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CASE REPORT

Atypical Clinical Manifestation of Secondary Syphilis in HIV patient

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Abstract

Syphilis is a sexually transmitted disease caused by *Treponema pallidum subsp. pallidum*, with a high incidence in patients living with HIV. HIV–syphilis coinfection may present with atypical cutaneous manifestations of secondary syphilis, including pustular, papulosquamous, photodistributed, nodular ulcerative (malignant syphilis), fungal-like, plaque-like, overlapping stages, and nodular forms. We report a case of a man with HIV diagnosed with secondary syphilis presenting with infiltrated erythematous-violaceous plaques. The differential diagnoses included leprosy, erythema nodosum, and cutaneous mastocytosis. Serology and skin biopsy confirmed the diagnosis. The patient received three weekly doses of benzathine penicillin, achieving complete resolution of the lesions after the first administration. At three months, serology showed a fourfold decline in rapid plasma reagin titers, confirming the therapeutic response. Subsequently, after antiretroviral therapy, the patient achieved viral suppression and immunological recovery. This case highlights the importance of recognizing the varied cutaneous manifestations of secondary syphilis in patients with HIV to guide timely diagnosis and adequate management.

Keywords: Cutaneous syphilis; HIV; Skin manifestations

Manifestación clínica atípica de sífilis secundaria en VIH

Resumen

La sífilis es una enfermedad de transmisión sexual causada por *Treponema pallidum subsp. pallidum*, con alta incidencia en pacientes con VIH. La coinfección VIH-sífilis puede presentar manifestaciones cutáneas atípicas en la sífilis secundaria, como formas pustulares, papuloescamosas, fotodistribuidas, úlceras nodulares (sífilis maligna), similares a micosis, en placas, con superposición de estadios o formas nodulares. Presentamos el caso de un hombre con VIH diagnosticado con sífilis secundaria y lesiones en placas eritemato violáceas infiltradas. Los diagnósticos diferenciales incluyeron lepra, eritema nodoso y mastocitosis cutánea. La serología y la biopsia confirmaron el diagnóstico. Se administraron tres dosis semanales de penicilina benzatina, con resolución completa de las lesiones tras la primera aplicación. A los tres meses, la serología mostró una disminución de cuatro diluciones, confirmando respuesta terapéutica. Posteriormente, con el inicio de la terapia antirretroviral, el paciente alcanzó supresión viral y recuperación inmunológica. Este caso resalta la importancia de reconocer manifestaciones cutáneas variadas de la sífilis secundaria en pacientes con VIH, para orientar un diagnóstico oportuno y un manejo adecuado.

Palabras clave: Sífilis cutánea; VIH; Manifestaciones cutáneas

Introduction

Syphilis is an infectious disease caused by *Treponema pallidum subspecies pallidum*, transmitted through sexual contact or vertical transmission during pregnancy[1]. The incidence of syphilis has increased, according to the World Health Organization (WHO), 7.1 million syphilis cases were reported globally in 2020. In the United States of America (USA), the Centers for Disease Control and Prevention (CDC) reported 176,000 cases in 2021[2], while in Colombia, 185,954 people were living with HIV in 2023, of whom 27% had a positive nontreponemal test result[3].

Syphilis is characterized by a wide spectrum of clinical manifestations, earning the name of "the great imitator." Both classic and atypical lesions have been described during secondary syphilis, and even more in the context of HIV co-infection[4–6]. Reported clinical variants include annular, pustular, frambesiform, papulosquamous, photodistributed, nodular ulcerative (malignant syphilis), fungal-like, plaque-like, overlapping stages, and nodular forms[4]. The cellular mechanisms underlying these manifestations remain unclear. Regarding the latent stage, its classification into early and late differs according to international guidelines: while American guidelines define early latency as infection of less than one year, the

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WHO extends this period up to two years. This discrepancy derives from the Oslo studies demonstrating that most recrudescences of secondary syphilis occur within the first year. Late syphilis, including latency beyond these cutoffs and tertiary disease, carries a low risk of transmission[1].

Previous case reports have described atypical cutaneous manifestations of secondary syphilis in people with HIV, such as necrotic and ulcerative lesions with extensive involvement of the face, scalp, and trunk[5], and palmoplantar psoriasiform plaques mimicking psoriasis[6]. Although these reports illustrate the broad clinical spectrum of secondary syphilis, their morphological features differ substantially from the infiltrated erythematous-violaceous plaques observed in our patient. Similar cases remain scarce, underscoring the clinical relevance of the present report.

Case Description

A 41-year-old man, diagnosed with HIV infection 24 days prior in the context of wasting syndrome, presented with a 2.5-month history characterized by erythematous-violet plaques, non-pruritic and non-scaling, of varying sizes, with infiltrated, edematous, well-defined borders, distributed throughout the body, predominantly on the chest and face (Figure 1A). He had not initiated antiretroviral therapy until the day of admission, when a regimen of tenofovir disoproxil fumarate/emtricitabine plus dolutegravir was started. On physical examination, the patient weighed 48 kg, with a height of 161 cm (BMI: 18.5 kg/m^2), showed no palpable lymphadenopathy, no mucosal lesions, no hepatosplenomegaly, no sensory involvement, and no signs of peripheral neuritis. He denied other significant medical history.

This led to suspicion of Hansen`s disease, secondary syphilis, and erythema nodosum. Admission lab tests revealed a plasma HIV-1 RNA level of 196,000 copies/mL with a CD4 T-cell count of 119 cells/µL, and the rapid plasma reagin (RPR) test was reactive at a titer of 1:128. A dermatology consultation suspected erythema nodosum, leprosy, cutaneous mastocytosis, and secondary syphilis, recommending a skin biopsy. The results described a moderate mixed inflammatory infiltrate perivascular and perianexial, predominantly lymphoplasmocytic.

Laboratory testing at admission revealed a CD8 and CD3 T-cell counts of 1,037 cells/µL and 1,267 cells/µL, resulting in a CD4/CD8 ratio of 0.12. Hepatitis B surface antigen, core antibody, and surface antibody were all absent, whereas antibodies against the hepatitis A virus were detected. Screening for hepatitis C antibodies was negative. The tuberculin skin test (PPD) was non-reactive, and three consecutive sputum bacilloscopies were negative for acid-fast bacilli.

Analyzing the results and due to the unknown duration of the syphilis, accompanied by unfulfilled or unclear diagnostic criteria for secondary syphilis (mucocutaneous palmar or plantar rashes, patchy alopecia, generalized lymphadenopathy, and malaise), and no prior treatment, the patient was administered three doses of benzathine penicillin G (2,400,000 IU) weekly for three weeks. After the first dose, the skin lesions resolved completely, as shown in Figure 1B. Three months later, a post-treatment follow-up showed a reactive RPR at 4 dilutions, confirming successful treatment. After five months of antiretroviral therapy, the patient achieved viral suppression and immunological recovery (CD4 T lymphocytes: 415 cells/µL - 12.03%). However, secondary syphilis diagnosis with atypical cutaneous manifestations was considered, taking into account the complete case presentation and giving importance to the present report.

Discussion

Secondary syphilis is characterized by the appearance of hyperchromatic and maculopapular skin lesions. These lesions primarily affect the palmar regions and soles of the feet or the dorsal region and do not cause pruritus. These lesions can last within a range of a few days to eight weeks, and by the time they may evolve into protuberances and pustular lesions or simply resolve on their own[1]. Highly contagious mucosal lesions, called mucous plaques, can also appear. In the mouth, especially on the tongue, areas devoid of papillae may appear, known as "mown lawn tongue," and on the scalp, areas of baldness, referred to as patchy alopecia, may occur. Çakmak and colleagues agree that secondary syphilis is known as the "great imitator" because it presents with any morphology and distribution of cutaneous lesions, including macular, plaque-like, papulonodular, pustular, annular, lichen planus-like, ulcerative, and nodular lesions that resemble tinea[4]. These forms can be more frequent in patients living with HIV[7].

In the present case, this could be considered secondary syphilis with a cutaneous manifestation in the form of atypical infiltrated plaques. Lesions in patients show T lymphocytes and dendritic cells with high expression of CCR5 and DC-SIGN, respectively, which explains a greater association with HIV co-infection[8]. These clinical differences may also be influenced by variations in the virulence of *Treponema pallidum* strains, in addition to host immune factors. Moreover, patients with secondary syphilis have shown alterations in the immunophenotype of monocytes, natural killer cells, and dendritic cells, especially the appearance of a subset of CD56-negative and high CD16 NK cells, which are known to be highly dysfunctional in patients with uncontrolled chronic viral infections[8].

The standard treatment for secondary syphilis is a single intramuscular dose of benzathine penicillin G (2.4 million units), as recommended by the CDC[2]. However, when the

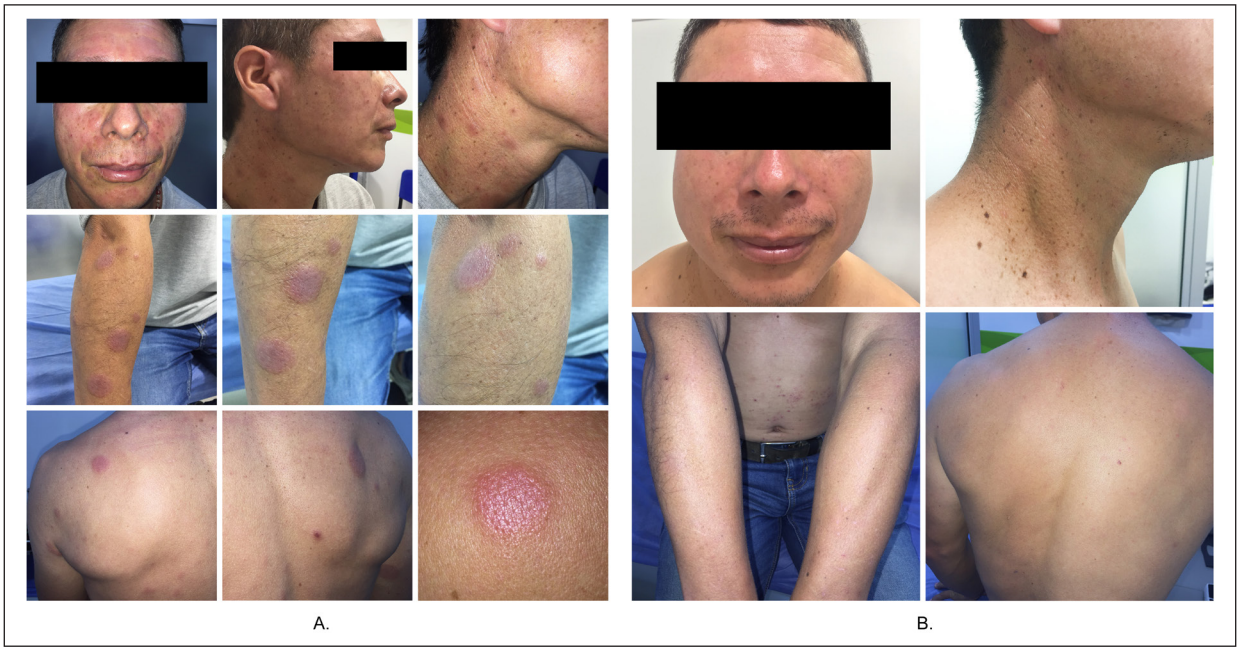

Figure 1. A. Plaque and nodular lesions observed upon patient's admission. B. Resolution of skin lesions after one week of treatment.

duration of the infection cannot be reliably established, the same guidelines recommend an extended regimen of three weekly doses (2.4 million units each). In this case, the clinical manifestations were not entirely consistent with secondary syphilis, but it didn't rule out the disease as a potential differential diagnosis, so we decided to administer three weekly doses of benzathine penicillin G to the patient, considering that the time of infection remained uncertain.

In the differential diagnoses, leprosy was considered because of the presence of erythematous plaque lesions with infiltrated, defined borders[9]; however, there was no sensory loss or neurological involvement. In addition, leprosy has been reported to cause positive results in nontreponemal tests[10]. Another differential diagnosis was erythema nodosum, which was considered because of the presence of nonulcerated bilateral symmetrical manifestations with preserved sensitivity in the patient, although its presentation is characterized by panniculitis with marked erythema, hyperthermia, and primarily pretibial involvement[11], rather than erythematous-violaceous plaques, as seen in the patient. Finally, with respect to cutaneous mastocytosis, it did not meet the criteria to be considered a differential diagnosis, as it is not a recurrent clinical condition, the patient did not belong to the typical age group for this pathology, and there were no clinical findings such as characteristic thickened skin or edematous "orange-peel" skin, associated pruritus, positive Darier's sign, and dermographism[12].

In addition to the aforementioned infectious diseases, cutaneous T-cell lymphomas must be considered, particularly mycosis fungoides, which is the most common subtype. In its plaque stage, this neoplasm may present with well-demarcated erythematous or violaceous infiltrated lesions that can clinically mimic the plaques observed in our patient. However, unlike secondary syphilis, these lesions usually follow a chronic and progressive course without rapid resolution after treatment initiation. Moreover, histopathology of cutaneous lymphomas reveals an atypical lymphocytic infiltrate, whereas in the present case, the findings corresponded to an inflammatory infiltrate, together with reactive serology for syphilis and a favorable response to penicillin, which allowed us to rule out cutaneous lymphoma as the cause of the lesions.

This report has some limitations. First, it describes a single case, which limits the generalizability of the findings. Second, no molecular confirmation of *Treponema pallidum* was performed, and no histopathological image of the biopsy specimen was available for illustration. In conclusion, non-recurrent plaque lesions should be considered in the clinical findings for secondary syphilis with an atypical presentation, particularly in populations living with HIV. A thorough physical examination can make the difference when carrying out clinical management and optimizing resources.

Ethical considerations

Protection of persons. The authors state that no experiments on humans or animals were performed for this case report.

Protection of vulnerable populations. This study does not involve vulnerable populations such as children, people with physical or intellectual disabilities, socially or economically vulnerable people, or institutionalized people.

Confidentiality. The authors declare that this article contains no data that would allow the patient to be identified.

Privacy. The authors have obtained informed consent from the patient mentioned in the article. This document is held by the corresponding author.

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