CASE REPORTS

Malignant Syphilis in an HIV-Infected Patient

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Abstract. Patients with HIV infection may develop common diseases with atypical clinical features. HIV infection may change the classic clinical course of syphilis and increase the incidence of a subtype of secondary syphilis named malignant syphilis.

A homosexual patient with HIV infection consulted us about a one-month history of general malaise and widespread cutaneous ulcerative lesions, some with thick hemorrhagic crusts. Serology for syphilis was positive at high titers. Based on clinical, histological and serological findings, a diagnosis of malignant syphilis was made and the patient started treatment with penicillin G benzathine with progressive resolution of lesions. Malignant syphilis is a rare subtype of secondary syphilis that presents special clinical and histological features and has been associated with several processes characterized by variable degrees of immunosuppression. It is necessary to take into account this entity among the possible diagnoses in HIV-infected patients with cutaneous lesions.

Key words: Syphilis, Lues, HIV, Malignant syphilis.

SÍFILIS MALIGNA EN UN PACIENTE CON INFECCIÓN POR EL VIH

Resumen. Los pacientes con infección por el virus de la inmunodeficiencia humana (VIH) pueden desarrollar enfermedades comunes con manifestaciones clínicas atípicas. La infección por el VIH puede alterar el curso clínico clásico de la sífilis y aumentar la frecuencia de aparición de un subtipo de sífilis secundaria denominado sífilis maligna. Un paciente homosexual con infección por el VIH consultó por un cuadro de un mes de evolución de afectación del estado general y lesiones cutáneas ulceradas generalizadas, algunas con gruesas costras hemáticas. La serología para lúes resultó positiva a títulos altos. En base a los hallazgos clínicos, histopatológicos y serológicos se estableció el diagnóstico de sífilis maligna y se inició tratamiento con penicilina G-benzatina, con resolución progresiva del cuadro.

La sífilis maligna es un infrecuente subtipo de sífilis secundaria que presenta peculiaridades clínicas e histopatológicas y se ha relacionado con diversos procesos que cursan con grados variables de inmunodepresión. Es necesario tener en cuenta esta entidad entre los posibles diagnósticos en los pacientes con infección por el VIH que presenten lesiones cutáneas.

Palabras clave: sífilis, lúes, VIH, sífilis maligna.

Introduction

The clinical manifestations of several diseases can take on atypical features in immunodepressed patients. Coinfection by the human immunodeficiency virus (HIV) and syphilis is a common and dangerous combination with important clinical consequences. Syphilis increases the risk of transmitting HIV and HIV can alter the classic course of syphilis. HIV-infected patients suffer from a secondary form of syphilis known as malignant syphilis—characterized mainly by its clinical presentation—more often than the general population. We report the case of an HIV-infected patient who developed malignant syphilis and describe the main features of this entity.

Case Report

A 30-year-old homosexual man who was diagnosed with HIV in 2003 and who had no current substance use presented with a 1-month history of general malaise, myalgia, and fever of up to 39.5ºC accompanied by the gradual appearance of lesions on the trunk, limbs, face, scalp, and genitals. Some of the lesions were painful. He

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Figure 1. Multiple lesions on the back.

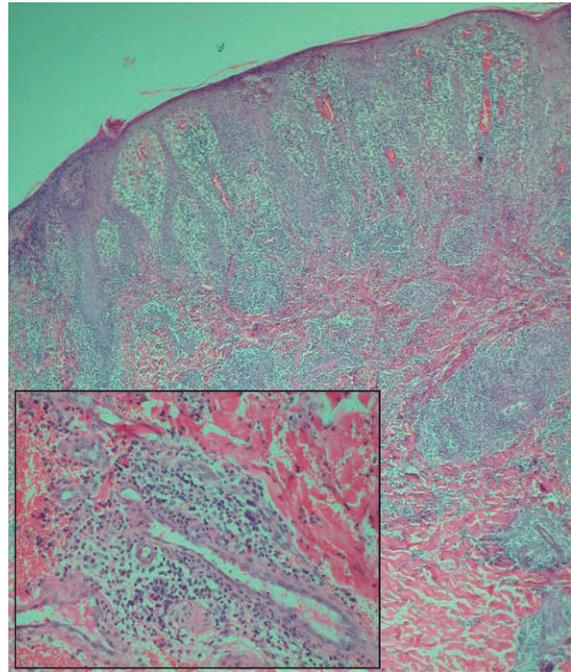**Figure 2.** Round lesion covered by a thick reddish scaly crust.

Figure 3. Dense inflammatory infiltrate in the upper dermis, mainly around the dermal vessels (hematoxylin-eosin, ×100). The box on the left shows swelling of the endothelia of the dermal vessels and a detail of the infiltrate, which is composed mainly of lymphocytes and plasma cells (hematoxylin-eosin, ×200).

did not complain of mucosal symptoms and did not recall previously having had lesions in the anal or genital regions. The main feature of the initial skin examination was the presence of multiple round lesions of different sizes on the back and front of the trunk (Figure 1), limbs, face, scalp, and genitals. Many had an ulcerous core covered by a thick raised reddish crust (Figure 2) with a peripheral inflammatory erythematous halo. Erythematous papular lesions could be seen on his neck—these were round and clearly delimited with a scaly collarette. Isolated erythematous papules measuring less than 0.5 cm were present on the patient's palms and soles. These were slightly infiltrated and not scaly. No lesions were observed on the mucosa.

Given the patient's general condition and history of HIV infection, he was admitted for further assessment and the only notable feature of the general physical examination was the presence of small bilateral enlarged inguinal lymph nodes that were neither adherent nor painful. The laboratory workup carried out on admission only revealed increased systemic inflammatory response parameters (erythrocyte sedimentation rate, C-reactive protein). Complete blood count, coagulation study, and urinalysis were normal. Studies to identify parasites in stool and acid-fast bacilli in sputum were negative. Stool culture revealed normal flora. The patient was seropositive for immunoglobulin G against rubeola, measles, herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, and parvovirus B19, but seronegative for hepatotropic viruses (hepatitis C virus and hepatitis B virus). Serology for syphilis was positive with high titers (positive rapid plasma reagin test, venereal disease research laboratory test 1/128, *Treponema pallidum* hemagglutination test 1/5120). The patient was seronegative for syphilis 1 month before admission, revealing a notably rapid and intense seroconversion. The last determination of viral load and CD4 count, carried out 2 weeks before admission, showed 750 000 copies/mL and 228 cells/μL, respectively.

Biochemistry and cytology of cerebrospinal fluid (CSF) were negative and the CSF was negative for syphilis.

Histology of an abdominal skin lesion revealed the presence of epidermal necrosis with irregular acanthosis and a marked inflammatory infiltrate in the upper dermis, mainly around the dermal vessels and composed of lymphocytes and abundant plasma cells (Figure 3). The dermal vessels showed prominent endothelia, and in some

cases the lumen was occluded by eosinophilic material. No granulomatous infiltrates or signs of vasculitis were observed. Warthin-Starry staining did not reveal spirochetes. Immunohistochemistry showed that the lymphocytes were almost all B cells.

Based on clinical, histological, and laboratory findings, the patient was diagnosed with malignant syphilis. Treatment was started with intramuscular penicillin G benzathine at 2.4 million units per week for 3 weeks, preceded by 20 mg oral prednisone; nevertheless, the patient developed a Jarisch-Herxheimer reaction.

The lesions and systemic symptoms improved quickly when treatment was started, although some hyperpigmented scars remained.

After discharge, the patient was referred to the infectious diseases section of our internal medicine department to begin antiretroviral therapy.

Serology testing a few months later revealed a return to negative values in the reactive tests and a marked fall in nontreponemal antibody titers (1/160).

Discussion

HIV infection and syphilis are sexually transmitted diseases with complex interactions and both are major public health problems, especially in the developing world.[1,2] In recent years, a considerable resurgence of syphilis has been observed, mainly as a result of sexual transmission between men.[2] This seems to be related for the most part to changes in the sexual behavior of some sectors of the population.[3,4]

Although most patients actually develop common clinical manifestations, it is currently accepted that HIV infection and immunodepression can alter the course of syphilis. Thus, HIV-infected patients experience more asymptomatic primary syphilis,[4] with the result that secondary manifestations are increasingly detected. Primary lesions can have an atypical presentation and secondary lesions can be more aggressive. In HIV-infected patients, ophthalmological involvement is more common in tertiary syphilis and neurosyphilis can present earlier[5]; therefore, in these cases lumbar puncture is necessary to evaluate syphilis serology in CSF and its characteristics, regardless of the patient's clinical status.[2]

In 1859, Bazin[6] was the first to use the term "malignant" to describe a subtype of secondary syphilis with peculiar clinical characteristics.

Malignant syphilis has been associated with several situations,[7] most of which involve varying degrees of immunodepression, including HIV and diabetes.[8] Even in the current resurgence of the disease, malignant syphilis is a very uncommon presentation.

Despite the fact that the possible involvement of more aggressive *T pallidum* serotypes has been posited,

immunodepression is currently considered to play a more important role in the pathogenesis.[9]

Romero Jiménez et al[10] reviewed 21 cases of malignant syphilis published in the literature until 2003 and observed that this form of syphilis presents mainly in young men, with a mean age of 34 years. The frequency of malignant syphilis was higher in HIV-infected patients than in the seronegative population.

In clinical terms, the condition is characterized by ulcerous skin lesions covered by thick crusts that can cause pruritus or pain and are usually accompanied by intense generalized disease (eye involvement, fever, enlarged lymph nodes, myalgia, etc). Lesions on the face and scalp are common, although the palms and soles of the feet are generally spared.[9,13]

Histology of the lesions usually reveals—as in our case—epidermal necrosis, dense dermal inflammatory infiltrate with predominant lymphocytes and plasma cells, and involvement of medium-caliber vessels with obliteration.[7,11] Detection of *T pallidum* in the lesions varies, although it seems to be less common in this form of secondary syphilis.[12] Our patient did not show definitive histopathologic signs of vasculitis, nor were granulomatous infiltrates present.

Serologic testing of malignant syphilis is normally strongly positive, although in HIV-infected patients unusual, even negative, results may be observed.[2,14]

Both the clinical findings and the marked seroconversion in such a short period (approximately 1 month) in our patient reveal an extremely aggressive and accelerated course of syphilis.

Treatment of syphilis in HIV-infected patients is the same as in seronegative patients,[2,15,16] although current recommendations for early secondary syphilis in the former group indicate a regimen of penicillin G benzathine similar to that used in late secondary syphilis (2.4 million units intramuscularly, once per week for 3 weeks).[17]

Our patient presented a significant degree of immunodepression (228 CD4/μL) and developed the characteristic manifestations of this type of secondary syphilis, with intense general involvement and generalized cutaneous lesions with thick scaly rupia crusts. The marked positive serology results, the histology findings, and the Jarisch-Herxheimer reactions observed for our patient are also common, although not characteristic of malignant syphilis.

In HIV-infected patients, the appearance of cutaneous lesions similar to those described in this case necessitates differential diagnosis with a variety of other entities, including toxicoderma, varicella, herpes simplex, herpes zoster, pityriasis lichenoides et varioliformis acuta, lymphomatoid papulosis, cryptococcosis, coccidioidomycosis, erythema multiforme, vasculitis, lymphomas, atypical mycobacteriosis, candidiasis, ecthyma, and ecthyma gangrenosum.[8,9,18,19]

Therefore, it is extremely important to consider the many presentations of syphilis—among them malignant syphilis—in the range of diagnostic possibilities in an HIV-infected patient who develops cutaneous lesions.

Conflicts of Interest
The authors declare no conflicts of interest.

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