Early malignant syphilis in an immunocompetent young man

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Abstract

Malignant syphilis, also known as lues maligna, is an atypical and aggressive form of secondary syphilis characterized by nodules and ulcers associated with a spectrum of nonspecific systemic manifestations. The underlying states of immunosuppression represent the primary risk factor. We present a 30-year-old immunocompetent man exhibiting dermatological lesions at various stages clinically and histologically consistent with the established criteria for malignant syphilis. He received antibiotic therapy with complete clearing. Furthermore, we emphasize the importance of proper interpretation of serological tests, both for diagnosis and systematic monitoring.

Keywords: malignant syphilis, immunocompetent, secondary syphilis

Introduction

Unusual or atypical forms of secondary syphilis have been described, including an aggressive nodulo-ulcerative variant described by Pierre Bazin in 1859, termed malignant syphilis, also known as lues maligna or rupioid syphilis. This form may present from 6 weeks to up to one year following initial manifestations of primary syphilis [1,2]. Most cases reported in the literature involve patients with HIV co-infection, considering that up to 7% meet criteria for this variant [3]. We present a young man who did not exhibit primary or secondary immunodeficiencies and presented with an early stage of malignant syphilis, based on clinical and histopathological findings.

Case Synopsis

A 30-year-old man was admitted to our hospital without known prior medical conditions. For the past four months, he had frequently consumed anabolic substances for aesthetic purposes without prescription, including methanolone enanthate, sustanon, and nandrolone. Throughout his life, he had engaged in high-risk sexual relationships without protective measures.

He presented with a cutaneous condition that had been evolving for two months. It began with the appearance of papules and nodules on the face and scalp, which then spread to the chest, abdomen, and limbs, with involvement of the palms and soles. Some of these lesions became ulcerated. He did not recall a primary lesion. Subsequently, he developed evening fevers and constitutional symptoms. He had

received minocycline antibiotic therapy without improvement. On admission, he exhibited dermatological lesions at various stages, including papules, crusted nodules, and some small psoriasiform plaques on the face (**Figure 1A**) as well as ulcero-necrotic papules, nodules, and plaques on the back (**Figure 1B**). There were no mucosal lesions. Cervical and retroauricular lymphadenopathy were noted.

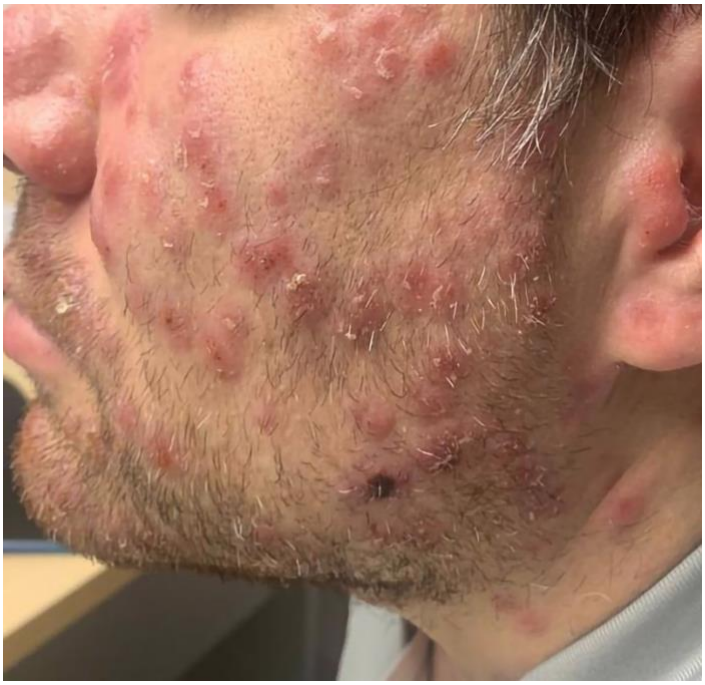

Figure 1A. *Skin examination at admission. Elevated erythematous, scaly and crusted papules, nodules and plaques.*

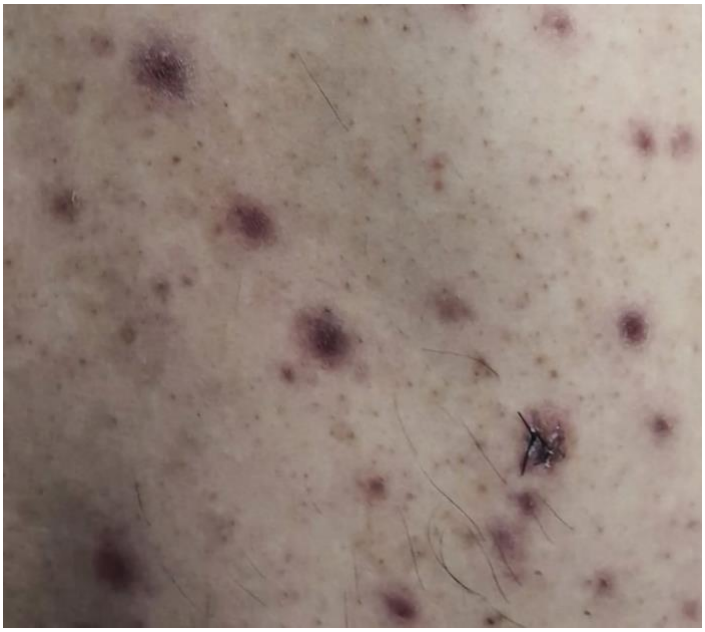

Figure 1B. *Ulcero-necrotic papules and nodules.*

Upon admission, an HIV test was requested using a fourth-generation, enzyme-linked immunosorbent assay, as well as a hepatitis B surface antigen test, both of which returned nonreactive results. A first qualitative Venereal Disease Research Laboratory (VDRL) test was requested, which also yielded a nonreactive result, from which no serial dilutions were performed. Additional laboratory tests showed elevated C-reactive protein levels at 85mg/l. Mpox was considered, and a polymerase chain reaction test was negative.

Histopathological examination of a skin biopsy revealed epidermal hyperplasia with a significant mononuclear lymphocytic and histiocytic infiltrate at the dermoepidermal junction (**Figure 2A**). Chronic perifolliculitis (**Figure 2B**) was noted, as well as vasculitis with vessel luminal obliteration, thickened endothelium, and perivascular infiltrate with a few plasma cells (**Figure 3**). Warthin-Starry staining did not identify spirochetes, possibly because of extensive inflammation and lack of silver staining. Other stains, such as periodic acid–Schiff and Ziehl-Neelsen, were negative.

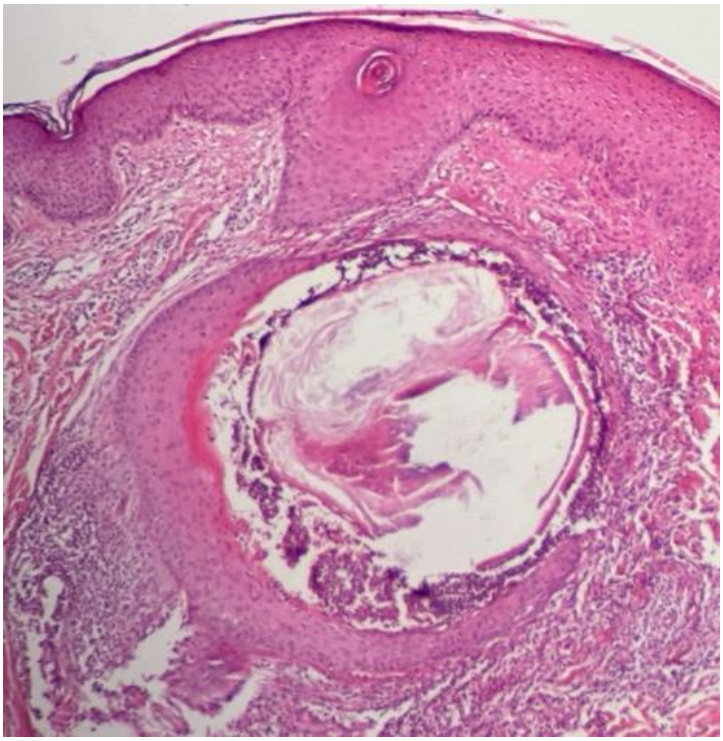

Figure 2A. *Skin biopsy stained with hematoxylin and eosin staining. Low-power view of skin biopsy showing epidermal hyperplasia, with abundant mononuclear infiltrate with lymphocytes and histiocytes at the dermoepidermal junction.*

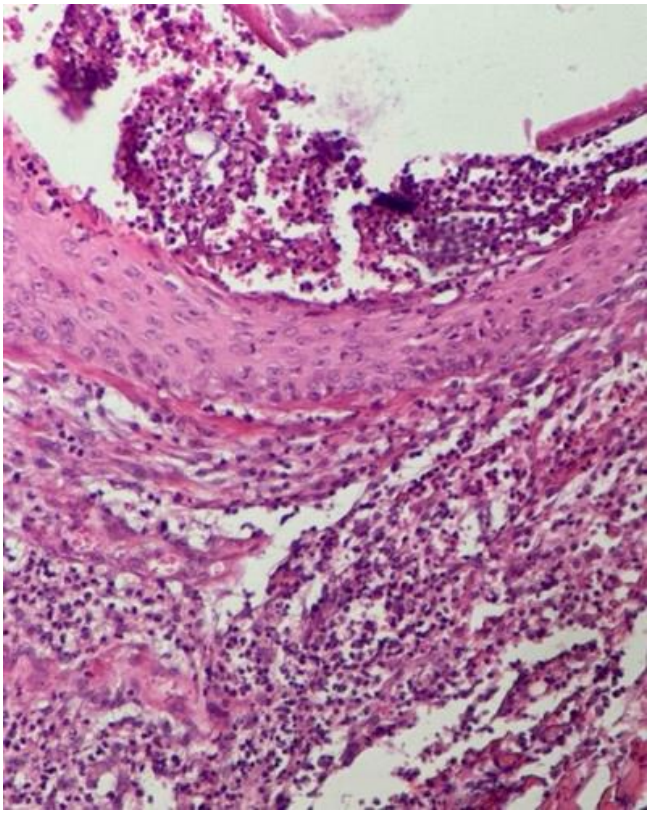

Figure 2B. *High-power perifolliculitis, showing extensive inflammatory infiltrate.*

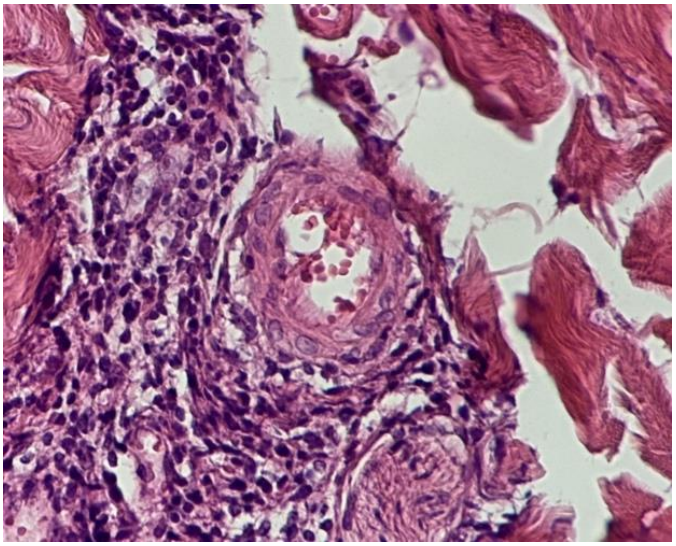

Figure 3. *Histopathological examination of skin. Hematoxylin and eosin staining. At higher magnification, it shows endothelial thickening and inflammatory infiltrate around the vessel with some plasmatic cells.*

Two weeks later, the patient presented with a new determination of VDRL from an external source, which was reactive at a titer of 1:64. Consequently, this test was repeated four days later at a state laboratory in our city, which reported reactive titers of 1:256. Additionally, a fluorescent treponemal antibody-absorption immunoglobin G serum test was requested, which returned positive results. The HIV test was repeated and remained nonreactive. Based on clinical, histopathological, and laboratory findings, a diagnosis of malignant syphilis was established and treatment for secondary syphilis was initiated with a single dose of intramuscular benzathine penicillin G (2.4 million units). There was no Jarisch-Herxheimer reaction. The patient showed rapid and complete resolution of lesions on follow-up and a decrease in VDRL titers at three and 6 months, with a value of 1:16 and 1:4, respectively.

Case Discussion

The spirochete bacterium Treponema pallidum subspecies pallidum is responsible for syphilis, transmitted sexually and vertically. The disease course is traditionally described in four stages: primary, secondary, latent, and tertiary per World Health Organization criteria, with the first three considered under the name "early syphilis" as an infection lasting less than one year. The US Center for Disease Control classifies latent syphilis of less than one year as early latent syphilis. Over one year, this is termed late latent or latent of unknown duration (if no symptoms/signs) or late syphilis [4]. Owing to its broad manifestations and its ability to evade the immune response, it is also known as the great imitator [1,5]. The global burden of syphilis infection is high, estimated at around 10.6 million cases annually [6]. Secondary syphilis is considered the most florid stage of the disease. There are atypical forms, among which is malignant syphilis, an unusual nodulo-ulcerative type. Other reported atypical forms include micropapular, follicular, vesicular, corimbiform, framboesiform, and psoriasiform [1,6].

The exact incidence of malignant syphilis is not known since it is a rare condition. In 1990, Held described the first case in 50 years of an immunocompetent woman who presented with this entity. In a retrospective study analyzing 322 syphilis cases over a four-year period, malignant syphilis

comprised only 1.2% of them. Most cases are reported in patients living with HIV, suggesting a possible interaction between the virus and Treponema pallidum that favors its presentation. In our case, the patient had a significant history of high-risk sexual encounters; however, no secondary immunocompromised state was identified, as evidenced by negative serology for HIV (fourth-generation, enzyme-linked immunosorbent assay) and hepatitis viruses. He also did not have other risk factors such as chronic alcoholism, malnutrition, or diabetes mellitus. However, no determination of complement or immunoglobulin levels was performed to search for a primary immunodeficiency state [2,7,8].

Among the dermatological manifestations of malignant syphilis, disseminated papules are initially described, followed by painful ulcero-necrotic, crusty plaques, predominantly on the trunk and extremities, which may appear similar to lesions in the tertiary stage. Our patient presented with lesions at different stages, localized in these sites, as well as on the face and scalp, without mucosal involvement. Our patient did not recall a primary dermatological lesion such as a chancre. Our patient experienced nonspecific symptoms such as fever, malaise, and lymphadenopathy, almost concurrently with the cutaneous lesions, which are reported as part of a prodromal phase that includes gastrointestinal manifestations and organomegaly [2,9]. To establish the diagnosis of malignant syphilis, the Fisher criteria have been proposed, which include 1) lesions that are clinically and histopathologically compatible, 2) elevated VDRL values, 3) the presence of Jarisch-Herxheimer reaction after starting penicillin treatment, and 4) rapid response to treatment. Our patient exhibited three criteria. It is relevant to note that the nontreponemal VDRL test was negative initially and became positive after two weeks with a titer of 1:64; this can be explained since this test can become positive within the first three months after infection [1,8]. One must also consider the prozone phenomenon, which refers to a false negative result when there is a large amount of circulating antibodies against T. pallidum. To avoid this, it is recommended to perform complementary serial dilutions in all cases [10].

The findings presented in our patient's histopathology are consistent with those described in the literature, such as an abundant mononuclear infiltrate with plasma cells and chronic vasculitis phenomena. In addition, pseudoepithelial hyperplasia with a paucity of spirochetes is very common. The Warthin-Starry staining, in this case, did not show the presence of spirochetes, which could relate to the extensive inflammatory infiltrate [9]. In the differential diagnosis of malignant syphilis, cutaneous T-cell lymphoma and other entities such as mycosis fungoides and lichen planus are included. It is important to highlight the relationship with other complications such as neurosyphilis and ocular syphilis that occur at any stage of syphilis and in patients with immunodeficiencies [4, 9,11]. Our patient showed no signs or symptoms of these and also exhibited full resolution of his malignant syphilis with directed treatment and continued to be periodically monitored in consultation.

Conclusion

Malignant syphilis, or lues maligna, is a rare and severe form of secondary syphilis, with few reported cases. It is mainly related to various underlying states of immunocompromise including HIV. Our case highlights the importance of early identification of this variant in patients with *Treponema pallidum* infection, even when they are immunocompetent, which requires a thorough medical history and complete physical examination, as well as proper interpretation of serological tests and histopathological findings.

Potential conflicts of interest

The authors declare no conflicts of interest.

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