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Secondary Syphilis Reinfection with Suspected Asymptomatic Neurosyphilis

Charles Kurnia Mahono^{1,2,*} and Nurdjannah Jane Niode^{1,2}

¹ Department of Dermatology dan Venereology, Faculty of Medicine, University of Sam Ratulangi, Manado 95115, Indonesia; charles.mahono@hotmail.com (C.K.M.); niodejane@unsrat.ac.id (N.J.N.)

² Department of Dermatology dan Venereology, Prof. Dr. R. D. Kandou, Central General Hospital, Manado 95115, Indonesia;

* Correspondence: charles.mahono@hotmail.com

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Abstract

Syphilis, a sexually transmitted disease caused by *Treponema pallidum*, poses a significant global health threat, with an annual incidence of around 12 million cases, predominantly affecting individuals aged 15-49. Reinfection occurs in 11 out of 120 patients, underscoring the importance of effective management. If untreated, 4-9% of cases may progress to early neurosyphilis, often presenting asymptotically. We present the case of a 22-year-old male with reddish-brown patches on the face, palms, and soles, along with erythematous papules on the genital region, following a history of recent promiscuity. Physical examination revealed distinctive manifestations, including nickels and dimes on the face, syphilitic roseola, Bielt's collarette on the palmoplantar region, and erythematous papules-plaques on the scrotal and penile areas. The VDRL test indicated a titer of 1:32, TPHA test >1:5120, and a non-reactive HIV rapid test. Initiating treatment with a single intramuscular injection of benzyl benzathine penicillin G (2.4 million IU) resulted in successful symptom resolution, accompanied by a four-fold decrease in VDRL titer to 1:8 by the third month. However, a subsequent increase to 1:32, following sexual intercourse in the sixth month, indicated reinfection and raised suspicions of asymptomatic neurosyphilis. The patient received oral doxycycline (100 mg twice daily) for 30 days. Unfortunately, treatment success could not be determined as the patient was lost to follow-up. This case report highlights that elevated VDRL titers signify reinfection, treatment failure, or neurosyphilis. Asymptomatic reinfection is common due to lead-time bias and partial immunity, especially with multiple episodes of syphilis. Early neurosyphilis may coexist with primary or secondary syphilis and is frequently asymptomatic. Continued efforts in monitoring and treatment adherence are crucial for effective syphilis management on a global scale.



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1. Introduction

Syphilis, a sexually transmitted disease caused by *Treponema pallidum*, is able to mimic several diseases and also known as “the great imitator” or “the clown” [1-3]. Transmission occurs through micro-abrasions in mucous membrane or skin during genito-genital, ano-genital, or

oro-genital sexual activity rapidly spreading through hematogenous means to other tissues [1].

It is estimated that there are 12 million new cases of syphilis worldwide every year, with an estimated age range of 15-49 years [2, 4]. The prevalence of syphilis is estimated to be 18 million cases [5]. According to the World Health Organization (WHO), the number of new

cases of syphilis in 2012 was 5.6 million worldwide and 886,000 in Southeast Asia [5, 6]. Kenyon *et al.* presented 11 out of 120 patients with syphilis experiencing reinfection [7]. Reinfection is often asymptomatic, causing a delay in diagnosis while infecting others [7, 8].

Stages of syphilis consist of early syphilis (primary syphilis, secondary syphilis, and early latent syphilis) and late syphilis (late latent syphilis and tertiary syphilis) [2]. Primary syphilis is the first stage of syphilis and progresses to secondary syphilis in 6 months after exposure [2]. Secondary syphilis occurs due to the multiplication and spread of *Treponema pallidum* [1]. Without any treatment, the symptoms of secondary syphilis will disappear spontaneously in 1-2 months and advance to latent syphilis [1]. Approximately one-third of untreated latent syphilis progresses to tertiary syphilis, while the other two-thirds remain in latency [2]. Tertiary syphilis consists of gummas, cardiovascular syphilis, and neurosyphilis. However, neurosyphilis may occur at any stage of the disease [2].

Neurosyphilis is one of the clinical syndromes of tertiary syphilis, in which *Treponema pallidum* invades the central nervous system [1, 2]. However, cerebral fluid abnormalities can be found in 13% of primary syphilis and 25-40% of untreated secondary syphilis [1]. Overall, as many as 4-9% of untreated syphilis patients may progress to neurosyphilis [1].

Here, we report a case of secondary syphilis reinfection with suspected asymptomatic neurosyphilis in a male patient treated in the outpatient of Dermatology and Venereology department of RSUP Prof. Dr. R. D. Kandou Manado Central General Hospital.

2. Cases

A 22-year-old male presented with reddish-brown patches on the face, palms of the hands, and soles of the feet, along with erythematous papules on the genitalia. Initially, the reddish-black patches appeared on the right lip and chin the previous month, followed by an increase in the number and spread to the palms and soles with pruritus the previous ten days. The patient denied any previous history of painless sores in genitalia. One week ago, the patient reported development of pruritic and non-tender flesh-colored to reddish papules in the genitalia, i.e., scrotum, and increased in number to the shaft of the penis. History of allergenic or irritating substances was denied. The patient applied a self-bought *pi kang shuang* cream for a month, but he did not use it regularly, and the lesions worsened. Sexual history revealed a multiple sexual intercourse with his current girlfriend in the past month without a condom. Additionally, he also did not know whether his girlfriend

had sexual intercourse with other people. Same-sex intercourse was denied. History of drug abuse and blood transfusion was denied.

The dermatological status revealed multiple well-circumscribed erythematous to hyperpigmented macules, lenticular to nummular in size without scales on the facial region; multiple well-circumscribed and partially diffuse erythematous to hyperpigmented macules, lenticular to nummular in size with scales on the palms and soles. The venereological status revealed multiple erythematous to skin-colored papules and plaques, miliary to lenticular in size without scales on the scrotal and penile region (Figure 1).

Supportive examination with rapid HIV test was non-reactive, while Venereal Disease Research Laboratory (VDRL) and *Treponema pallidum* Hemagglutination Assay (TPHA) examinations were reactive (1:32 and >1:5120). A diagnosis of secondary syphilis was made, and treatment with a single dose of benzyl benzathine penicillin G (BBPG) 2,4 million IU intramuscularly was initiated. Follow-up at the first month showed a two-fold decrease in VDRL titer to 1:16. Successful treatment was obtained in the third month, marked by the disappearance of symptoms and a four-fold decrease in VDRL titer to 1:8. Follow-up at the sixth month, he admitted to having high-risk sexual activities and the VDRL titer increased to 1:32 without any symptoms and the result of HIV rapid test was still non-reactive. Thereafter, he was prescribed oral doxycycline 100mg twice daily for 30 days due to the unavailability of BBPG. The outcome of this treatment could not be determined because he had no VDRL and TPHA re-examination, and the patient was lost to follow-up.

3. Discussions

This case reported a 22-year-old male working as a private employee. Primary and secondary syphilis often occur at the age of 20-29 years [2]. According to the Centers for Disease Control and Prevention (CDC) 2017, syphilis cases are more common in men (16,9 per 100,000) than women (2,3 per 100,000) [9]. The higher cases of syphilis in men were mainly due to men who have sex with men (MSM) that have syphilis for 82% of cases [2, 9]. In this case, previous sexual intercourse with the same sex was denied.

The patient denied any previous history of genital ulcer. The characteristic of primary syphilis ulcer is usually small, from millimeters to 2 cm, clean base, and painless, leading to an unreported ulcer [2]. In this case report, current clinical manifestations include multiple well-circumscribed erythematous to hyperpigmented



Figure 1. The efflorescence on the facial, palms, soles, penile, and scrotal region.

macules, lenticular to nummular in size without scales on the facial region; multiple well-circumscribed and partially diffuse erythematous to hyperpigmented macules, lenticular to nummular in size with scales on the palms of the hands and soles of the feet. Palmoplantar involvement in secondary syphilis is 40-80% of cases [10]. According to clinical manifestations of secondary syphilis, his symptoms are known as *nickels and dimes* on the face, while on both palms and soles, known as roseola syphilitic is characterized by a symmetrically distributed copper-colored rashes [2]. Scales at the edge of the lesion (collarette scales) is a typical pathognomonic sign of secondary syphilis, known as *Bielt's sign* or *Bielt collarette* [2, 11, 12]. The venereological status was multiple erythematous to skin-colored papules and plaques, miliary to lenticular in size without scales on the scrotal and penile region. The symptoms of flat-topped or papulosquamous may be found on the genital, although rarely [2].

At the initial examination, the VDRL and TPHA titer were reactive, 1:32 and >1:5120, respectively. In the third month after the BBPG 2,4 million IU injection single dose, the VDRL titer decreased four-fold to 1:8, with a constant TPHA; he also remained asymptomatic, indicating a good response. A four-fold decrease in VDRL titer indicated a successful treatment has been achieved, while the TPHA titer may remain high and/ or reactive even for a lifetime despite having an adequate treatment [1-3]. Follow-up in the sixth month revealed sexual intercourse with the previous sexual partner three to four times in the last three months. Although he remained asymptomatic, a four-fold VDRL titer from 1:8 to 1:32 was noted. This may occur due to reinfection, failed therapy, and neurosyphilis [2, 3]. Reinfection is characterized by increasing nontreponemal titer \geq four times that has previously been diagnosed with syphilis and received adequate therapy by decreasing nontreponemal titer \geq four times [3, 7]. Reinfection is often asymptomatic, which is suggested due to lead-time bias and partial immunity

of the host [7, 8]. Lead-time bias showed screening serologic examination of syphilis patients when it is in the incubation period, leading to no symptoms [8]. Asymptomatic is more often found in patients who often have several episodes of syphilis because *Treponema pallidum* can induce partial immunity, triggering reinfection [7]. Individuals with multiple episodes of syphilis make a degree of immunity to *Treponema pallidum* infection and each episode of syphilis has an additive effect to form immunity and weaken the host immune response [7].

Neurosyphilis may co-exist with primary and secondary syphilis and is generally asymptomatic [1]. Asymptomatic neurosyphilis is characterized by a positive serology titer and an increase in CSF cell count and/ or protein, a positive TPHA-CSF/serum, and a positive VDRL-CSF test, but without clinical symptoms [13]. He refused to have a CSF examination, so the diagnosis of neurosyphilis could not be excluded. Thus, the working diagnosis was reinfection with suspected asymptomatic neurosyphilis.

First-line therapy is BBPG 2,4 million IU single dose intramuscularly [1-3, 5]. BBPG is the first choice therapy because blood levels of treponemicide penicillin can last for 21-28 days [1]. Patients who are allergic to penicillin, refused an injection, and the unavailability of BBPG can be treated with other antibiotics [1-3, 5]. An alternative antibiotic is oral doxycycline 100 mg twice daily for 14 days in primary or secondary syphilis and 30 days for latent syphilis [3, 5]. Doxycycline is considered effective for early-stage syphilis with an 83-100% seroconversion success rate and is able to penetrate well into the CSF [1, 2]. Doxycycline is easily available, cheaper, and easier to use because it is an oral preparation [2]. In this case report, at the time of the four-fold increase in titer, BBPG 2,4 million IU was not given due to unavailability, and the diagnosis of neurosyphilis was not established; therefore, the patient had oral doxycycline 100mg twice daily for 30 days as an alternative therapy for tertiary

syphilis. A success with doxycycline could not be determined because the patient did not do nontreponemal re-examination and the patient was lost to follow-up.

The prognosis of *quo ad vitam* and *quo ad functionam* was bonam; meanwhile, *quo ad sanationam* was dubia. These were based on the success of therapy at the third month follow-up. The patient had an increasing four-fold VDRL titer in the sixth month, and after a month of doxycycline orally, the patient was lost to follow-up. Thus, the prognosis could not be re-evaluated.

4. Conclusions

This case report highlighted a case of a 22-year-old male with secondary syphilis reinfection and suspected asymptomatic neurosyphilis. The VDRL and TPHA titer showed reactive. Injection of a single dose of BBPG 2,4 million IU showed a successful treatment with a four-fold decrease of VDRL titer in the third month, but there was an increasing four-fold VDRL titer in the sixth month, indicating reinfection. Neurosyphilis can occur along with primary or secondary syphilis and is generally asymptomatic. However, the patient refused to have a cerebrospinal fluid examination. Thus, neurosyphilis could not be established.

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