

A Case Of A 32-Year-Old Male With Rare Presentation of Secondary Syphilis*

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ABSTRACT

Nodular secondary syphilis is a rare condition with only 12 cases reported from 1980 to 2005⁵. Cutaneous nodular granulomatous lesions, a positive serologic test for syphilis, and rapid resolution of symptoms with administration of Benzathine Penicillin are usually seen in previous cases^{3,4,5,6}. We report a case of a 32-year old male with clinical manifestations and laboratory findings consistent with nodular secondary syphilis, and concurrent manifestations of primary and secondary stages. This is the first documented case in East Avenue Medical Center and possibly in the Philippines, highlighting the need for meticulous historytaking, physical examination and laboratory work-up to determine the correct diagnosis.

Keywords: Secondary syphilis, nodules, HIV, sexually transmitted disease

INTRODUCTION

Syphilis is a sexually transmitted infection characterized by a variety of clinical manifestations depending on the stage of the disease. Mucocutaneous manifestations vary from genital ulcers to widespread papulosquamous eruptions to granulomatous nodules. We report a rare case of a 32-year old male with clinical manifestations and laboratory findings consistent with nodular secondary syphilis, and concurrent manifestations of primary and secondary stages.

CASE REPORT

A 32 year old man, Filipino, from Quezon City was seen at the dermatology out patient department of East Avenue Medical Center for evaluation of nodular skin lesions on his face, trunk, genitalia, upper and lower extremities.

History of present illness started one month prior to consult when he noted an asymptomatic papule on his glans penis. No pain, pruritus nor urethral discharge were noted. This was followed by the appearance of bilateral, non-tender, inguinal lymphadenopathy with the left side more grossly enlarged. No medications were taken and no consult was done at this time.

One week prior to consult, the patient noted sudden eruption of pinkish papules and nodules on his face accompanied by non-tender bilateral cervical lymphadenopathy. He initially thought that these papules were pimples. However, he noted increase in size of the lesions, spreading to the scalp, trunk, genital area, and extremities. Persistence of symptoms prompted consult.

Review of systems showed no pertinent systemic findings aside from loss of appetite. He denies weight loss, body weakness, eye pain or redness, changes in vision, and any history of mouth sores or thrush. Past medical history was unremarkable. Patient denies similar lesions among other members of the family. He works as a sales clerk in a grocery store. He is a non-smoker and occasional alcoholic beverage drinker. For the sexual history, his first contact was at 15 years of age and he claims to have had approximately 30 male sexual partners, most of which were casual encounters. He denies use of condoms and contact with prostitutes.

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On cutaneous examination, there were numerous well defined, round, pink erythematous to hyperpigmented papules and nodules, some with erosions on the face, nape, trunk, upper and lower extremities sparing the mucous membranes, palms and soles (see figure 1). There was also a solitary, well-defined, round, pink, eroded papule on the glans penis (see figure 2). On physical examination, there were bilateral non-tender, firm, movable cervical lymph nodes along with a grossly enlarged matted lymph node on the left inguinal area (*buboe*). Cardiac and neurological examination was unremarkable.

A working diagnosis of syphilis, rule out other sexually transmitted infection was made based on the patient's sexual activity profile and clinical picture. Skin biopsy was taken on a new lesion on the left arm which revealed an ulcer surmounted by a crust and fibrin with a zone of neutrophils at the base. The adjacent epidermis showed spongiosis, subcorneal pustule, irregular acanthosis and a foci of slight basal layer vacuolization. There is also a superficial and deep perivascular moderately dense mixed- cell infiltrate consisting of lymphocytes, histiocytes, neutrophils, and numerous plasma cells forming nodular aggregates in the upper dermis. There was exocytosis of lymphocytes and neutrophils into the dermis. Endothelial swelling was noted. The overall findings were consistent with *secondary syphilis*.

Laboratory tests showed that complete blood count, urinalysis, Chest X-ray, Anti-HIV, Anti-HCV, Anti-HBV antibodies were normal. There was also a highly reactive rapid plasma regain test (RPR) strengthening the diagnosis of secondary syphilis. One dose of Benzathine Penicillin G 2.4 million units was administered via intramuscular injection. Anti-histamine was given for pruritus and patient was advised to apply a skin barrier repair cream on lesions. He was advised to abstain from any form of sexual activity, to contact all sexual partners for the past six months, and to use protection on future sexual contacts.

Upon follow up, we noted resolution of lesions with post-inflammatory hyperpigmentation of the papules. Lymphadenopathies were no longer palpable. Repeat HIV test was requested despite the initial negative result in order to remove the potential

false negative result in a patient that was tested within the window period. The window period is a 3-4 week delay between a newly acquired HIV-1 infection and development of antibodies to HIV. During the window period a person can be infected with HIV and be very infectious but still test HIV negative.

DISCUSSION

Syphilis dates back to the time of Columbus, when pandemics of the disease were first documented. Since then, syphilis remained prevalent until the discovery of Penicillin in 1928, which became widely available for the treatment of syphilis during the postwar era¹. In the United States, the Center for Disease Control (CDC) reports that in 2000 and 2001, the national rate of reported primary and secondary cases of syphilis was 2.1 cases per 100,000 population which is the lowest rate since reporting began in 1941. After being on the verge of elimination in 2000, syphilis cases have rebounded which is attributed to the increase in cases primarily among men, and particularly among men who have sex with men (MSM). The increase in syphilis cases among MSM is a major public health concern, particularly because syphilis and the behaviors associated with acquiring it increase the likelihood of acquiring and transmitting human immunodeficiency virus (HIV)⁸. In the Philippines, the exact prevalence and incidence of syphilis is lacking although 589 new cases of syphilis were reported in the Philippine Dermatological Society Health Information System Database (PDS- HIS) from 2011 to 2017.

Syphilis is a disease caused by the spirochete *Treponema pallidum*. It is most commonly acquired sexually when a person comes in contact with infectious lesions of syphilis on another person. Syphilis can also be acquired through nonsexual contact such as blood transfusion, accidental inoculation in an occupational setting, or through exposure in utero¹. According to CDC, it has been observed historically that increase in the number of cases of congenital syphilis paralleled the increase in primary and secondary cases among women in 2014–2015 (27.3%) and during 2011–2015 (55.6%)⁸. This is of particular importance because early diagnosis and treatment would prevent the devastating effects of syphilis.

Most of the manifestations of syphilis are cutaneous, making it of particular interest to dermatologists. Persons infected with syphilis pass through four distinct clinical phases. The primary lesion develops 10-90 days after infection and classically presents with a painless chancre at the site of inoculation. In 60-70% of cases of *primary syphilis*, painless regional lymphadenopathy arises which is usually unilateral early in the course of the disease, with bilateral involvement later in the course. The chancre heals in 3-6 weeks without treatment, and within 1-2 weeks with treatment¹. The lesions of *secondary syphilis*, corresponds to a phase of infection characterized by widespread dissemination of spirochetes. Clinical manifestations are famously varied, reinforcing the reputation of this infection as "The Great Imitator"³. The cutaneous lesions of secondary syphilis are diverse, while the most being macular, maculopapular, papulosquamous, and annular often located on the palms and soles, sometimes accompanied by fever, lymphadenopathy, weight loss, arthralgias and myalgias⁴. A *latent period* of varied duration is characterized by the absence of signs or symptoms of disease, with only serologic tests as evidence of infection. The *tertiary stage* is characterized by the presence of a small number of organisms and a high cellular immune reactivity against the organisms. The microorganisms may invade the central nervous and cardiovascular systems as well as the skin, leading to delayed type hypersensitivity responses which produce local inflammation and gummas in affected tissues².

Serology is the most reliable method for laboratory diagnosis of syphilis, regardless of the stage of infection⁹. According to the CDC, a presumptive diagnosis of syphilis requires use of two tests: a nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or Rapid Plasma Reagin [RPR]) and a treponemal test (i.e., fluorescent treponemal antibody absorbed [FTA-ABS] tests, the *T. pallidum* passive particle agglutination [TP-PA] assay, various enzyme immunoassays [EIAs], chemiluminescence immunoassays, immunoblots, or rapid treponemal assays). The traditional algorithm for the diagnosis of syphilis recommends the use of nontreponemal test to screen for syphilis. Once positive, diagnosis is confirmed by treponemal tests¹².

The recommended treatment for most types of syphilis is benzathine penicillin G, with dose and administration schedule determined by disease stage. Treatment success is generally defined as clinical improvement accompanied by a fourfold decline in serologic nontreponemal titer within a specified timeframe depending on the stage of infection and HIV status of the infected person¹.

This case is noteworthy because lesions of primary and secondary syphilis are concurrently present. As mentioned, syphilis goes through several stages, often described in time intervals that come one after another, but the presence of two stages is not usually seen. Are these two stages present at the same time? Did we catch the patient during the transition of primary and secondary stages? According to literature, simultaneous presentation of primary and secondary syphilis has been reported and that chancre can persist into the secondary stage especially in HIV positive patients⁷. In fact, HIV infected persons are more likely to present with secondary syphilis with a primary chancre¹. Hence, retesting for HIV as done in this case is even more necessary because of the patient's clinical presentation. Our patient shows us that the clinical manifestations of syphilis, which are classically divided in literature according to stages, may not appear in the orderly manner as we thought and may occur simultaneously.

Aside from the simultaneous occurrence of primary and secondary syphilis, our patient's manifestation of secondary syphilis was very unusual. He presented with few papules accompanied by nodules. There were no lesions on the palmoplantar areas, which are usually involved in secondary syphilis. Nodular lesions are rare in secondary syphilis. In fact, only 12 cases of nodular secondary syphilis have been reported from 1980 to 2005⁵. The most commonly reported histological patterns in nodular secondary syphilis are mainly diffuse dermal infiltrates and a granulomatous inflammation⁵. The pathogenetic interpretation of nodular granulomatous lesions in secondary syphilis is not clear. Some authors suggest that this kind of lesion represents a reaction of specific hypersensitivity to treponemal infection, while others believe that the formation of dermal granulomata should be correlated with the duration of the disease, representing a transition

eruption to the tertiary phase⁶. This becomes especially important because nodular secondary syphilis could be a precursor of tertiary syphilis, a potentially morbid condition. A high degree of clinical suspicion, a careful sexual history and thorough physical examination, followed by serological testing permits accurate diagnosis, thus facilitating prompt treatment of these cases¹¹. The response to treatment was the same as in the typical secondary syphilis⁵.

Comparing the above mentioned information on secondary nodular syphilis with the clinical and histopathologic findings seen in our patient, we can say that almost all characteristic findings of nodular secondary syphilis is evident in our patient, except for the histopathologic finding of granuloma formation. The question now is, is this a case of the rare nodular secondary syphilis?

Except for the histopathologic findings described above, there are no guidelines described in literature on how to accurately give a diagnosis of nodular secondary syphilis because very few cases have been reported. A possible explanation why granuloma formation is not appreciated in this case is because skin biopsy was taken from a fairly new lesion on the right arm. Granuloma may not have developed yet, but the true etiology of the condition which is secondary syphilis is persistently evident. The authors are postulating that if biopsy was taken from the old nodular lesions, granuloma formation might have been appreciated. This also emphasizes the importance of clinicohistopathologic correlation in the diagnosis of syphilis. Although granuloma formation was not evident in histopathology, the clinical presentation and laboratory findings still points to a diagnosis of nodular secondary syphilis.

CONCLUSION

Syphilis remains a public health concern. Syphilis is curable at any stage of the disease with devastating effects if left untreated. This case report outlines the diagnosis and management of a patient with a rare condition of nodular type of secondary syphilis. Although patients with this condition are not frequently seen in general practice, physicians must be made aware to avoid misdiagnosis and incorrect treatment. Aside from administration of curative drug, supportive treatment such as patient

education, counselling, and contact tracing is just as important. This case report stresses the importance of meticulous historytaking, physical examination and laboratory work-up to come up with the correct diagnosis when presented with a patient with a rare condition. Furthermore, a thorough review of the literature especially existing case reports and case series is essential.

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APPENDIX

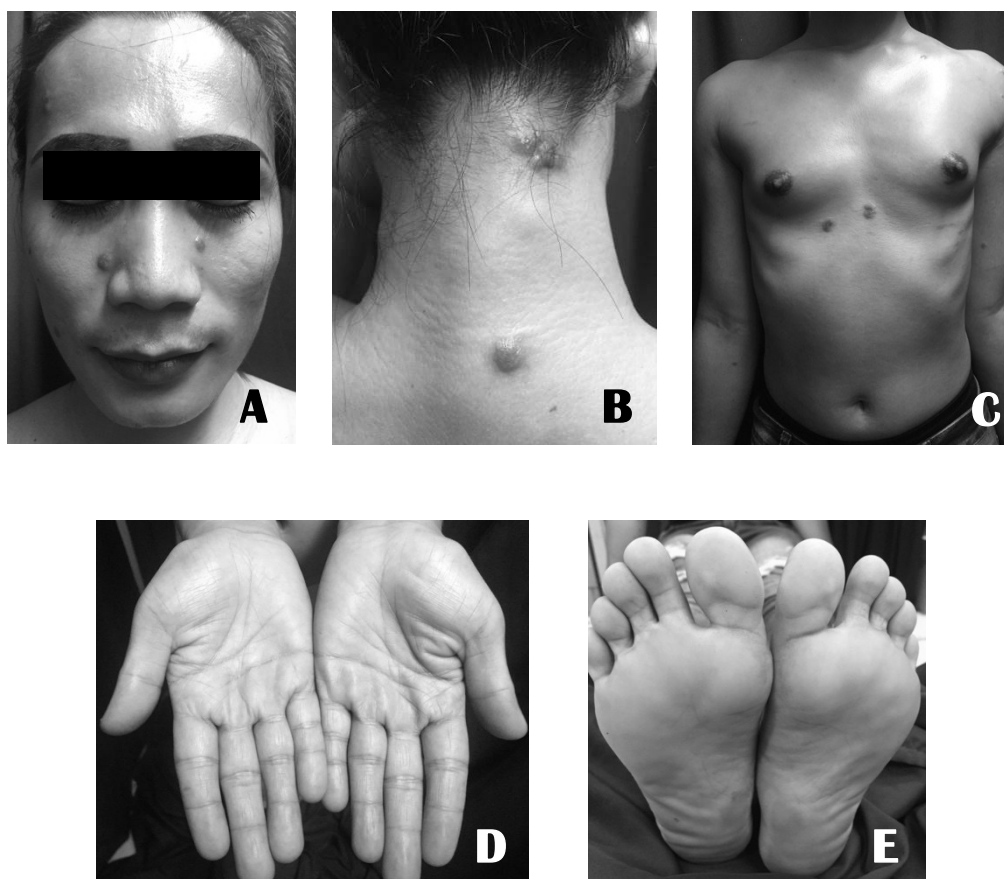


Figure 1. Multiple, well defined, round, pink erythematous papules and nodules, some with central erosion distributed on the face, nape, trunk (A,B,C), upper and lower extremities sparing the palms and soles (D,E).



Figure 2. Nodular lesion on the glans penis where chancre was previously located (A). Grossly enlarged lymph node on the left inguinal area or *Buboe* (B).



Figure 3. Resolution of erythematous nodules and lymphadenopathies of secondary syphilis three months' post treatment with Benzathine Penicillin G.