

Secondary Syphilis and HIV Co-infection: A Case Series

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Abstract: The abstract should summarize the contents of the paper and should contain at least 70 and at most 200 words. The interaction between syphilis and HIV infection is complex and a dangerous combination. Atypical nontreponemal serologic test results (i.e., unusually high, unusually low, or fluctuating titers) might occur regardless of HIV-infection status. Despite several advances in the understanding of the interaction between HIV infection and syphilis achieved during the past few years, the clinical treatment of coinfecting patients remains challenging. Clinically relevant differences in presentation, diagnosis, and management strategies must be recognized by clinicians. The present communication describes two different cases of secondary syphilis and HIV co-infection in young men, which shows difference in clinical manifestation and serological response after treatment.

1 INTRODUCTION

Syphilis is a sexually transmitted disease caused by *Treponema pallidum* subspecies *pallidum*. It has been called the “great imitator” in reference to its ability to cause a wide range of manifestations in nearly every organ system. Men who have sex with men (MSM) and bisexual men have the highest risk for syphilis infection. Other significant risk factors include HIV infection, thus coinfection is common, and the two diseases affect each other in several ways. The clinical manifestations of syphilis are divided into primary, secondary, latent, and tertiary stages. These coinfections may also alter the symptoms and signs, the progression of the disease, and the risk of progressing to the tertiary stage. Studies have shown that 16–30% of individuals who have had sexual contact with a syphilis-infected person in the preceding 30 days become infected, and in some cases the transmission rates may be much higher (Holman et al., 2012; Mendoza et al., 2011).

Syphilis and HIV have played an important role in public health. These two infections overlap, interact, and share significant characteristics. A recent review of studies conducted worldwide reported a 9.5% prevalence of syphilis among adults living with HIV infection. In 2013, the incidence of primary and secondary syphilis rose to 5.3 cases per 100,000 people in the US, more than doubling the

lowest rate of 2.1 per 100,000 in 2000. We report two cases of secondary syphilis in MSM patient with HIV coinfection. These cases reveal a specific dermatological lesion of secondary syphilis and confirmed by serological testing. This report discusses about the clinical presentation, diagnosis, treatment, and serological response.

2 CASE

Case 1 : 24-year-old male complained of redness macules on his body, including the palm and soles for 1-month. The rash was neither painful nor pruritic. He also complained of hair loss resulting in “moth eaten” alopecia which occurred simultaneously with skin rash. One month before the rash appeared, he had a ulcer on his genital which resolved without treatment. His HIV infection was diagnosed in 2014 and had been sexually active with homosexual partners since 2010. From dermatological examination on thorax anterior et posterior, scalp, palmar manus dextra, plantar pedis dextra et sinistra region, there were multiple violaceous macule, sharply marginated, vary in size, covered with thin scales. There was the ‘moth-eaten’ syphilitic alopecia. There was hyperpigmented macule, unsharply marginated on genital area. No evident lip or buccal mucosal

lesions were noted. The VDRL titer was 1:32 and TPHA was 1:20480 with CD4 count of 88 cells/ μ l.

Case 2 : Thirty-three years old man came with chief complaint multiple rash on his trunk and extremities since 1 months before, painless and not itchy. At first the lesion was found in his arms and spreads to other site of body. Patient had multiple sexual partner (bisexual), and there were history of ulcer at his penis 3 months ago that healed spontaneously in a few days. The patient diagnose with HIV about 1 years ago and taking Anti Retroviral (ARV) routinely. From dermatological examination, on regio trunk and extremities superior dextra et sinistra there were multiple erythematous macule sharply marginated, 0,5-1 cm in diameter, some covered with thin scale. The serology titer of Venereal Disease Research Laboratory (VDRL) test was 1: 128 and *Treponema Pallidum* Hemagglutination Assay (TPHA) was 1:1280.

In these two cases, patient was treated with Benzathine Penicillin G 2,4 million Unit intramuscular single dose. Serologic examination was reevaluated in 3, 6, 9 and 12 month after treatment. In case 1 fourfold decline was achieved at sixth month follow-up, but in case 2 serologic value still persist until twelve month.

3 DISCUSSION

Syphilis infections have increased in recent years internationally, especially among MSM. The surge in syphilis among MSM is troubling, considering the morbidity associated with untreated syphilis, including neurosyphilis and cardiovascular sequelae. Furthermore, syphilis is associated with both HIV transmission and acquisition, and a disproportionate number of syphilis diagnoses occur in HIV infected MSM (Petrosky et al., 2008).

Syphilis infection has been divided into primary, secondary, latent, and tertiary stages. The clinical manifestations of syphilis in HIV patients can be very similar to those seen in an otherwise healthy host (Mendoza et al., 2011). Clinical manifestation of syphilis is not affected very much in HIV-infected populations. Thus, the manifestation is almost similar with those without HIV infection. However, there are some differences which can be seen in HIV-infected patients. As defined by CDC surveillance case definitions, primary syphilis is a stage of syphilis characterized by one or more chancres, in the presence of laboratory evidence from tissues or sera consistent with syphilis. At the inoculation site, a chancre develops after an incubation period that

ranges from 10 to 90 days (average, 3 weeks) and is associated with painless regional lymphadenopathy arises 7–10 days after the chancre appears, especially when the chancre's location is genital. Unilateral lymphadenopathy is more common earlier in the course of disease, with bilateral involvement later in the course. This chancre is a unique, firm, usually painless, nonpurulent, indurated, round ulcer located in the inoculation area. It initially presents as a small papule that ulcerates very rapidly. Genital ulcers primarily increase the transmission of HIV caused by the loss of the epidermal barrier and local inflammation. In HIV-positive patients, primary syphilis can present with multiple ulcers that are similar to herpetic lesions (soft chancre). These lesions are deeper, persist longer, may leave a scar upon healing, and may lead to perforations in the prepuce or labia majora (Mendoza et al., 2011; Katz et al., 2012; Wahab et al., 2013; Hu et al., 2014).

Secondary syphilis is a stage of syphilis characterized by localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy, in the presence of laboratory evidence from tissues or sera consistent with syphilis. Secondary syphilis, which occurs in roughly one-fourth of all untreated syphilis cases, results from the multiplication of disseminated *T. pallidum* and formation of lesions at multiple sites in the skin and internal organs, despite the presence of a significant antibody response. The rashes are quite varied in appearance but have certain characteristic features. The lesions are usually widespread, involving the entire trunk and the extremities, including palms of the hands and soles of the feet, symmetrical in distribution, frequently pink, coppery, or dusky red (particularly the earliest macular lesions) usually 0.5–2 cm in diameter with involvement of the palms and soles. They are generally nonpruritic, although occasional exceptions have been reported (Das et al., 2015; Jansen et al., 2016; Solomon et al., 2015). The diverse manifestations of human syphilis also demonstrate the invasiveness of *T. pallidum*. Secondary syphilis presents after hematogenous dissemination from the chancre has occurred, usually 4–10 weeks after appearance of the primary chancre in the immunocompetent patient. It usually manifests as mucocutaneous lesions with systemic symptoms. However, 75% of coinfecting HIV patients present with secondary syphilis while the chancre is still present. Systemic symptoms include fever, anorexia, muscle pain, depression, arthritis, and weight loss. Without treatment, the secondary stage typically recedes in 4–12 weeks (Mendoza et al., 2011). In these cases, we noted that the patient presented with

genital ulcer followed by rash on his body, palm and soles simultaneously. This situation is observed more common in HIV infected persons than those without HIV.

The scalp may be involved, resulting in alopecia. The eyebrows and beard area can be affected as well. The 'moth-eaten' pattern is the most frequent clinical manifestation of syphilitic alopecia (SA) and represents one of the most characteristic signs of secondary syphilis. In the event of suspected secondary syphilis, the patient should be examined for the presence of signs compatible with SA, questioning about any perceived sign of hair loss or alopecia and examining the scalp in the parieto-occipital areas, where these signs are more frequently observed. In case 1, the patient was having hair loss with moth eaten pattern associated to syphilis infection, which completely disappeared 8 weeks after the end of the therapy (Mendoza et al., 2011; Piraccini et al., 2015).

For most HIV infected persons, serologic tests are accurate and reliable for the diagnosis of syphilis and for following a patient's response to treatment. Regardless, both treponemal and nontreponemal serologic tests for syphilis can be interpreted in the usual manner for most patients who are coinfecting with *T. pallidum* and HIV. However, atypical nontreponemal serologic test results (i.e., unusually high, unusually low, or fluctuating titers) might occur regardless of HIV-infection status. When clinical findings are suggestive of syphilis but serologic tests are nonreactive or their interpretation is unclear, alternative tests such as biopsy of a lesion, dark-field examination, and PCR of lesion material might be useful for diagnosis (Waugh, 2015; CDC, 2015).

Persons with HIV infection and primary or secondary syphilis should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy. Increased risk of serological failure has been reported to be more common among those with late stage of syphilis and HIV-infected patients (CDC, 2015). In Case 1, VDRL titer declined fourfold after 6 month completed therapy. However, the subsequent follow up sample is needed for further confirmation of this condition. Different with case 2, the serologic test is fluctuated and at month-12 the titer is not decrease to 4-fold. The subsequent follow-up sample is needed for further confirmation of this condition. Furthermore, the determination of the immunocompromised state may be helpful to explain this phenomenon.

The CDC guidelines for treatment of primary, secondary, tertiary, and early latent syphilis less than 1 year in HIV patients are very similar compared to

those of HIV-negative patients. Most reports show that HIV infection does not markedly affect response to benzathine penicillin therapy. The U.S. Public Health Service continues to recommend a single dose of 2.4 million units benzathine penicillin in this situation. Penicillin is the antibiotic of choice and it is recommended antibiotic in HIV infected population because it can reach high concentration in central nervous system for treatment of neurosyphilis which is more common in this population. Penicillin remains not only the most effective treponemicide, but it is easy to administer, has few side effects and is relatively inexpensive. Results continue to be excellent for all forms and stages of treponemal disease, and there are no signs that *T. pallidum* has developed resistance to this antibiotic (Mendoza et al., 2011; Wahab et al., 2013; CDC, 2015; Kinghorn et al., 2016). In our case also, the treatment with a single dose of 2.4 million units benzathine penicillin was given according to stage of syphilis and patient recovered well after the treatment by decreasing of the rash on his body and regrowth of hair, but further evaluation of serological test is needed. It is recommended that attempts be made to identify, trace and offer further investigation to at-risk sexual contacts (Kinghorn et al., 2016).

4 CONCLUSIONS

The importance of our cases is not only about syphilis and HIV co-infection but to highlight some of the differences in clinical manifestations and serological results of syphilis that might be important for management of such patients.

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