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Case Report

Syphilitic Unorthodoxy: A Case of Lues Maligna in a Human Immunodeficiency Virus-negative 28-year-old Filipino Male

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Abstract

Lues maligna, also known as malignant syphilis, is an uncommon variant of syphilis at the secondary stage – more commonly reported in immunocompromised patients or those with concomitant human immunodeficiency virus (HIV) infection. In this report, we present a case of a 28-year-old HIV-negative male with a 9-month history of multiple, well-defined, irregularly-shaped, erythematous papules, and small plaques evolving to ulcerated plaques and nodules with crusts, associated with pain, pruritus, and episodes of fever, arthralgia, and weight loss. Positive treponemal and nontreponemal tests, aided by histopathologic findings consistent with syphilis led to the diagnosis of lues maligna. Significant improvement of lesions was noted with 3 weekly doses of 2.4 million units of benzathine penicillin G. For patients presenting with painful and pruritic erythematous ulcerated plaques with crusts associated with systemic symptoms, and with a significant sexual history despite testing negative for HIV infection, a high index of suspicion for uncommon presentations of other sexually transmitted infections such as syphilis could aid in early diagnosis and subsequent treatment.

Keywords: Human immunodeficiency virus-negative, lues maligna, malignant syphilis, secondary syphilis

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Introduction

Syphilis is a sexually transmitted infection that occurs in several stages, each presenting with recognizable mucocutaneous manifestations. However, there is a variant with particular rarity, making diagnosis a challenge for dermatologists.

Lues maligna, also known as malignant syphilis or ulceronodular syphilis, is an uncommon variant of the disease at the secondary stage. This is a rare, aggressive form that accounts for 1.2% of all patients diagnosed with syphilis, more commonly reported in immunocompromised patients or those with concomitant human immunodeficiency virus (HIV) infection.[1] In this report, we present a case of lues maligna in a 28-year-old HIV-negative male.

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Case Report

A 28-year-old Filipino male presented with a 9-month history of multiple, well-defined, irregularly shaped, erythematous papules and small plaques evolving to

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ulcerated plaques and nodules with crusts, associated with pain, pruritus, and episodes of fever (maximum temperature of 38.7°C), arthralgia, and weight loss. The patient was a heavy alcoholic beverage drinker and had a significant sexual history of more than 10 lifetime partners. He was also classified in a high-risk population (men having sex with men). Previous consults with an internist and a dermatologist were done wherein the patient was managed as a case of immunocompromised host with reactive arthritis. He was given prednisone 20 mg/day, sulfasalazine 50 mg/tablet twice a day, and a calcium supplement for 1 week. A concomitant deep fungal infection was also considered, for which he was given itraconazole 100 mg/capsule twice a day for 1 week for two cycles, clindamycin 300 mg/cap every 6 h for 10 days, and unrecalled topical medications with good compliance. However, the patient only noted minimal improvement in addition to the continued development of new lesions. At the presentation, the patient was weak-looking and was unable to stand for anthropometrics. Cutaneous physical examination showed the above-described cutaneous findings on the face, trunk, and all extremities, sparing the palms and soles. Multiple erythematous erosions on the palate were also present [Figure 1].

On laboratory work-up, the rapid plasma reagin (RPR) quantitative test was reactive at a 1:4 dilution and treponema pallidum enzyme immunoassay test was also reactive. HIV antigen test, which was done twice (1 month and 3 months after the patient's last sexual contact), tested negative. Skin punch biopsy revealed epidermal orthokeratosis and dermal lichenoid and nodular granulomatous inflammatory mixed-cell infiltrates of lymphocytes, histiocytes, neutrophils, and numerous plasma cells with extravasated erythrocytes [Figure 2]. Clinicopathologic findings were consistent with secondary syphilis, specifically lues maligna. The patient was given 2.4 million units of benzathine penicillin G intramuscularly for three doses at weekly intervals and supportive treatment with plain normal saline solution compress, facilitating the healing of lesions. After 2 weeks of admission, the patient was discharged with partially-resolved lesions. Follow up visits were scheduled after 1 week [Figure 3] and then at 2 weekly intervals until the lesions were fully resolved.

Case Discussion

Lues maligna, which was first described in 1859, has an estimated incidence of 0.12%–0.36%, leading to its classification as a rare and severe variant of secondary syphilis commonly described in patients with severe malnourishment and chronic alcoholism.[2] In a systematic review by Wibisono *et al.*,[3] out of 45 published case reports of the disease from 2014 to 2018, 73% occurred in

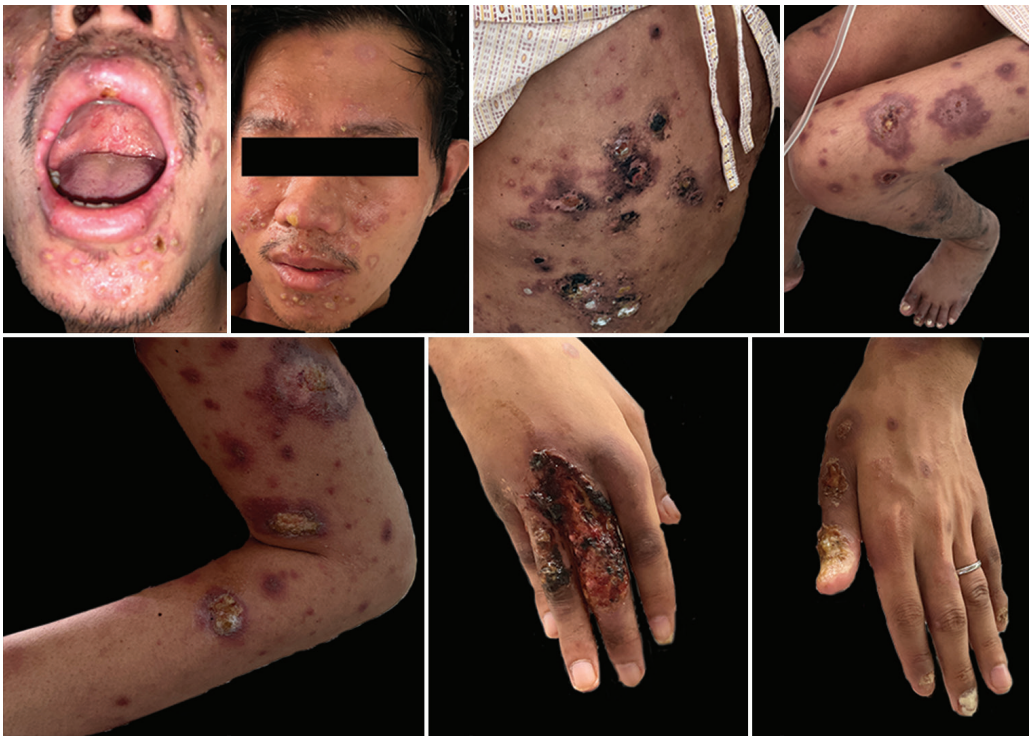

Figure 1: Physical examination findings of a 28-year-old male diagnosed with lues maligna. The lesions are described as multiple well-defined annular to irregularly shaped erythematous ulcerated plaques and nodules with crusts on the face, trunk, and extremities. Multiple erythematous erosions on the palate were also observed in the patient

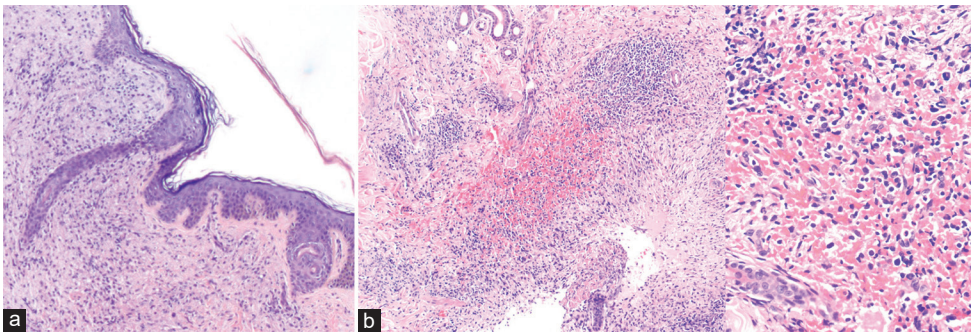

Figure 2: Histopathologic findings of lues maligna. (a) Epidermal orthokeratosis in low power magnification and (b) dermal lichenoid and nodular granulomatous inflammatory mixed-cell infiltrates of lymphocytes, histiocytes, neutrophils, and numerous plasma cells with extravasated erythrocytes in low and high power magnification

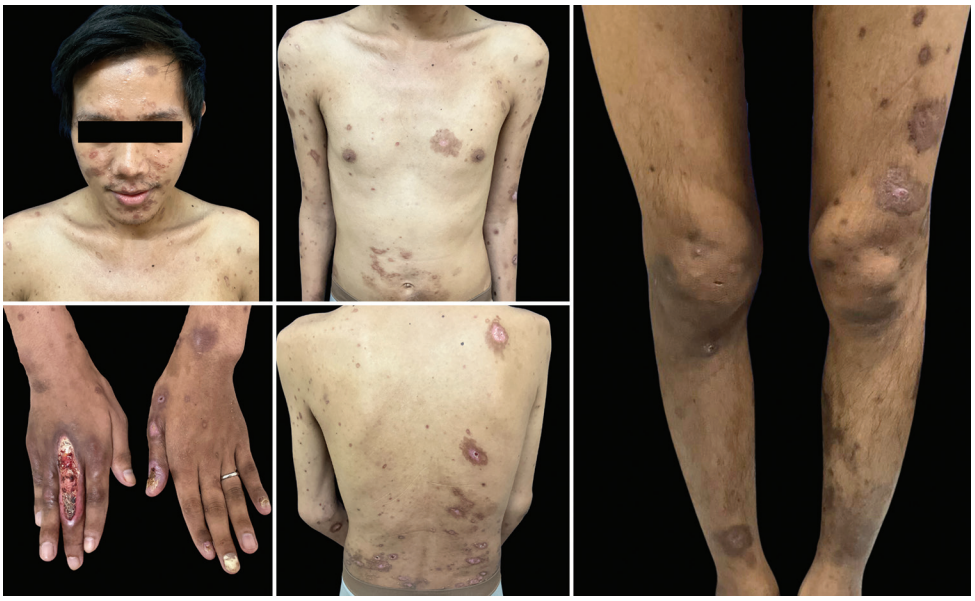

Figure 3: Physical examination findings of the patient 1-week postadmission and postadministration of the last dose of benzathine penicillin G 2.4 million units (total of three doses given at weekly intervals). Lesions resolved to multiple hyperpigmented patches

HIV-positive individuals. Out of the 27% reported cases in HIV-negative individuals, half had comorbidities, including diabetes mellitus, alcoholism, drug abuse, psoriasis, and hepatitis. In the presented case, the 28-year-old male had a history of liver cirrhosis associated with chronic and heavy alcoholism. In 2014, a similar case of lues maligna characterized by noduloulcerative lesions in a chronic alcoholic HIV-negative patient was also reported.[4]

In contrast to the more common cutaneous findings in secondary syphilis called syphiloderms, which is characterized by a maculopapular or papulosquamous rash on the trunk and extremities, especially the palms and soles, lues maligna presents with crusted or scaly papules and plaques with an oyster shell-like surface that later on ulcerate or becomes necrotic.[5] This manifestation of syphilis is commonly associated with high nontreponemal titers and systemic symptoms, which were observed in our patient who presented with fever, arthralgia, weight loss, and a reactive RPR test.

Due to its unusual presentation, several other diseases may be considered as potential diagnoses, leading to delay in treatment initiation and increased morbidity. Among these, differential diagnoses for the disease include bacterial, fungal, and mycobacterial infections, sarcoidosis, and lymphoproliferative skin disorders including cutaneous T-cell lymphoma.[6] As a guide to clinical diagnosis, Fisher *et al.* in 1969 proposed the following criteria for lues maligna: (1) Comparable gross and microscopic morphology, (2) positive syphilis serologies, (3) the Jarisch-Herxheimer reaction, and (4) dramatic responsiveness to antibiotic therapy.[7] Histopathological diagnosis is also of significance as skin biopsy of malignant syphilis follows the typical histopathologic features of syphilis including dermal plasma cell and lymphocytic infiltrate, with occasional

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granulomatous and vascular damage. This allows a clinician to rule out other differential diagnoses not presenting with such findings. In this case, all of the aforementioned criteria were fulfilled with the exception of the Jarisch–Herxheimer reaction, as the febrile episodes of the patient associated with postadministration of penicillin were nonspecific. In addition, worsening of the lesions of the patient after penicillin injection was not well-documented.

As for other diagnostics, reports show that immunohistochemistry provides a sensitivity of up to 92% and excellent specificity in the diagnosis of secondary syphilis.[8] This is superior to silver-staining for detecting Treponema pallidum, as interestingly, there is limited to no spirochete detection in lues maligna biopsies despite it being associated with high treponemal titers. However, in the absence of these immunohistochemistry tests, clinical pathologic correlation in addition to a low threshold for requesting serologic tests for syphilis provides a more accessible yet critical way to early diagnosis and initiation of treatment for these patients. As similar to any other undiagnosed stage of syphilis, delayed diagnosis and treatment initiation could lead to late manifestations and complications of the disease including the appearance of gummas and cardiovascular syphilis as in tertiary syphilis, and neurosyphilis; although the latter could occur at any stage of the disease.

Currently, there are no separately established guidelines or recommendations for the treatment of lues maligna. In the reports published to date, the most common regimen administered is benzathine penicillin G 2.4 million units for three doses given at weekly intervals, similar to the treatment given in late latent syphilis.[3] Successful treatment with aqueous crystalline penicillin G at various dosing regimens (i.e., single intramuscular injection, 3 weekly injections, and 2-week injection of parenteral penicillin) has also been reported.[2] Similar to the case presented, the prognosis is good in the majority of patients, showing complete resolution of lesions with minimal to no scarring. For resistant or relapse cases, extended therapy with high doses of penicillin has shown some benefit. Response monitoring is recommended through regular follow-up clinical examination and testing for RPR titers. Finally, for high-risk HIV-negative individuals, a repeat HIV test may be warranted.

Conclusion

Lues maligna, also called malignant syphilis, is a rare aggressive form of secondary syphilis commonly reported in immunocompromised individuals. The challenge to dermatologists is its unusual presentation described as ulceronodular lesions with oyster shell-like crusting, which could mimic other diseases including deep fungal infections and lymphoproliferative disorders. Hence, prompt diagnosis is most important to initiate immediate treatment. In this report, we presented a case of malignant syphilis in a 28-year-old HIV-negative male with a history of chronic alcoholism. The diagnosis was confirmed through the clinical presentation supported by positive treponemal and nontreponemal tests, as well as histopathologic findings. Successful treatment was observed with three doses of benzathine penicillin G 2.4 million units given at weekly intervals. The patient was discharged with significantly improved lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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