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Journal

Dermatology Online Journal, 28(5)

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Publication Date

2022

DOI

10.5070/D328559250

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A rare case of lues maligna in an HIV-negative woman

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Abstract

We describe an HIV-negative 43-year-old woman presenting with a diffuse ulceronodular eruption and positive serological tests for syphilis consistent with lues maligna. Lues maligna is a severe and rare variant of secondary syphilis characterized by prodromal constitutional symptoms followed by the formation of multiple well-circumscribed nodules with ulceration and crust. This case depicts a particularly rare presentation as lues maligna usually involves HIV-positive men. The clinical presentation of lues maligna can pose a diagnostic challenge, with infections, sarcoidosis, and cutaneous lymphoma as just a few entities in its broad differential diagnosis. However, with a high index of suspicion, clinicians can diagnose and treat this entity earlier and reduce morbidity.

Keywords: HIV, lues maligna, malignant syphilis, ulceronodular

Introduction

Lues maligna, also termed malignant syphilis or ulceronodular syphilis, is a rare and severe form of secondary syphilis first described in 1859 [1]. Most reported cases involve an immunocompromised state, usually HIV, and/or men [2-5]. We present a rarer case of a woman presenting with lues maligna and found to be HIV-negative.

Case Synopsis

A 43-year-old woman with a history of type two diabetes mellitus, homelessness, schizophrenia, and

polysubstance dependence presented with a diffuse painful and pruritic eruption of one month duration. Although she was not taking any medications for her diabetes, her hemoglobin A1C was within normal limits. A review of systems was negative for systemic symptoms. Physical examination revealed diffuse well-circumscribed erythematous nodules and plaques of varying sizes; some exhibited rolled borders, ulceration, and superficial crusting (**Figure 1**). Lesions involved the face, neck, chest, abdomen, back, and all extremities, sparing the palms and soles. Palpable inguinal lymphadenopathy was also present.

The rapid plasma reagin (RPR) titer was 1:128, and the treponemal immunoglobulin G antibody test was positive. Human immunodeficiency virus (HIV) antigen and antibodies were negative. A skin biopsy revealed epidermal acanthosis with a diffuse dermal infiltrate comprised of plasma cells (**Figure 2A**). Immunohistochemistry for *Treponema pallidum* showed abundant spirochetes within the epidermis

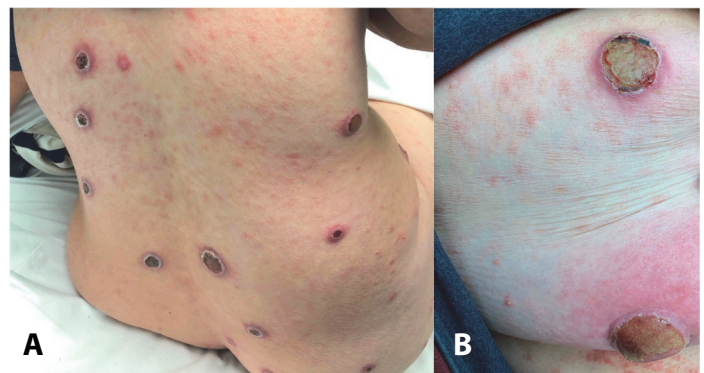


Figure 1. A) Numerous well-circumscribed erythematous flat nodules and plaques of varying sizes exhibiting rolled borders, ulceration, and crust. **B)** Primary morphology of individual lesions showed a well-defined plaque with rolled borders and central erosion.

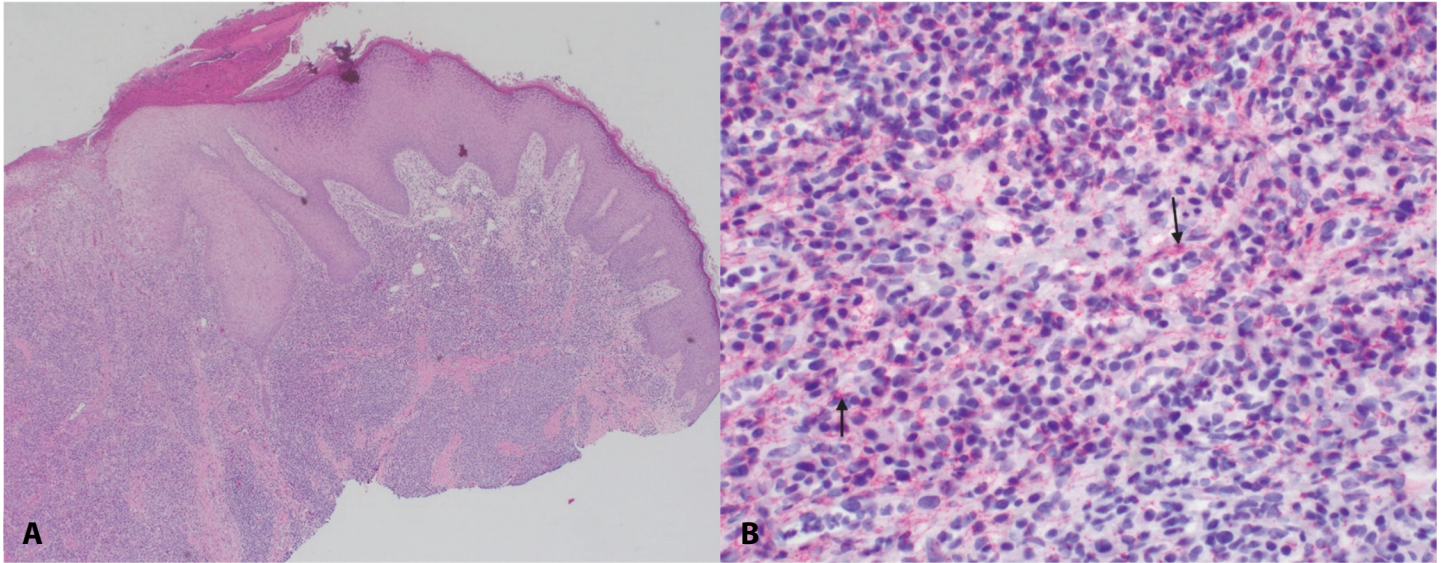


Figure 2. Pathology images of biopsied abdominal lesion. **A)** Low power magnification reveals epidermal acanthosis with a diffuse dermal inflammatory infiltrate comprised of numerous plasma cells. H&E, 4 \times . **B)** Higher power magnification with immunohistochemistry for *Treponema pallidum* shows abundant spirochetes stained red (arrows) within the dermis, consistent with a diagnosis of syphilis. H&E, 40 \times .

and dermis. Gram, acid-fast bacillus, and Periodic acid–Schiff stains were negative (**Figure 2B**). A diagnosis of syphilis, specifically lues maligna, was made. The patient was given 2.4 million units of penicillin G benzathine intramuscularly and demonstrated an RPR titer of 1:32 two weeks later. However, clinical improvement of the rash could not be fully assessed as the patient was subsequently lost to follow-up. Subsequent emergency department visits noted absence of rash and continued HIV-negative status one year after presentation.

Case Discussion

Clinicians should be aware of this atypical presentation of this common entity. As opposed to the papulosquamous eruption of typical secondary syphilis, lues maligna presents as multiple well-circumscribed papules, papulopustules, or nodules with ulceration and a lamellar or rupioid crust on the trunk and extremities [2]. The skin lesions may be preceded by weeks-to-months of constitutional symptoms such as fevers, arthralgias, and weight loss, although this was not seen in our patient. This clinical presentation can pose a diagnostic challenge, with bacterial, fungal, and mycobacterial infections, as well as sarcoidosis, pityriasis

lichenoides, leukemia cutis, and cutaneous lymphoma among the potential diagnoses [2,6]. Fisher et al. proposed the following criteria to make the diagnosis of lues maligna: congruent gross and microscopic characteristics, positive syphilis serologies, the Jarisch-Herxheimer reaction, and responsive to antibiotic treatment [7]. The Jarisch-Herxheimer reaction is a self-resolving febrile reaction that occurs within the first 24 hours of treatment of spirochetal infections, such as syphilis [8]. Our patient exhibited all of Fisher et al.'s criteria except the Jarisch-Herxheimer reaction, similarly seen in other reported cases [2,9].

The typical histopathological features of syphilis include dermal plasma cell infiltrate and perivascular infiltrate. Vessel obstruction with histologic features of vasculitis may be seen as well [7]. Interestingly, *Treponema pallidum* organisms are commonly not visualized by silver stains in lues maligna biopsies, but immunohistochemistry has increased sensitivity and specificity [2,9]. Since microscopy of lesions commonly reveal nonspecific findings and often have an absence of organisms with staining, clinical pathologic correlation paired with a low threshold for serologic testing for syphilis is key to prompt diagnosis and management [6]. As seen in our workup, additional histological stains should be used to rule out other infectious etiologies. Clinicians

should also be aware of potential false-negative RPR results related to high antibody titers that prevent proper antigen-antibody complex formation and visualization [10]. This reaction is known as the prozone phenomenon and may be seen especially in lues maligna patients as they can have markedly high antibody titers [11]. If suspected, clinicians may request the dilution of the specimen to obtain more accurate results.

A review by Sands et al. identified only 14 reported cases of lues maligna prior to 1988 [12]. These were commonly associated with alcoholism, diabetes mellitus, and malnourishment, like our patient [4]. An otherwise healthy woman presenting with lues maligna is exceedingly rare and had not been reported in 50 years prior to Held et al.'s report in 1990 [13]. Of note, our patient may have been more susceptible to syphilis owing to her diabetes, which has been shown to increase risk of infection through dysregulating the immune system [14]. Lues maligna has become more common following the HIV epidemic, though it is still rare. HIV-positive patients are 60 times more likely to develop lues maligna and conversely, lues maligna may also represent the initial manifestation of HIV [2]. With this strong association in mind, HIV status should be tested in all patients with lues maligna.

Fortunately, lues maligna responds well to multiple penicillin regimens with complete resolution of

lesions and minimal-to-no scarring [9]. Before treatment, clinicians should caution the patient of the self-limited Jarisch-Herxheimer reaction. Along with fever, this reaction may be associated with worsening of the rash or other systemic symptoms such as chills, headache, and myalgias. Also, HIV-positive patients should continue anti-retroviral therapy during treatment [15]. Response should be monitored with regular clinical examinations and down-trending RPR titers [2]. A repeat HIV test may be warranted for HIV-negative patients with lues maligna that fail to respond to treatment.

Conclusion

Herein, we report a rare case of lues maligna in an HIV-negative woman. Clinicians should always consider lues maligna in a patient with HIV or risk factors for HIV presenting with ulcerated nodules. Clinical pathological correlation and serologic tests for syphilis are key to early diagnosis and treatment to reduce patient morbidity. Lastly, it is imperative to test for HIV infection in all lues maligna patients if it has not already been diagnosed.

Potential conflicts of interest

The authors declare no conflicts of interest.

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