Case Report

Annular Secondary Syphilis with Histopathologic Features of Granuloma Annulare

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Abstract

Syphilis is one of the most common sexually transmitted diseases in the world. It is known as "the great mimicker" due to its varied cutaneous presentations, which can make it challenging to diagnose. We report a case of a 20-year-old female presenting with a nonhealing, pruritic, annular plaque on the left malar area of 3-month duration. She was initially treated as a case of tinea faciei. The lesion was unresponsive to topical antifungals and steroids with continued increase in size and number. Skin biopsy revealed secondary syphilis with histopathologic features of granuloma annulare. Degenerated collagen, not a feature of secondary syphilis, was seen, prompting further studies to confirm the diagnosis of secondary syphilis. Alcian blue stain was negative, which helped rule out granuloma annulare. She was then given benzathine penicillin G 2.4 million U, which led to a significant decrease in the size of the lesion noted 1 week posttreatment. Only postinflammatory hyperpigmentation was noted after 1 month of treatment. Clinically, secondary syphilis may present as an annular lesion that can mimic tinea. This can also present with atypical histopathologic features and an in-depth investigation is needed to further confirm the diagnosis.

Keywords: Annular secondary syphilis, annular syphilis, granuloma annulare, syphilis

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Introduction

Syphilis is a sexually transmitted infection which has four clinical phases, namely primary, secondary, latent, and tertiary. Humans are the only known natural hosts. This disease is caused by the spirochete *Treponema pallidum* subspecies *Pallidum*. Known as the great mimicker, it has numerous clinical manifestations[1] presenting as different dermatological diseases. It has become a challenge in diagnosis[1,2] causing a delay of proper treatment. It can affect different organs necessitating immediate diagnosis and treatment.

In the Philippines, a total of 778 patients, 630 of which were males and 148 were females, were diagnosed with secondary syphilis from 2011 to 2021 among the Philippine Dermatological Society Institutions.

This study aims to report a case of annular secondary syphilis in a Filipino female with histopathological features of granuloma annulare and to review published literature on previous cases with similar presentation.

Case Report

A 20-year-old female presented with a nonhealing annular plaque on the left malar area. Eight months before consult, she had a history of a solitary ulcer on

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her left labia majora which was clinically diagnosed by a gynecologist as genital herpes. She was prescribed acyclovir 5% cream 5 times a day for 10 days and unrecalled antibiotics for 1 week. The ulcer resolved after 2 weeks.

Three months before the consult, the patient noted a solitary erythematous papule on her left cheek [Figure 1]. There was no consult done or medications applied. There was no history of fever, generalized body malaise, and muscle or joint pains. During the interim, she noted that the lesion enlarged in size. Similar lesions were also noted on the left lower eyelid, left inner canthus, and right upper eyelids. There was associated occasional pruritus but no pain or hypoesthesia was noted. There was no genital lesion, oral ulcer, or other mucosal lesion noted at this time. The lesions persisted and continued to gradually increase in size, which then progressed into an annular plaque. The patient consulted a dermatologist in a private hospital and was prescribed miconazole 2% cream and betamethasone valerate 0.1% ointment twice a day, which were applied for 2 weeks. She noted decrease in the size of the lesions on the bilateral lower eyelid but the erythematous annular plaque on her left cheek continued to increase in size, approximately 2 cm [Figure 1]. She was then referred to a tertiary institution for further evaluation and management.

Cutaneous examination showed a concentric lesion composed of an outer pinkish erythematous annular plaque measuring 6 cm in diameter, topped with minute scales, an inner hyperpigmented annular patch, and a central hyperpigmented patch over the left cheek. There were also few well-defined erythematous arcuate plaques on the left lower eyelid and bilateral inner canthi. Further examination revealed the presence of oral ulcers [Figure 2]. There was no palmar or plantar lesion. She had cervical lymphadenopathy on levels I and II.

The patient had her coitarche at the age of 18. Her last sexual contact was 1 week before the initial consult. She had a total of 2 male sexual partners. She practiced monogamy with her current partner. She did not use contraception and had no known history of sexually transmitted diseases or human immunodeficiency virus. Upon further investigation, potassium hydroxide and acid-fast smears were both negative. Screening for syphilis revealed a reactive rapid plasma reagin (RPR) (1:16) and a positive fluorescent treponemal antibody absorption (FTA-ABS) test. Her HIV test was negative. Dermoscopic findings were white homogenous structures with peripheral erythema, red dots, yellow clods, and tan foci of pigmentation [Figure 3].

Histopathological examination of the lesion revealed mounds of parakeratosis with neutrophils in the stratum corneum, hyperplastic epidermis with spongiosis, moderately dense superficial and deep perivascular infiltrates of lymphocytes, histiocytes, and numerous plasma cells with some eosinophils in the dermis and extended to the lower reticular dermis. There were also plasma cells and histiocytes around the follicular, eccrine, sebaceous glands, and arrector pili muscle on the upper dermis. Finally, there were focal areas of degenerated collagen with surrounding histiocytes; however, they were not arranged in a palisaded array and no plasma cells were seen [Figure 4]. The initial diagnosis was secondary syphilis, rule out granuloma annulare. Further staining with Alcian blue stain was negative for mucin arguing against granuloma annulare. The patient was then given a single dose of 2.4 million units of benzathine penicillin G. There was noted significant decrease in size after 1 week,

Figure 1: Six-centimeter concentric lesion composed of an outer erythematous annular plaque topped with few scales, an inner hyperpigmented annular patch, and a central hyperpigmented patch over the left cheek

Figure 2: Painless oral ulcers on the inner upper and lower lip

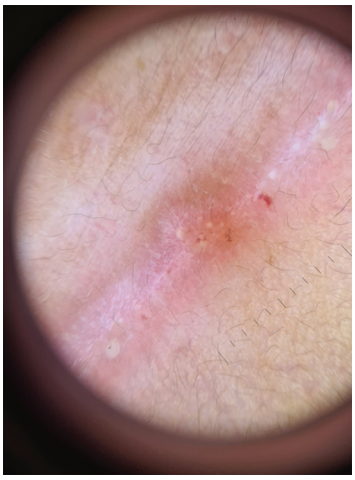

Figure 3: White homogenous structures with peripheral erythema, red dots, yellow clods, and tan foci of pigmentation

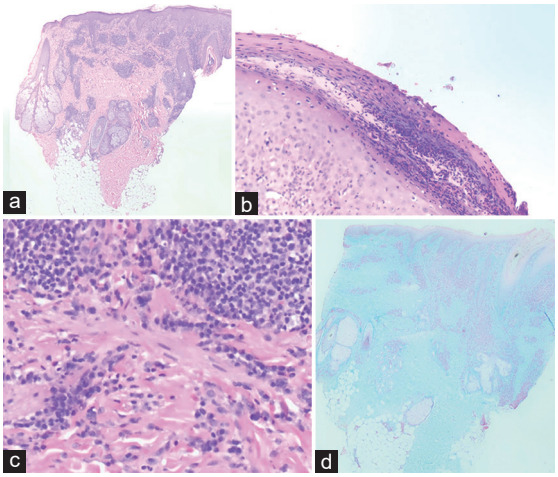

Figure 4: Histopathology of the border of the annular plaque on the left cheek of the patient showed (a) superficial and deep perivascular infiltrates of lymphocytes, histiocytes, and numerous plasma cells. There were also noted (b) parakeratosis with neutrophils, and (c) focal areas of degenerated collagen with surrounding histiocytes. (d) Alcian blue stain was negative for mucin

with resolution to postinflammatory hyperpigmentation after 1 month.

Discussion

Syphilis, despite being one of the most common sexually transmitted diseases, has varied presentations which makes the diagnosis challenging.[2]

An annular lesion for secondary syphilis accounts for approximately 5.7%–13.6% of cutaneous manifestations.[1] This is usually seen in children and patients of African descent in the late secondary stage[3] and usually affects the face near the corners of the mouth.[4] The annular shape is formed when a lesion is localized at one area and then would spread radially.[5] The thickness of the lesions can vary from slightly raised scaly lesions to verrucous plaques.[5] The patient's lesion appeared on her left malar area. A localized annular lesion may cause a diagnostic dilemma since the patient lacked the usual cutaneous features of secondary syphilis.[6] Mucosal lesions may be present in secondary syphilis. The usual areas affected are the tongue, gingiva, soft palate, and lips. Oral ulcers usually present as oval reddish macules or maculopapular eruptions[7] which were present in our patient.

Cutaneous manifestations are vital clues for the diagnosis of syphilis which are present in 80% of patients.[6] Due to its ability to mimic different diseases, it should be included as a differential diagnosis for lesions with atypical presentations.[8] Patients often seek dermatologic consults due to these concerns[9] and it is vital that dermatologists would have a high index of suspicion when it is warranted.

Serologic tests are usually performed to diagnose syphilis. They are classified as nontreponemal and treponemal tests. Nontreponemal tests such as RPR and Venereal Disease Research Laboratory are often used to diagnose and monitor response to treatment and treponemal tests such as FTA-ABS is used to rule out the possibility of false-positive nontreponemal tests. Biopsy and the use of immunohistochemistry and silver staining are not often used but are sometimes requested for atypical lesions. However, some lesions remain negative which makes serologic tests essential.[1] Other tests such as HIV antigen test and hepatitis B profile may also be requested to rule out other sexually transmitted diseases. For the patient's hepatitis B markers, the anti-HBs, anti-HBe (reverse), anti-HBc IgM, and anti-HBc IgG (reverse) were reactive, which may mean that the patient has a chronic infection on top of a resolving acute infection.

From a histopathologic perspective, having features of both syphilis and granuloma annulare is rare. One case report revealed a similar finding where biopsy of nonpruritic

macular and papular rash revealed interstitial arrangement of the histiocytes with occasional multinucleated giant cells between collagen bundles which is a feature of granuloma annulare. However, due to the clinical features, the patient was diagnosed as syphilis, and serum sample tested positive.[10] Although granulomatous inflammation is usually seen in the tertiary stage, one case report revealed palisading granulomas with central necrosis and degenerated collagen on a patient with nodular secondary syphilis.[11] Another case report revealed a patient with nodular tertiary syphilis mimicking granuloma annulare histologically, however, all biopsy specimens were negative for mucin.[12]

Dermoscopy is often nonspecific but a main finding is Biett's collarette – a circular, thin, scaling edge progressing in an outward direction and surrounded by an erythematous halo, which was not found in the patient.[3]

The treatment regimen for early syphilis is still 2.4 million U of benzathine penicillin G. Annular secondary syphilis generally has good response to penicillin.[1] The thickness of the patient's lesions decreased in size within 1 week after administering 2.4 million U of benzathine penicillin G. Only postinflammatory hyperpigmentation was left a month after the treatment. Early detection and treatment are warranted to prevent complications of this disease entity. Partners who were exposed within 90 days to patients with primary, secondary, and early latent syphilis should also be tested for syphilis. Aside from medical management, we should also counsel the patient on safe sexual practices to prevent the recurrence of the disease.

Conclusion

Syphilis can present with a variety of skin lesions. It can mimic almost any disease entity which makes it occasionally challenging to diagnose. A high index of suspicion is needed for patients who have atypical cutaneous manifestations and are in the high-risk group. A thorough and in-depth history is needed and aids in the diagnosis of syphilis. Early, accurate diagnosis is important to prevent progression to the tertiary stage. Despite having many presentations, it is easy to treat. Proper health education should be given to patients to prevent future infections.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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