Annular secondary syphilis with HIV coinfection that resembles other dermatoses

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Abstract

Syphilis is a sexually transmitted infection with manifestations that can mimic other diseases, leading to misdiagnosis. Annular syphilis is a rare atypical secondary syphilitic lesion that seldomly involves the face. Human immunodeficiency virus (HIV) coinfection can increasingly lead to atypical manifestations of syphilis and complicate the diagnosis. Herein, we describe a 29-year-old man with a diagnosis of annular secondary syphilis and HIV coinfection. He had clinical manifestations of annular erythematous papules and plaques with white scales at the edges, distributed and scattered on the face, neck, and upper back. The skin lesions went undetected on several visits and were misdiagnosed owing to similarities with other dermatoses. Serological examination showed positive *Treponema pallidum* particle agglutination assay and venereal disease research laboratory test titer 1/512, confirming syphilis infection. Results from the histopathological examination supported the diagnosis of secondary syphilis. Positive anti-HIV rapid test results indicated concurrent HIV infection. He was treated for syphilis and given antiretroviral therapy, and showed a good response as demonstrated by improvement of the lesions and serological titers. This case highlights the importance of recognizing the possibility of annular secondary syphilis and HIV coinfection which can have atypical manifestations.

Keywords: annular syphilis, atypical, secondary

Introduction

Syphilis is a sexually transmitted infection caused by the spirochete *Treponema pallidum,* with an estimated incidence of 12 million individuals infected annually worldwide. This infection is more common in men who have sex with men (MSM), although the incidence is increasing in heterosexual individuals [1]. In 2016, the incidents of primary and secondary syphilis were higher in men (15.6 cases per 100,000 men) than in women; 58.1% of cases that occurred in MSM. Syphilis coinfection with HIV was reported at 47% in MSM, 10.7% in heterosexual men, and 4.1% in women [2]. The incidence shows that syphilis is still a global burden.

Secondary syphilis is called the *great imitator* because it can mimic other dermatoses [1]. Annular syphilis is a rare and atypical form of secondary syphilis. These lesions rarely involve the face [3]. Syphilis infections are often associated with HIV infection because they can increase the risk of comorbidity with the other disease and cause atypical manifestations [4]. As a result, diagnosis and therapy are often delayed due to forms that resemble other diagnoses [1,3].

We report a case of annular secondary syphilis on the face, nape, and upper back as an atypical manifestation of secondary syphilis with HIV coinfection. The diagnosis of secondary syphilis was misdiagnosed on several visits. The atypical presentations and predilections in our case have been rarely reported. Accordingly, it is essential to

prevent delayed diagnosis and treatment by early and informed recognition of possible mimicking manifestations resulting from the coinfection.

Case Synopsis

A 29-year-old man came to the outpatient clinic with the chief complaints of red bumps and rash on his face, nape, and upper back. A month and a half earlier, the eruption had appeared under his right eye, that was sore without itching. He went to the doctor and was diagnosed with acne vulgaris. He was given neomycin sulfate 0.5% and betamethasone ointment 0.1% twice daily, but the complaints persisted. Three weeks later, an erythematous eruption spread to his entire face, nape, and upper back without pain or itching. There was no history of photosensitivity. He returned to the doctor and was diagnosed with guttate psoriasis. He was then referred to our hospital.

Based on previous history, he last had sexual intercourse two months before the complaints and never used a condom. Sexual orientations included oro-genital, genito-genital, and anogenital intercourse with women and men. There were similar complaints in a previous sexual partner with red rash on her body, but his partner's treatment and HIV status were unknown. Our patient was unaware of any previous genital lesions.

On physical examination, the face, nape, and upper back showed erythematous papules and plaques of annular, partially oval shapes with varying sizes. In some, thin white scales appeared on edges of the multiple scattered lesions (**Figure 1**). There were no lesions on the palms and soles, which usually are locations with typical manifestations of syphilis. On the ventral side of the penile corpus, a solitary oval hypertrophic scar was seen. No lymph node enlargement was found.

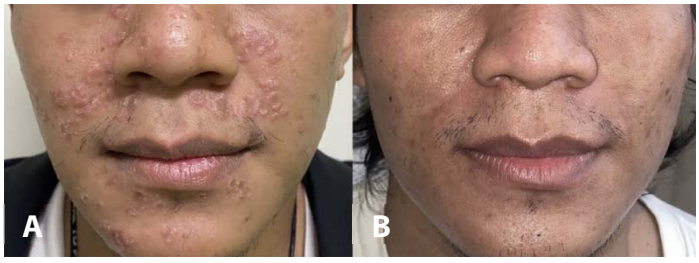

Figure 1. ***A)*** *Erythematous papules and plaques of annular and oval shape with white scales before therapy.* ***B)*** *After seven months of treatment with benzathine penicillin injection.*

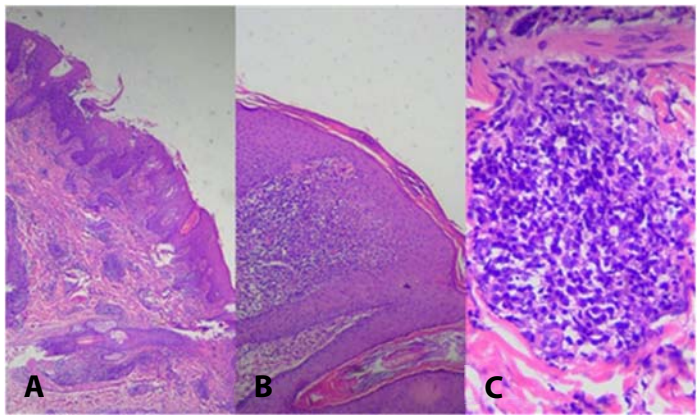

Figure 2. *Histopathological examinations showed basket-weave type orthokeratosis, focal parakeratosis, and moderate spongiosis. Dense inflammatory cell infiltration, especially in the perivascular and peri adnexa. H&E,* ***A)*** *10×,* ***B)*** *40×,* ***C)*** *100×.*

Potassium hydroxide (KOH) examination showed no fungal elements. *Treponema pallidum* particle hemagglutination (TPHA) serological test showed reactive results and the venereal disease research laboratory (VDRL) titer was 1/512. Biopsies were taken from two locations, the left cheek region and the upper back. Histopathological examination in both areas showed that the epidermis had basket-weave type orthokeratosis with partial focal parakeratosis, moderate spongiosis, and neutrophil exocytosis. Upper to lower dermis appeared with edema with dense inflammatory cell infiltration consisting of lymphocytes, histiocytes, plasma cells, and neutrophils, especially perivascular and peri adnexa (**Figure 2**). Direct immunofluorescence examination did not show any deposits of IgM, IgG, IgA, or C3 complement at the basement membrane (**Figure 3**). An anti-HIV rapid test showed a positive result. He underwent a CD4 examination with a result of 752cells/µl.

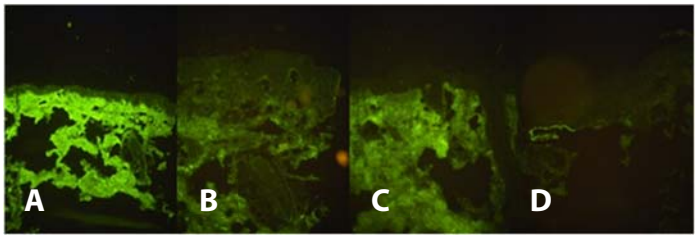

Figure 3. *Direct immunofluorescence showed no deposits at the basement membrane of* ***A)*** *IgG, 10×;* ***B)*** *IgM, 40×;* ***C)*** *IgA, 10×; and* ***D)*** *C3c, 40×.*

The patient's diagnosis was suitable for annular secondary syphilis with HIV coinfection. He was given a single injection of benzathine penicillin 2.4 million units intramuscularly. Antiretroviral drugs with tenofovir, lamivudine, and dolutegravir were given. Evaluation results 5 and 7 months after therapy showed that the skin lesions had disappeared and the VDRL titer decreased to 1/8, which showed a good improvement.

Case Discussion

Cutaneous secondary syphilis manifests generally as an erythematous maculopapular eruption on the trunk, palms, and soles without itching [3,5]. These typical lesions occur in 50-70% of cases [6]. A facial predilection is rarely reported [3,5]. Besides a rare predilection, atypical forms may also occur in secondary syphilis, making definitive diagnosing more difficult. Atypical forms such as lichen planus-like lesions, follicular rash, vesicular rash, corymbiform rash, and psoriasiform rash have been reported in their early stages. In late secondary syphilis, the atypical forms described include nodular, annular, pustular, frambesiform, papulosquamous on sun-exposed areas, and nodular-ulcerative lesions (malignant syphilis). Atypical annular lesions are rare and reported in 6-14% of cases [6,7]. In our case, annular secondary syphilis was found on the face, nape, and upper back. These are atypical lesions in secondary syphilis with a rare shape and predilection. Skin lesions on the face are usually more noticed by the patients because they are more visible. Therefore, the patient in our case had the facial complaint checked by a doctor at the previous visit. Furthermore, atypical forms of secondary syphilis can lead to misdiagnosis and delay diagnosis and therapy [8]. Our patient was previously examined by several doctors and was misdiagnosed with other diseases because the lesions were atypical and resembled other dermatoses.

The incidence of syphilis has a strong correlation with HIV coinfection. Syphilis can be a risk factor for HIV and vice versa [4,9]. Pathogenicity that can explain the relationship between syphilis and HIV is very complex and not yet fully understood [10]. In HIV with primary syphilis, atypical manifestations can be found in multiple chancroid-like ulcers. In HIV with secondary syphilis, overlapping stages and atypical skin manifestations can be found [4,7]. Factors influencing the atypical forms of syphilis are host susceptibility, bacterial and transmission characteristics, and patient immunity [4]. In our case, the patient was diagnosed with secondary syphilis and HIV coinfection. The presence of HIV infection was one of the risk factors for the atypical manifestations in our patient.

Based on European syphilis guidelines, the diagnosis of secondary syphilis is established by positive treponemal and non-treponemal test results [11]. *Treponema pallidum* cannot be cultured in vitro. Hence, the diagnosis and therapeutic evaluations depend on serological examinations [12]. Treponemal tests include *Treponema pallidum* particle agglutination or *Treponema pallidum* hemagglutination assay and IgM/IgG enzyme immunoassay. Non-treponemal tests include the rapid plasma reagin or VDRL test [4,6,11]. The treponemal test is the first test to show a positive result two weeks after infection and will remain positive throughout life. Non-treponemal tests are used to evaluate therapy and indicate disease stage. In general, high titers indicate more active (early) lesions; low titers indicate latent lesions or signs of infection that have been treated [6]. Our patient had a positive *Treponema pallidum* hemagglutination assay result with a high VDRL titer of 1/512, confirming the diagnosis of secondary syphilis.

Patients with atypical manifestations of syphilis often require a histopathological examination to rule out other conditions in the differential diagnosis [12]. The histopathology of secondary syphilis is nonspecific. It can show hyperkeratosis, irregular acanthosis, elongated rete ridges, and neutrophil exocytosis. Dense inflammatory cells tend to infiltrate the upper dermis of lymphocytes, histiocytes, and plasma cells, especially in the superficial and deep perivascular regions [12,13]. The histopathology of our case showed focal parakeratosis, moderate spongiosis, neutrophil exocytosis, and dense infiltration of inflammatory

cells (lymphocytes, histiocytes, plasma cells, and neutrophils) in the upper and lower dermis, especially perivascular and peri adnexa, suggestive of syphilis over the other possibilities such as guttate psoriasis, granuloma annulare, subacute cutaneous lupus erythematosus, and tinea faciei et corporis. Guttate psoriasis is a variant of psoriasis which is a chronic auto-inflammatory disease [14]. Guttate psoriasis lesions are acute, with small erythematous papules and plaques accompanied by white scales that form like droplets. Histopathological findings can confirm the diagnosis of guttate psoriasis, which shows a psoriasiform reaction, dilated superficial blood vessels, hypergranulosis, and parakeratosis. Munro microabscesses can be found in the stratum corneum and spongiform pustule of Kogoj in the stratum spinosum [15]. These histopathological findings were not found in our case and were unsuitable for diagnosing guttate psoriasis.

Granuloma annulare is a rare non-infectious granulomatous disease [16]. Predilection is most common on the hands and feet, but generalized, subcutaneous, or perforated forms can be found [17]. The lesions are often asymptomatic in erythematous or skin-colored papules with annular forms. The annular erythematous papules were similar to the skin manifestations in our case. The diagnosis of granuloma annulare is established by histopathological examination in which palisade or interstitial histiocytic granulomas, mucin in the dermis, collagen degeneration, and sometimes multinucleated giant cells. In some cases, elastophagocytosis, eosinophil infiltrates, and vessel wall thickening can also be found [16]. In our case, no histopathological finding was suitable for granuloma annulare.

Subacute cutaneous lupus erythematosus (SCLE) is an autoimmune disease, and considered a subacute form of cutaneous lupus. Clinical manifestations of SCLE can be annular or papulosquamous [18]. The distribution of the lesions tends to be symmetrical in sun-exposed areas such as the neck, shoulders, chest, and extensor surfaces of the extremities. There is photosensitivity of the face, neck, upper back, and shoulders. The annular skin lesions and distribution were similar to our case but without photosensitivity. Histopathological examination and direct immunofluorescence can confirm the diagnosis of SCLE, which shows interface dermatitis, dense perivascular infiltrates, epidermal atrophy, and prominent basal cell vacuolization. Basement membrane thickening can also be found. On direct immunofluorescence examination, IgG and complement deposits are identified along the basement membrane [18,19]. However, histopathological features in our case and immunofluorescence results did not support the diagnosis of SCLE.

Tinea faciei is a dermatophyte infection on the face other than the beard area, whereas tinea corporis is a dermatophyte infection on the skin other than the hands, feet, head, beard, face, groin, and nails [20,21]. Cutaneous manifestations include pruritic lesions in the form of annular erythematous plaques with white scales on the edges [22]. The skin lesions were similar to our case but without itching. Our case predilection was on the face, nape, and upper back, which may still be a predilection for fungal infections. Potassium hydroxide examination can help establish the diagnosis by finding unpigmented, thin, and transparent hyphae [21]. Histopathological examination can show orthokeratosis, neutrophils in the stratum corneum, papillary dermis edema, and hyphae between the two cornified cell zones (sandwich sign), [23,24]. There were no hyphae on KOH and histopathological examination in our case.

First-line therapy for syphilis with or without HIV is intramuscular benzathine penicillin (penicillin G). The dosage and duration of therapy depend on the stage of syphilis. In early syphilis, including primary, secondary, and early latent syphilis, a single dose of 2.4 million units of benzathine penicillin G can be given. The goals of therapy for syphilis are clinical and serological titer improvement [8]. Titer improvement is successful if the non-treponemal test decreases 4-fold within 6-12 months post-therapy in early syphilis, and 12-24 months post-therapy in late syphilis [8,11]. Our patient showed a decrease in titer from 1/512 to 1/8 and a disappearance of lesions within five months post-therapy, indicating a remarkably successful therapy. Making the correct diagnosis can help clinicians

provide appropriate and adequate therapy, thereby increasing the success of therapy.

Conclusion

We report a patient with annular secondary syphilis on the face, nape, and upper back, a rare atypical manifestation of secondary syphilis with HIV coinfection. The patient had been misdiagnosed with other dermatoses on several visits. The definitive diagnosis was then established by serological examination of syphilis and skin biopsy. Syphilis may coexist with HIV infection and lead to atypical manifestations, as in our patient. It is essential to recognize the atypical presentations of secondary syphilis, especially in patients with HIV infection.

Potential conflicts of interest

The authors declare no conflicts of interest.

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