

Concomitant Primary and Secondary Syphilis: A Case Series from STD Clinic, Siriraj Hospital

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ABSTRACT

Objective: To emphasize the importance of dermatologists in identifying the presence of concomitant primary and secondary syphilis in the same patient in order to effectively diagnose the disease and provide adequate treatment.

Case presentation: The diversity of the clinical manifestations of syphilis is very common; however, atypical presentations of syphilis have a chance to occur. Such concomitant primary and secondary syphilis, which develops chancre concomitant rash is an uncommon manifestation. Cases of atypical syphilis have been described most frequently in patients with concomitant human immunodeficiency virus (HIV) infection and men who have sex with men (MSM). This report presents the cases of 8 patients with primary and secondary syphilitic lesions. These cases are representative because of their clinical presentation, age range, gender distribution and diagnostic approach.

Conclusion: The concomitant presence of primary and secondary syphilis in the same patient is unusual. The importance of our cases is to highlight some of the differences in clinical manifestations in HIV-infected men and HIV-uninfected men that might be important for early diagnosis for managing and curing such patients.

Keywords: Concomitant primary and secondary syphilis; syphilis (Siriraj Med J 2018;70: 81-86)

INTRODUCTION

Syphilis is a sexually transmitted infection caused by the spirochete *Treponema pallidum*. Humans are the only natural host for this organism.¹ Transmission occurs mainly through microabrasions in mucosal membranes or skin, enabling the organisms to rapidly enter the bloodstream to disseminate to other tissues.² Syphilis has three clinical stages. The primary stage is characterized by a single chancre that manifests approximately 90 days after exposure and remits spontaneously within two to eight weeks. The secondary stage occurs between 2 and 12 weeks after exposure, when a rash develops on several parts of the skin.

The rash subsides spontaneously with no treatment when the condition enters its latent stage. Also, called late phase and rarely observed today, the tertiary stage is characterized by gummata and/or neurosyphilis that emerge

three years or later after exposure.³ The pathogenesis of syphilis begins with *T. pallidum* replication at the site of initial inoculation, dividing once every 30-33 hours, inducing a local inflammatory response that results in a painless chancre approximately 3-6 weeks after initial infection. In each chancre, proliferating spirochetes are surrounded by immune cells, including CD4+ and CD8+ T cells, plasma cells, and macrophages, which produce IL-2 and IFN- γ cytokines, indicating a Th1-skewed response. Tissue necrosis and ulceration occur due to small vessel vasculitis, and trafficking of immune cells causes a non-tender regional lymphadenopathy. Within 3-8 weeks, the chancre heals, indicating clearance of *T. pallidum* locally. However, by this time, *T. pallidum* has spread systemically to multiple tissues and organs, setting the stage for secondary syphilis.² Accordingly, the concomitant presence of primary and secondary

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Received 16 February 2017 Revised 20 April 2017 Accepted 26 April 2017

doi:10.14456/smj.2018.14

syphilis in the same patient is unusual.⁴ Both primary and secondary syphilis diagnoses are accomplished by serologies or darkfield microscopy.^{5,6}

Recently, an increase in the rate of syphilis has been observed in MSM having HIV coinfection.^{7,8} In Thailand, syphilis has been considered as a major sexually transmitted infection.⁹ Prevalence of syphilis in MSM is significantly associated with young population and people with HIV infection.¹⁰ Moreover, in the early stage of syphilis, men infected with HIV and genital ulcers



Fig 1. Multiple discrete erythematous maculopapular rash on trunk

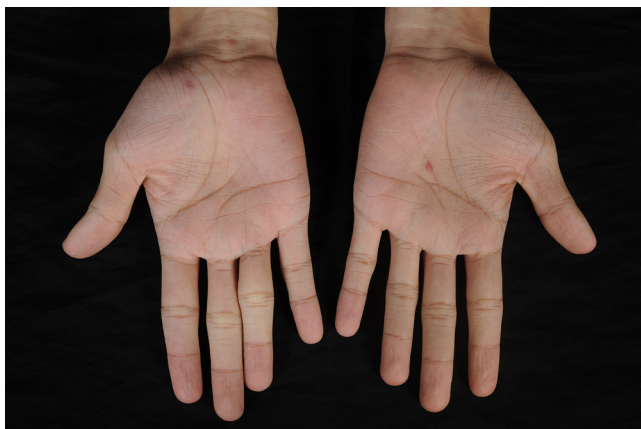


Fig 2. Maculopapular rash on both palms



Fig 3. Multiple discrete erythematous plaque with shallow ulcer on scrotum and shaft of penis

resulting from syphilis may have secondary syphilis with concurrent primary chancres, and multiple chancres.¹¹ Here, we have discussed eight cases of concomitant primary and secondary syphilis identified at Sexual Transmitted Disease (STD) clinic, Siriraj Hospital with different risk factors and unusual clinical manifestations.

The study would help in curing similar patients with appropriate treatment.

CASE PRESENTATION

Case 1: A 23-year-old male presented to the STD clinic with complaint rash over both palms and soles for three-week duration. He had history of MSM, which included unprotected sexual intercourse with multiple sex partners.

On a physical examination, he was afebrile and had no lymphadenopathy. There were multiple discrete erythematous macules and papules on both palms and soles together with painless solitary whitish papule on erythematous base at his perianal area. There was no oral lesion or other abnormalities.

The Venereal Disease Research Laboratory test (VDRL) was reactive at the titer of 1:64. The Treponema pallidum particle agglutination assay (TPHA) was also reactive at the titer more than 1:80. Perianal ulcer was scraped positive for spirochetes on dark field microscopy. HIV serology of the patient was negative. He was diagnosed with concomitant primary and secondary syphilis. The patient was treated with a single dose of intramuscular benzathine penicillin 2.4 mega units. The follow up of VDRL test three months after completion of the treatment showed remarkably decreased titer to 1:2. The repeated VDRL titer after six months was weakly reactive.

Case 2: A 17-year-old male known with amniotic band syndrome presented to the STD clinic with complaint rash over trunk, extremities, palms, soles and a genital chancre for one-month duration. He had previous history of heterosexual activity and unprotected sexual intercourse with multiple sex partners.

On a physical examination, he was afebrile, had multiple 1-2 cm palpable lymph nodes at both groins and generalized discrete erythematous papules and plaques on the trunk, extremities, palms and soles with multiple erosions and whitish patches on the glans penis.

VDRL test was 1:64, with positive TPHA test as well. Chancre at glans penis was scraped positive on dark field microscopy. Urine PCR for chlamydia trachomatis was positive. Urine PCR for gonococcal urethritis and HIV serology were negative.

The patient was diagnosed as concomitant primary

and secondary syphilis with nongonococcal urethritis. He was treated with single dose intramuscular injection of 2.4 mega units benzathine penicillin, 2 g ceftriaxone and 1 g orally of azithromycin. The follow up of VDRL test three months after completion of the treatment showed remarkably decreased titer to 1:8.

Case 3: A 34-year-old male with HIV infection (126 CD4 cells/mm³, HIV viral load 2,100,100 copies/ml), involved in bisexual activity and unprotected sexual intercourse with multiple sex partners, presented to the STD clinic with pharyngeal discomfort for 2 weeks. He had history of late latent syphilis and was treated with intramuscular injection of benzathine penicillin 2.4 mega units weekly for three doses in the past 5 years.

On a physical examination, he was afebrile, had no lymphadenopathy and had few discrete scaly erythematous plaques on both palms and soles, multiple whitish patches at posterior pharynx, ill-defined erythematous erosion at glans penis and skin colored verrucous papules at perianal area.

VDRL test was reactive at 1:256. TPHA was also reactive with the titer more than 1:80. Whitish patch at posterior pharynx was scraped positive for spirochetes on dark field microscopy. Tzanck's smear and HSV Ag tests on specimen taken from posterior pharynx were negative. He was diagnosed reinfection of concomitant primary and secondary syphilis with HIV infection. The patient was treated with intramuscular injection of benzathine penicillin 2.4 mega units weekly for three doses because he had recurrent syphilitic infection and HIV infection. The follow up of VDRL test one month after completion of the treatment showed remarkably decreased titer to 1:128. The repeated VDRL titer after three months was not available because he was lost to follow-up.

Case 4: A 25-year-old male with HIV infection (400 CD4 cells/mm³) was involved in homosexual activity and unprotected sexual intercourse with multiple sex partners. He had history of latent syphilis and was treated with intramuscular benzathine penicillin 2.4 mega units weekly for three doses in the past 1 year. He presented to STD clinic with complaint rash on palms, soles and genitalia for 12 days.

On a physical examination, he was afebrile, had no lymphadenopathy and had multiple discrete scaly erythematous patches and plaques on both palms and soles with discrete erythematous plaques on shaft of penis and scrotum.

VDRL test was reactive at titer of 1:64. TPHA was

also reactive with the titer more than 1:80. Dark field microscopy of a specimen scraped from an erythematous plaque at the genitalia was positive. He was diagnosed reinfection concomitant primary and secondary syphilis with HIV infection.

The patient was treated with intramuscular benzathine penicillin 2.4 mega units single dose. The follow up of VDRL test three months after completion of the treatment showed the titer of 1:16.

Case 5: A 21-year-old male student with a history of HIV infection (400 CD4 cells/mm³) was involved in homosexual activity, protected sexual intercourse with multiple sex partners and intravenous drug usage. He had history of early syphilis and was treated with benzathine penicillin 2.4 mega units intramuscular injection single dose. He presented to the STD clinic with complaint of generalized erythematous rash on palms, trunk and extremities for 3 days.

On a physical examination, he was afebrile, had no lymphadenopathy and had generalized discrete erythematous maculopapular rash on his trunk, both palms, lower extremities and multiple discrete erythematous maculopapular rash with ulcer on the scrotum and shaft of penis. No other abnormalities were observed.

VDRL test was reactive at 1:256, with positive TPHA test as well. Chancre at his scrotum was scraped positive for spirochetes on dark field microscopy. Tzanck's smear was negative for multinucleated giant cell. The patient was treated with intramuscular benzathine penicillin 2.4 mega units single dose. The follow up of VDRL titer was not available because he was lost to follow-up.

Case 6: A 37-year-old male was involved in homosexual activity and protected sexual intercourse with multiple sex partners. He presented to STD clinic with erythematous erosion on the genitalia for 2 weeks.

On physical examination, he was afebrile with ill-defined erythematous erosion on the shaft of penis. He was diagnosed herpes simplex virus infection. The patient was treated with acyclovir 1200 mg/day.

One week later genital rash was improved but he had new rash on both hands and legs. On a physical examination, he had palpable 1-2 cm lymph nodes at both groins, few discrete erythematous macules at both palms and soles with ill-defined erythematous erosion at glans of penis.

VDRL test was reactive at 1:128. TPHA was also reactive at the titer more than 1:80. Chancre at glans penis was scraped positive for spirochetes on dark field microscopy. HIV serology of the patient was not done

because he refused to do the test. The patient was treated with intramuscular benzathine penicillin 2.4 mega units single dose. The follow up of VDRL test three months after completion of the treatment showed remarkably decreased titer to 1:16. The repeated VDRL titer after six months was 1:8.

Case 7: A 22-year-old male presented to the STD clinic with genital rash for six months and rash on both palms and soles for one month. He had history of heterosexual, unprotected sexual intercourse with sexual partner with secondary syphilis. On a physical examination, he was afebrile and had no lymphadenopathy. There were multiple discrete brownish patches and plaques on both palms and soles with multiple discrete erythematous plaques on the scrotum. There was no oral lesion or other abnormalities.

VDRL was reactive at the titer of 1:32, with positive TPHA test as well. Genitalia was scraped positive for spirochetes on dark field microscopy. HIV serology of the patient was negative. He was diagnosed as concomitant primary and secondary syphilis. The patient was treated with intramuscular benzathine penicillin 2.4 mega units for single dose. The follow up of VDRL test three months after completion of the treatment showed remarkably decreased titer to 1:8.

Case 8: 24-year-old male with HIV infection (560 CD4 cells/mm³) was involved in homosexual activity and unprotected sexual intercourse with multiple sex partners. He presented to the STD clinic with rash on genitalia and both palms and soles for one-week duration. He had history of late latent syphilis and was treated with intramuscular benzathine penicillin 2.4 mega units weekly for three doses in the past 5 years. On a physical examination, he was afebrile, had no lymphadenopathy and had few discrete scaly erythematous plaques on both palms and soles, ill-defined erythematous erosion at glans penis, multiple whitish patches at posterior pharynx and skin colored verrucous papules at perianal area.

VDRL test was reactive at 1:512, with positive TPHA test as well. Whitish patch at posterior pharynx was scraped positive for spirochetes on dark field microscopy. Tzanck's smear and HSV Ag test were negative in specimen scraped from posterior pharynx. He was diagnosed reinfection concomitant primary and secondary syphilis with HIV infection.

The patient was treated with intramuscular benzathine penicillin 2.4 mega units weekly for three doses because he had recurrent syphilitic infection and history of HIV infection. The follow up of VDRL test was not available because he was lost to follow-up.

DISCUSSION

These 8 cases of concomitant primary and secondary syphilis highlight the diversity of clinical presentations and potentially devastating consequences of this syndrome. Although the majority of recently published cases are in HIV-infected men who had sex with men¹², it can also happen in a HIV-negative man. This clinical feature is challenging to diagnose because concomitant primary and secondary syphilis is an uncommon manifestation of syphilis.¹³ Secondary syphilis with concurrent primary chancre is more likely to develop in HIV-infected men than HIV-uninfected men. This scenario can happen because of rapid progression of the disease from primary to secondary stage in HIV infected patient or delayed healing of genital ulcer.¹²

Our cases here showed that concomitant primary and secondary syphilis were detected among 6 MSM cases and 4 HIV-infected cases. In case of syphilis and HIV coinfection, all cases had past history of syphilis.

However, in this case series, we also found 3 cases of concomitant primary and secondary syphilis in HIV-negative men with unknown pathogenesis.

Treatment of syphilis in HIV-infected and non-HIV cases is similar. Penicillin continues to be the first-line therapy for all stages of syphilis.¹⁴ A single dose of benzathine penicillin G 2.4 million units intramuscularly is currently used to treat primary, secondary, and early latent syphilis. If nontreponemal titers do not decline 4-fold, if there is a 4-fold increase, or if signs or symptoms persist or recur, treatment is considered to fail. In those cases, CSF should be sampled, and treatment should be administered as in HIV-uninfected patients (weekly injections, unless CSF examination indicates neurosyphilis). If additional follow-up cannot be ensured, additional treatment is recommended.¹⁵ Our third case was treated with benzathine penicillin G 2.4 million units intramuscularly once weekly for 3 weeks due to history of recurrent syphilis and HIV infection. In conclusion, the concomitant presence of primary and secondary syphilis in the same patient is unusual. The importance of our cases is to highlight some of the differences in clinical manifestations in HIV-infected men and HIV-uninfected men that might be important for early diagnosis for managing and curing such patients.

ACKNOWLEDGMENTS

The authors are grateful to Professor Kanokvalai Kulthanan, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University for patients' information.

TABLE 1. Summary of Key Factors in Each Case

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Patient age, sex	23, male MSM	17, male Heterosexual	34, male MSMW	25, male MSM	21, male MSM	37, male MSM	22, male Heterosexual	24, male MSM
HIV status CD4	Negative	Negative	Positive 126 cells/mm ³	Positive 400 cells/mm ³	Positive 400 cells/mm ³	Not available	Negative	Positive 560 cells/mm ³
Presenting symptoms	Rash for 3 months	Rash and chancre for 1 month	Discomfort at pharynx for 2 weeks	Rash for 12 days	Rash for 3 days	Rash for 2 weeks	Rash for 1 month	Rash for 1 week
Physical examination	Multiple discrete erythematous macule and papule on both palms and soles, Painless solitary whitish papule on erythematous base at perianal area	Generalized discrete erythematous papule and plaque at trunk, extremities, palms and soles with multiple erosion and whitish patches at glans penis	Few discrete scaly erythematous plaque at both palms and soles, multiple whitish patch at posterior pharynx, illdefined erythematous erosion at glans penis, and skin color verrucous papule at perianal area	Multiple discrete scaly erythematous patch and plaque on both palms and soles with discrete erythematous plaque at shaft of penis and scrotum	Generalized discrete erythematous maculopapular rash on trunk, both palms, lower extremities and multiple discrete erythematous maculopapular with ulcer at scrotum and shaft of penis	Few discrete erythematous macule at both palms and soles with ill-defined erythematous erosion at glans of penis	Multiple discrete brownish patch and plaque on both palms and soles with multiple discrete erythematous plaque on scrotum	Discrete scaly erythematous plaque at both palms and soles, ill-defined erythematous erosion at glans of penis, multiple whitish patch at posterior pharynx and skin color verrucous papule at perianal area.
Baseline VDRL	1:64	1:64	1:256	1:64	1:256	1:128	1:32	1:512
Treatment	PCN IM weekly x1	PCN IM weekly x1	PCN IM weekly x3	PCN IM weekly x1	PCN IM weekly x1	PCN IM weekly x1	PCN IM weekly x1	PCN IM weekly x3
Clinical outcome	Symptom resolution	Symptom resolution	Lost to follow-up	Symptom resolution	Lost to follow-up	Symptom resolution	Symptom resolution	Lost to follow-up

Abbreviations: Pt = indicates patient; MSMW = man reporting sex with men and women; MSM = man reporting sex with men; PCN = penicillin.

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