis could be cardiovascular syphilis, neurosyphilis, or gummatous syphilis^{1,19}. We did not find these findings on our patient. This case is secondary syphilis with HIV co-infection caused by sexual partner transmission. Dermatological examination of the palms and soles showed multiple red macules with clear boundaries, with varying sizes between diameter 0.5cm-1cm. and multiple red macules in face,no abnormalities were found in the oral mucosa. Secondary syphilis occurs in 2-8 weeks after the painless lesions from primary syphilis on his genitals that disappeared without treatment. Meanwhile, the boyfriend didn't have any symptoms of secondary syphilis.

Diagnosis is usually based on combination of clinical findings with pathology and using serologic tests. From the anamnesis, clinical examination and serology, using a combination treponemal and non-treponemal tests [VDRL and TPHA]. The most common test for syphilis is VDRL. VDRL has 78% sensitivity for primary syphilis and 100% sensitivity for secondary syphilis with 98% specificity. TPHA has 85% sensitivity for primary syphilis and 100% sensitivity for

secondary syphilis with 96% specificity. TPHA are manual indirect hemagglutination assays, usually done in microtiter plates using sheep and fowl erythrocytes. Combining TPHA and VDRL yields better sensitivity and specificity especially in difficult cases¹². The patient's initial TPHA and VDRL tests revealed of TPHA Positive and VDRL 1:64 before treatment. Two months after treatment there is a decreased VDRL 1:8 and TPHA Positive.

Infections of HIV/AIDS currently has become very serious problems for the world health. this virus were given the name of the human immunodeficiency virus (HIV) that can be found the body fluid especially blood, a liquid sperm, vaginal discharge, and water milk mother.¹⁴ symptoms from HIV divided into 4 steps: acute infection stage, asymptomatic stage, symptomatic stage [light to severe], AIDS stage, for skringing usually used enzym-linked immunosorbent assay (ELISA).

Co-infection of syphilis and HIV - each facilitate infection by the other, and aggravate one another's clinical course⁸. Persons with HIV infection and primary and secondary syphilis using ART per current HIV guidelines might improve clinical outcomes among persons coinfecting with HIV. Syphilis was associated with a decrease in CD4 cell counts and an increase in HIV-RNA levels that both improved after treatment of syphilis¹⁷. Co-infection of syphilis and HIV can dramatically affect the clinical manifestations and course of either disease. Sexual orientation affects the risk of co-infection with syphilis and HIV. One of the main routes of transmission of HIV/AIDS is through unsafe sex with an HIV-infected partner, be it heterosexual or homosexual²¹. Men who were HIV Positive had a three-fold higher risk of having serological evidence of active syphilis. Risk sexual practices among HIV-positive persons is of concern. Targeted prevention efforts and prompt treatment and prevention of syphilis and other STDs may positively impact the incidence and seroprevalence of syphilis and HIV co-infection.¹³. Syphilis therapy does not depend on the patient's HIV status, titers may decrease slowly in HIV patients. All syphilis patients should be tested for HIV, and all HIV patients should be tested for syphilis²².

Persons with HIV infection who have primary or secondary syphilis should be treated as those without HIV infection. The recommended regimen drug for all secondary syphilis stages is benzathine penicillin G, 2.4 million units IM in a single dose^{3,8}. As an alternative, the patient could be prescribed Penicillin-prokain 600.000 U/days for 10-14 days IM/IV. Patient who refuses injection can be prescribed doxycycline 100 mg orally twice a day for 14 days or Erythromycin 500 mg four times a day for 14 days have been used for many years to treat syphilis patients who allergic to penicillin^{15,20}. All persons with HIV infection and syphilis should have a careful neurologic exam to prevent more severe manifestations. After treatment, a Jarish-Herxheimer reaction may occur, in the form of chills, fever, joint pain, headache²⁰. The reaction occurs due to massive release of treponema, starting 4-6 hours after injection and will disappear slowly over 24 hours, All these reactions were treated with aspirin and ibuprofen.

Follow-Up persons with HIV infection and primary or secondary syphilis should be evaluated clinically and serologically at 3, 6, 9, 12, and 24 months after therapy, but until this case report was published we only followed the patient in the two month after treatment. Therapy is successful if there is a decrease in the VDRL titer $\geq 4x$ compared with the initial titer. The criteria for treatment failure (i.e., signs or symptoms that persist or recur or a sustained [>2 weeks] fourfold or greater increase in titer) should be managed in the same manner as persons without HIV infection.²⁰ Retreatment can be considered for persons whose nontreponemal test titers do not decrease fourfold within 24 months of therapy. If CSF examination is normal, treatment with benzathine penicillin G administered as 2.4 million units IM at weekly intervals for 3 weeks is recommended^{3,16}. All persons with HIV infection and primary and secondary syphilis should undergo a thorough neurological, ocular, and otic examination, csf examination should be performed in those with an abnormal neurological examination to prevent more severe manifestations of neurosyphilis³.

4. Conclusion

Concomitant syphilis and HIV infection are particularly common with a high risk among men who have sex with men, intravenous drug abusers, and prostitutes. Although syphilis presentation in patients with HIV is largely similar to that in patients without HIV, differences in disease manifestation may be present. Persons with HIV infection who have primary or secondary syphilis should be treated as those without HIV infection and using ART per current HIV guidelines might improve clinical outcomes among persons coinfecting with HIV. The patient received treatment for secondary syphilis stages is benzathine penicillin G, 2.4 million units IM in a single dose from the dermatologist. The syphilis treatment has been shown to effectively reduce VDRL levels in secondary syphilis cases occurring alongside HIV infection. Syphilis patients with HIV co-infected needs comprehensive and regular evaluations (follow up to 24 month after therapy), but even with successful treatment, treponema can potentially contribute to reinfected immunosuppression individuals who did unsafe sex and classified as high risk. Health reproductive education, partner notification, and screening in high-risk populations are crucial elements in controlling the infection and prevention.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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