CASE REPORT

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Secondary syphilis with HIV infection in Men Who Have Sex with Men (MSM) patient treated with azithromycin and doxycycline: a case report

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ABSTRACT

Background: Syphilis frequently presents in tandem with HIV and the prevalence is increasing, particularly in men who have sex with men (MSM). The most common and recognizable manifestations are usually the secondary stage, characterized with or without constitutional symptoms. This case study aims to evaluate secondary syphilis with HIV infection in MSM patient treated with azithromycin and doxycycline

Case Presentation: A 22-year-old man with secondary syphilis and HIV infection. The diagnosis was established based on erythema and hyperpigmented maculopapular lesions with the scale on the forearms, palms, back, feet, and soles without pruritic sensation, a history of the same-sex sexual partners, and the titer of VDRL 1:64, TPHA 1:2560. The patient also has a low CD4 level and HIV-1 RNA were detected on a blood test. Patients received azithromycin 2 grams orally and continued by doxycycline twice a day for 30 days and treated for the HIV Infection. Skin disorders have improved rapidly and are significantly accompanied by decreased VDRL titer.

Conclusion: The therapy of 2-gram azithromycin improved clinical manifestation on the skin. The following treatment of 30 days doxycycline showed clinical improvement and significant decline in a nontreponemal serologic test.

Keywords: Azithromycin, Doxycycline, HIV, MSM, Syphilis.
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INTRODUCTION

Syphilis is a disease caused by the spirochete *Treponema pallidum* subspecies *pallidum*, which is usually sexually transmitted.[1] The disease has been divided into stages based on clinical findings: primary, secondary, tertiary, and latent syphilis infections.[2] Syphilis frequently presents in tandem with conditions such as HIV and the prevalence is increasing, particularly in men who have sex with men (MSM).[3-5] The incidence of HIV is three times higher in MSM with syphilis rather than with no syphilis.[6] Based on CDC data in 2017, of 30.644 reported primary and secondary syphilis cases, 17.736 (57.9%) were among MSM and 45.5% of cases among MSM were HIV-positive.[5] A study in Bali 2016, found the prevalence of syphilis among MSM is 22% and 28.57% among MSM with HIV-positive.[7]

The most common and recognizable manifestations are usually cutaneous, marked by skin rashes with or without mucous membrane lesions.[1,2] Skin lesions may be mild or florid rashes, not usually pruritic, that may cover the palms and soles.[8] Secondary stage typically recedes in 4-12 weeks if not treated.[1] Treatment of secondary syphilis is the same as for primary syphilis. Alternative therapy could be chosen when an allergic reaction occurs or the unavailability of the first-line drugs happens.

According to outpatient medical records data in Dermatovenereology Clinic Dustira Hospital Cimahi, from January 2018–January 2019, 7 cases of syphilis were reported. About 6 of them were male and the other one is female. There were 2 male patients who reported HIV-positive and one of them was known as MSM.

This case study aims to show clinical manifestation and evaluate the efficacy of alternative therapy in treating syphilis with HIV co-infection in an MSM patient.

CASE REPORT

A 22-year-old man was consulted with erythematous, hyperpigmented, nonpruritic macules and papules on forearms, palms, back, feet, and soles. Symptoms first appeared one week before examination with the presence of fever in the last 3 days. The patient had no ulcer on the penis, anus, or mouth in history. No neurological abnormality was found and he had never treated the skin complaints before. He loses 6 kg in the last one month and complains of coughing with white sputum during the previous 2 weeks. The patient is single and his first sexual intercourse was at the age of 10 by genito-genital sex with a different sex partner. The patient had 2 same-sex partners for

Figure 1. The clinical manifestations before taking any treatment (1a, 1b, and 1c). Erythematous macules and papules size 0.2x0.2 cm–0.7x0.7 cm in diameter on the forearms, palms, and back (1d and 1e). Erythematous and hyperpigmented macules and papules with 0.2x0.2cm-0.5x0.5cm in diameter with scales on feet and soles.

Figure 2. One month after taking 2-gram azithromycin (2a and 2b), no skin lesions occurred in both forearms and palms (2c, 2d, and 2e)—several hyperpigmented macules on the feet and soles.

the last 4 years, and the previous sexual intercourse was about 2 months ago, without a condom, and it was anogenital sex. The history of sexually transmitted disease in partners was unknown.

The patient was *compos mentis*, a vital sign was normal, no abnormalities in physical examinations. Erythematous macules and papules were observed on the forearms, palms, and back, with erythematous and hyperpigmented macules and papules with scales on feet and soles (**Figure 1**). Leucocytes were slightly increased (10.400/mL while other complete blood count components within the normal limit. The first differential diagnosis was secondary syphilis followed by hand and foot mouth disease. No therapy was given on this day. VDRL, TPHA, and anti-HIV were suggested to test the following day and a chest X-ray is also requested.

During the 2nd day of examination, the patient had similar complaints and skin manifestations as before. VDRL was reactive, anti-HIV (rapid) was reactive, with the view of bronchitis and right bronchopneumonia from chest X-ray. The patient was then consulted to the VCT clinic and pulmonary department. VDRL and TPHA with titer were suggested to test and azithromycin 2 grams were given this day after taking the blood test.

In addition, on the 3rd day of examination, the same complaints as before were found with fading erythematous and hyperpigmented macules on the skin. TPHA 1:1280, CD4: 257, HIV-1-RNA: virus detected, 2.2900 copies/ml. The patient was given the first HIV therapy (cotrimoxazole and FDC) and ambroxol. On the 9th day of examination, the patient had no complaint and skin lesions mostly faded away. TCM result was negative for *Mycobacterium tuberculosis.* The patient was suggested to continue the HIV and bronchitis therapy. Working diagnosis could be concluded by then: secondary syphilis with stage 2 HIV infection and bronchitis.

There were no complaints during the 32nd day of examination, and skin lesions on the forearms and palms were found. Some hyperpigmented macules were observed on the feet and soles. VDRL 1:64, TPHA 1:2560. The patient was given

doxycycline 200 mg daily for 30 days and suggested to continue taking HIV therapy. However, on the 62nd day of examination, there were no complaints, no skin lesions. VDRL 1:4, TPHA 1:160. The patient was advised to continue taking HIV therapy. VDRL and TPHA were suggested to test in the next 2 months (**Figure 2**).

DISCUSSION

It is known that syphilis frequently presents in tandem with conditions such as HIV and the prevalence is increasing notably in men who have sex with men (MSM).[3-5] A study by Solomon et al. in 2014 said the incidence of HIV is three times higher in MSM with syphilis rather than with no syphilis.[6] And according to Funnye AS et al. in 2003, men who were HIV-positive had a three-fold higher risk of having serological evidence of active syphilis.[9] The subject of this case study was men who have sex with men with secondary syphilis and HIV-positive.

It has been reported that syphilis presents differently in persons infected with HIV. There seems to be a higher rate of asymptomatic primary syphilis among HIV-infected patients, and infection progresses more rapidly from primary to secondary stages.[10] Patients might not be aware of chancres incredibly if painless and located in an area that is not visible such as the anus or oral cavity.[1] In such a scenario, primary syphilis would be undiagnosed and untreated and, therefore, more likely to progress into secondary and tertiary stages.[10]

Secondary syphilis is a stage characterized by localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy, in the presence of laboratory evidence.[2] Lesions typically erupt 3-12 weeks after the chancre appears (6 months after exposure).[1] Skin lesions may be mild or florid and most commonly include a wide morphologic variety of rashes that may cover the palms and soles.[8] As mentioned in this case before, erythematous macules and papules were observed on the forearms, palms, and back. Erythematous and hyperpigmented macules and papules with scales were found on feet and soles. Constitutional symptoms such as sore throat, low-grade fever, malaise, myalgias, arthralgias also may be present.[8] Fever in the past 3 days could be counted as constitutional symptoms.

The complaints of 2 weeks cough with white sputum and 6 kg weight loss in one month made the suspicion of pulmonary TB infection. HIV-positive patients are at high risk of being infected by pulmonary TB, in which 27.5% of all studied cases by Shanmuganathan R and Subramaniam ID in 2015 marked by prolonged cough and weight loss.[11] After taking a chest X-ray and molecular gene Xpert test, the suspicion could be removed. Stage 2 HIV infection based on WHO classification was diagnosed by weight loss of less than 10% of total body weight, the reactive anti-HIV, and total CD4: 257 cell/ml.[12]

In secondary syphilis, patients may present with fever and painless rash, which may be misdiagnosed as a mild viral infection.[13] Differential diagnostic could be removed with the reactive serological test. The result was VDRL 1:64 and TPHA reaching 1:2560.

Parenteral penicillin G is the recommended treatment for all cases of syphilis.[1] Despite several advantages of this regimen, some disadvantages include pain, penicillin allergy, and the need for injection equipment and medically trained personnel. Azithromycin is a promising candidate to overcome the disadvantages associated with injectable penicillin G benzathine. According to Riedner R et al., single-dose oral azithromycin effectively treats syphilis and may be particularly useful.[14] The unavailability of penicillin G benzathine was the reason why alternative therapy was chosen. According to the previous study, 200 mg doxycycline given orally for 30 days could be used as an alternative treatment.[15]

Clinical and serologic follow-up is important to monitor response to treatment. CDC recommends follow-up every 3 months during the first year in HIV-infected patients. Treatment success is generally defined as a fourfold decline in serologic nontreponemal titer in the absence of persistent signs or symptoms of syphilis.[1] One week after taking 2-gram azithromycin, clinical improvement occurred, but the treatment success couldn't be concluded since it was not enough data of nontreponemal serologic test before. Within a month of follow-up, there is an improvement in clinical symptoms and a sixteen-fold decline in nontreponemal tests after taking 30 days of doxycycline. Another 2 months follow-up is needed to monitor the treatment success.

CONCLUSION

The therapy of 2-gram azithromycin improved clinical manifestation on the skin. The following treatment of 30 days doxycycline showed clinical improvement and significant decline in a nontreponemal serologic test.

CONFLICT OF INTEREST

There was no competing interest regarding the manuscript.

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AUTHOR CONTRIBUTIONS

All authors equally contribute to the study by selecting the case, data acquisition, evaluating the outcome, and analyzing the case study results through publication.

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