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Secondary syphilis as first presentation of HIV: a case report

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Abstract

The simultaneous occurrence of HIV and syphilis poses an increasing difficulty due to the dynamic interplay between these two diseases. In recent years, the worldwide prevalence of co-infection between these two major global health issues has increased, partly because each infection can facilitate the acquisition of the other. We report a case of a 36-year-old diabetic male presenting to our clinic with scattered erythematous papules and plaques with a collarette of scale on the palms, soles, and genital area. The patient had geographic tongue with linear white plaques and fissuring. Virology showed positive herpes simplex virus IgG antibodies for types 1 and 2, and skin biopsy demonstrated vacuolar interface dermatitis, acanthosis, lymphocyte exocytosis, and thinning of the rete ridges. Additionally, the HIV serology test was positive. A diagnosis of secondary syphilis on top of HIV was established. Given the significant consequences that the co-infection of syphilis and HIV has on impacted individuals, it is crucial to allocate more time, effort, and resources to investigate this condition.

Introduction

Belonging to the family Spirochaetaceae, *Treponema pallidum* is the bacterium responsible for one of history's most prevalent sexually transmitted infections: syphilis.[1] Syphilis primarily presents as a painless, hardened ulcer called a chancre at the site of infection. Secondary syphilis, which occurs 2 to 8 weeks after the chancre disappears, is characterized by various systemic manifestations that can affect any part of the body.[2] For centuries, syphilis has been associated with stigma and disgrace, with affected populations often blaming neighboring countries for its origin.[3]

HIV, which belongs to the *Retroviridae* family and is classified under the *Lentivirus* genus, has inflicted severe stigma on its patients since it was first discovered 40 years ago.[4,5] Originally thought to be transmitted exclusively among homosexual individuals, this sexually transmitted infection has claimed the lives of tens of millions of people.[6] The co-infection of HIV and syphilis presents an escalating challenge due to the dynamic interaction between these two infections. This interaction not only increases the risk of acquiring and transmitting both diseases but also accelerates disease progression, posing additional risks.[7] In recent years, a higher global rate of co-infection between these two global health problems has been observed, as both infections facilitate the acquisition of each other.[8] This is supported by a Danish study that showed that 10% of men diagnosed with syphilis acquired HIV infection within five years after the diagnosis of syphilis, and 58% of men who have sex with men diagnosed with syphilis were found to have concurrent HIV.[9]

This alarming coexistence makes screening for HIV among syphilis patients a real necessity, particularly within high-risk populations. It is still uncertain whether cases of HIV infection are accurately reported among individuals diagnosed with syphilis, especially considering the impact of the COVID-19 pandemic.[10] Therefore, it is crucial to prioritize HIV screening among syphilis patients in order to ensure comprehensive and timely detection. The escalating and progressive high rate of co-infection, along with the synergistic interaction between these two diseases, highlights the need for a thorough understanding and comprehension of these infections.

We report a case of a 36-year-old male patient who presented to our clinic with scattered erythematous papules and plaques with a collarette of scale as the first manifestations of HIV.

Case Report

A 36-year-old Saudi male was referred to our clinic from the emergency department complaining of erythematous papules and plaques. The patient was vitally stable, afebrile, and fully conscious, although mild tachycardia was noted with a heart rate of 118 bpm. According to the patient, a similar rash occurred approximately one year ago and resolved spontaneously over several weeks. The current rash appeared one week ago and has persisted for a few days. The patient has not used any treatment for this episode. Lesions on the body caused no pruritus, pain, discharge, or irritation. However, the patient had an active complaint of oral ulcers, causing an inability of oral intake due to pain and a burning sensation.

Examination of the oral mucosa revealed geographic tongue with linear white plaques and fissuring (Figure 1). Furthermore, on examination, there were scattered erythematous papules and plaques with a collarette of scale present on the palms (Figure 2), soles, and genital area. When checking for adenopathy, bilateral submandibular lymphadenopathy was observed.

Medical history revealed that the patient is a known case of type 1 diabetes mellitus, with no other reported comorbidities. On further history taking, the patient reported no prior surgical interventions and no significant family medical history. Regarding his sexual history, the patient stated that approximately one year ago he experienced similar symptoms, which resolved spontaneously without treatment following anal intercourse. He reports having multiple heterosexual partners and inconsistent use of barrier protection. He denies any history of sexual abuse.

Based on the previous clinical data a differential diagnosis was made with secondary syphilis on the top of the list along with Reiter's Syndrome, pustular psoriasis, and erthyema multiform major. To confirm the diagnosis a biopsy was taken from the left hand with blood and urine workup done as well.

Laboratory results show markedly elevated inflammatory markers, with a C-reactive protein level of 34.9 mg/L (reference range: <5 mg/L) and an erythrocyte sedimentation rate of 63 mm/h (reference range: 0-20 mm/h). *Treponema pallidum* antibodies were positive. The *Treponema pallidum* Hemagglutination Assay was reactive with a titer >1:2560 (reference range: <1:80). Rapid Plasma Reagin was also reactive with a titer >1:128 (reference range: non-reactive). Complete blood count revealed neutrophilia with neutrophils at 79% (reference range: 30-70%) and relative lymphopenia with lymphocytes at 17% (reference range: 23-60%). When looking into renal function tests, all items were within normal limits aside from creatinine 56 (reference range: 64-104 μmol/L) and CO_2 20.10 (reference range: 22-29 mmol/L). Hepatic function test on the other hand were all non-significant apart from biliruben 28.80 (reference range: 3.40-20.50 μmol/L).

Coagulation profile revealed a prothrombin time of 16.1 seconds (reference range: 11.9-15.9 s) and a mildly elevated international normalized ratio of 1.18 (reference range: 0.87-1.16), while activated partial thromboplastin time remained within normal limits.
Virology showed herpes simplex virus IgG (types 1 and 2) antibodies positive at 30 (reference range: <0.9 index), while herpes simplex virus IgM (types 1 and 2) antibodies were negative. HIV serology was positive. QuantiFERON was negative, as were hepatitis B and hepatitis C tests.

Urine examination showed red blood cells at 1/high-power field (HPF; reference range: 0-10) and white blood cells at 3/HPF (reference range: 0-10). However, bacteria were present on the examination.
Skin biopsy showed vascular interface dermatitis, acanthosis, lymphocyte exocytosis with thinning of the rete ridges, perivascular and periadnexal inflammation, and neutrophils in the stratum corneum (Figures 3 and 4). Overall, the histologic features are consistent with secondary syphilis.

As a result of the history of the patient, clinical examination, laboratory workup, and skin biopsy, a diagnosis of secondary syphilis was established. Patient was given doxycycline 100 mg twice daily for 14 days and triamcinolone 0.1% paste, paracetamol 500 mg tablets, tacrolimus 0.1% ointment, magic wash (lidocaine, diphenhydramine, and aluminum hydroxide and magnesium hydroxide), and emollients.

While the Local Guidelines for Gonorrhea and Syphilis still recommend penicillin as the primary treatment for such cases, doxycycline stands as an acceptable alternative. Given the unavailability of penicillin, the patient received doxycycline.

The patient was referred to the infectious diseases clinic in which he was given trimethoprim/sulfamethoxazole and bictegravir/emtricitabine/tenofovir alafenamide.

Discussion

The economic, social, medical, and psychological burdens imposed by both syphilis and HIV on their patients are immense, and these burdens significantly affect their quality of life.[11] The coexistence of both infections can be even more devastating and debilitating for patients. As this phenomenon is becoming more prevalent, it is crucial to allocate additional time, effort, and consideration to address this issue effectively.

Syphilis testing, particularly in cases of HIV co-infection, remains a challenging area in need for improvement. Dark field microscopy, though desirable, is rarely accessible due to its unpracticality, and serological tests primarily rely on humoral immune responses, posing risks and concerns regarding interpretation.[10] In spite of the fact that rapid testing is an option, it is limited to treponemal antibodies and therefore does not differentiate between active and treated infections. There is still no Food and Drug Administration-approved rapid test combining both non-treponemal antibodies and treponemal antibodies.[12] The issue of inadequate testing arises even more in the context of individuals living with HIV. Researchers from Australia have further elaborated on this point by integrating opt-out syphilis serology into HIV monitoring tests. By doubling the frequency of testing from once to twice yearly, this modification resulted in a significant rise in the detection rate of early-stage syphilis cases, increasing from 21% to 85%.[13] As the case of HIV, practical, efficient, cheap, and available diagnostics could revolutionize the prevention and management of syphilis. Furthermore, healthcare providers may contribute to early detection and easier management through implementing opt-out testing methodology mainly when dermatological manifestations of immune suppression are present.

As one of the great mimickers and imitators, it is even more crucial to give extra attention to syphilis in HIV positive patients. The presentation of syphilis in HIV-positive patients is difficult to predict, as it can manifest with classic symptoms, as in our case, but may also present with atypical and unusual

features.[14] A number of case reports have shown ocular involvement of syphilis with decreased bilateral vision in HIV positive patients.[15] Other reports have demonstrated pulmonary affection of secondary syphilis with HIV co-infection.[16] Another article have reported a case of secondary syphilis presented as erthymia multiform in a homosexual HIV patient.[17] In general when discussing HIV patients it is possible to see multiple, larger or deeper ulcers with overlapping of primary and secondary syphilis.[18] Physicians should maintain an open mindset regarding the diverse presentations and systemic involvement of secondary syphilis, particularly among HIV-positive patients.

Although current guidelines recommend the standard treatment of early syphilis with a single intramuscular (IM) dose of benzathine penicillin G (BPG), and three weekly doses of 2.4 million units IM BPG for late latent syphilis regardless of HIV status, many clinicians question this approach.[19] The synergistic interaction between these two infections and the possible immunosuppression in such co-infected patients may prompt a reevaluation of current guidelines and treatment modalities.[20] Furthermore, there is an increased risk of progression to neurosyphilis, as well as a higher likelihood of developing asymptomatic neurosyphilis among HIV-positive patients. Therefore, this supports further reconsideration of syphilis treatment in HIV-positive individuals.[21]

Conclusions

Due to the massive impact the co-infection of syphilis and HIV has on affected individuals, it is crucial to allocate more time, effort, and resources to investigate this condition. Additionally, providing practical and efficient diagnostics and considering clinical rather than serological outcomes are essential to effectively treat and prevent syphilis. Furthermore, physicians should be aware of the various atypical presentations and the possibility of systemic involvement of syphilis among HIV-positive individuals. Lastly, further research is needed to evaluate and assess the existing guidelines for treatment of co-infected patients.

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Figure 1. Geographic tongue with linear white plaques and fissuring of the tongue.

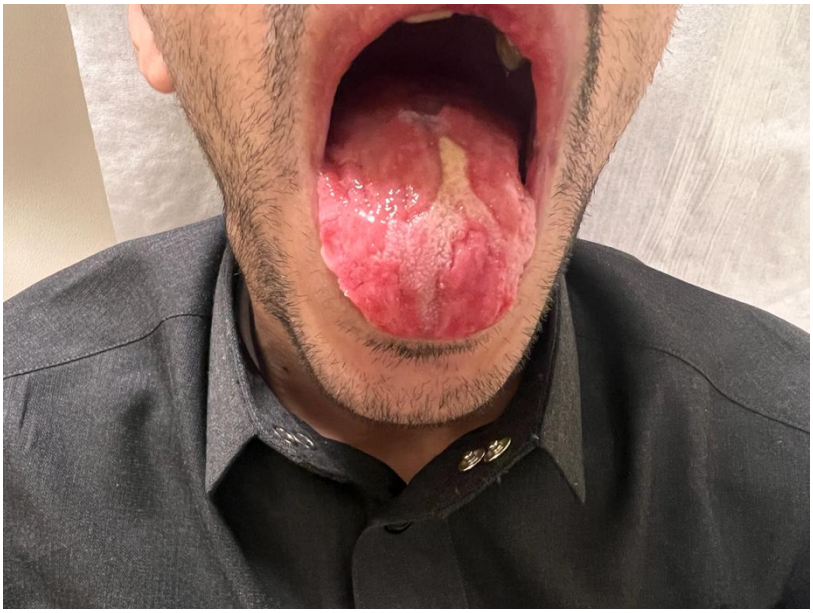

Figure 2. Scattered erythematous papules and plaques with collarette of scale present on the palms.

Figure 3. Vascular interface dermatitis, acanthosis, lymphocyte exocytosis with thinning of the rete ridges.

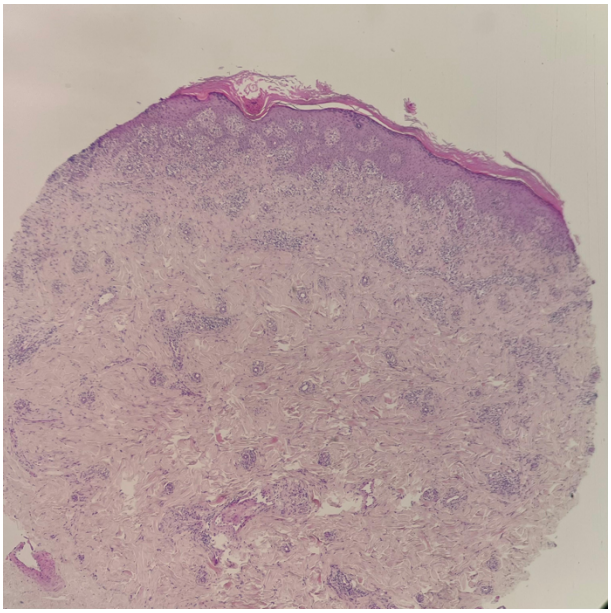

Figure 4. Perivascular and periadnexal inflammation and neutrophils in the stratum corneum.