JAMA Dermatology Clinicopathological Challenge

Diffuse Eruption of Necrotic Papules and Nodules

Patrick A. Armstrong, BS; Jason S. Reichenberg, MD; Dayna G. Diven, MD; Alde Carlo P. Gavino, MD

A white woman in her 30s presented with a 2-month history of widespread erythematous, hyperkeratotic papules, and nodules with necrotic ulceration involving her face, trunk, and extremities (**Figure**, A and B). Her groin, buttocks, and oral mucosa were spared. In addition, there were hyperpigmented, ulcerated papules and nodules on her palms and soles. The eruption started as asymptomatic papules on her right forearm that spread progressively to the rest of her body and began to ulcerate. The patient did not have fevers, chills, or weight loss. She denied any history of sexually transmitted diseases, foreign travel, alcoholism, or immunodefiiency. Her last sexual encounter was with a reportedly monogamous partner 5 months prior. She did not seek medical care and received no treatments at the onset of her disease; however, she developed madarosis, low-grade fevers, and chills, prompting her to finally seek medical care. A biopsy specimen was taken from a nodule on her back (Figure, B and C).

What is your diagnosis?

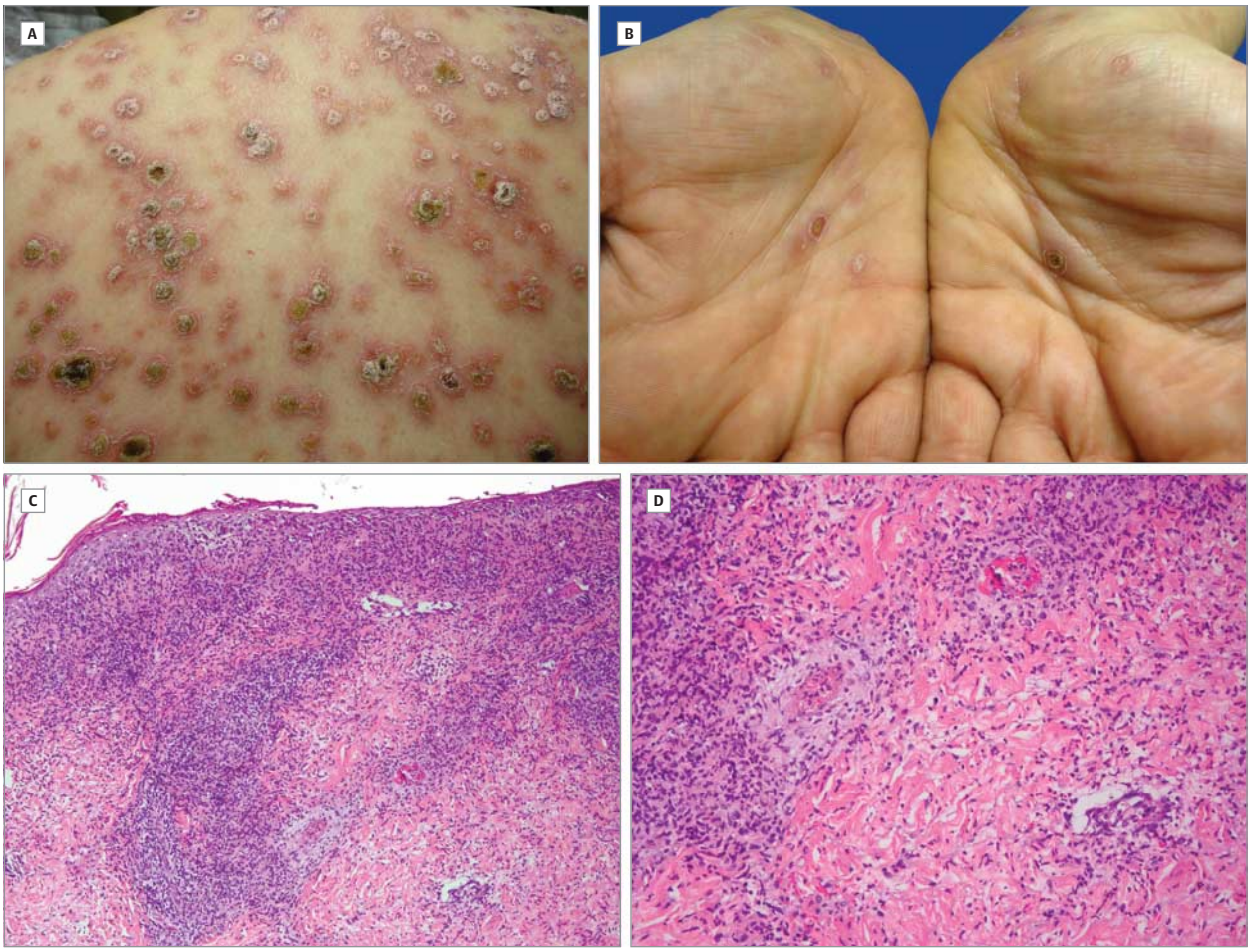

Figure.

Diagnosis

Lues maligna (malignant syphilis) with granulomatous histologic characteristics

Microscopic and Serologic Findings

Biopsy findings revealed an acanthotic epidermis with underlying superficial and deep perivascular and periadnexal granulomatous inflammatory infiltrate admixed with plasma cells. There was evidence of vasculitis with fibrin deposition and lymphocytic and neutrophilic inflammation within blood vessel walls and lumina. Special stains, including periodic acid–Schiff (PAS), Grocott methenamine–silver (GMS), and acid-fast bacilli (AFB), were negative for organisms. A *Treponema pallidum* immunohistochemical stain revealed abundant corkscrew-shaped organisms consistent with spirochetes within the epidermis, follicular epithelium, and blood vessels. Serologic studies showed a highly elevated rapid plasma reagin titer of 1:8192, which was later confirmed by a positive result from a microhemagglutination assay. Human immunodeficiency virus (HIV) antibodies were not detected. Lues maligna was diagnosed, and the patient was immediately treated with 2.4 million U of penicillin G benzathine.

Discussion

Lues maligna, also known as nodulo-ulcerative or malignant syphilis, is a very rare manifestation of an infection caused by the spirochete *T pallidum*. It has been defined as a variant of secondary syphilis and often has a prodrome of fever, headache, and myalgia followed by a rapidly progressing papulopustular eruption that evolves into sharply marginated necrotic ulcers with rupioid crusting.[1] Histopathologically, lues maligna is typically characterized by a dermal infiltrate of plasma cells admixed with lymphocytes, histiocytes, and neutrophils[1] but can rarely exhibit granulomatous inflammation.[2]

Prior to the advent of the HIV epidemic, the incidence of lues maligna was exceptionally uncommon, with only 14 reports from 1900 to 1988 in the English literature.[3] Although recent attention has focused on lues maligna in HIV-infected patients, several cases have been reported in HIV-negative patients,[4-7] most of whom had comorbid health problems of alcoholism or malnutrition.

The pathophysiologic mechanisms responsible for the development of lues maligna are not well understood. It seems to be host-dependent, since it has been demonstrated that patients with lues maligna are infected with *T pallidum* of normal virulence by sexual partners who do not display the same severe symptoms.[8] It is likely that functional and quantitative deficits in both the humoral and cell-mediated components of immunity are involved.[1] Patients without obvious immunosuppression may have an unidentified functional deficit or variation in immune function that gives a predisposition to lues maligna.

Clinically, syphilis was high in the differential diagnosis of the present case, primarily based on the finding of cutaneous involvement of the patient's palms and soles. However, it is important to note that lues maligna can spare palmar and plantar skin.[4,7] The common histopathologic pattern for syphilis is superficial and deep lymphocytic inflammation with plasma cells.[9] However, as corroborated by the present case, syphilis may exhibit a predominantly granulomatous pattern.[2] In addition, characteristic plasma cells are sometimes sparse or completely absent on histologic examination.[9] Thus, it is important to consider syphilis in the differential diagnosis of dermal granulomas, especially when results from PAS, GMS, AFB, and Fite stains are negative for organisms, and even when plasma cells are not present. Careful assessment and correlation of the clinical, serological, and histopathologic findings are critical in establishing the proper diagnosis.

ARTICLE INFORMATION

Author Affiliations: School of Medicine, University of Texas Medical Branch, Galveston (Armstrong); University of Texas Southwestern–Austin, Austin (Reichenberg, Diven, Gavino).

Corresponding Author: Alde Carlo P. Gavino, MD, Department of Dermatology, The University of Texas Southwestern–Austin, 601 E 15th Street, CEC 2.470, Austin, TX 78701 (carlogavino.md@gmail.com).

Section Editor: Mary S. Stone, MD; Assistant Section Editors: Soon Bahrami, MD; Carrie Ann R. Cusack, MD; Molly A. Hinshaw, MD; Arni K. Kristjansson, MD; Lori D. Prok, MD.

Published Online: October 16, 2013. doi:10.1001/jamadermatol.2013.4717.

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Kumar B, Muralidhar S. Malignant syphilis: a review. *AIDS Patient Care STDS*. 1998;12(12):921-925.

2. Morar N, Ramdial PK, Naidoo DK, Dlova NC, Aboobaker J. Lues maligna. *Br J Dermatol*. 1999;140(6):1175-1177.

3. Shulkin D, Tripoli L, Abell E. Lues maligna in a patient with human immunodeficiency virus infection. *Am J Med*. 1988;85(3):425-427.

4. Held JL, Ross M, Beltrani V Jr, Kohn SR, Grossman ME. Noduloulcerative or "malignant" syphilis occurring in an otherwise healthy woman: report and review of a dramatic dermatosis. *Cutis*. 1990;45(2):119-122.

5. Kumar B, Gupta S, Muralidhar S. Mucocutaneous manifestations of secondary syphilis in north Indian patients: a changing scenario? *J Dermatol*. 2001;28(3):137-144.

6. Watson KM, White JM, Salisbury JR, Creamer D. Lues maligna. *Clin Exp Dermatol*. 2004;29(6):625-627.

7. Bayramgürler D, Bilen N, Yildiz K, Sikar A, Yavuz M. Lues maligna in a chronic alcoholic patient. *J Dermatol*. 2005;32(3):217-219.

8. Cripps DJ, Curtis AC. Syphilis maligna praecox: syphilis of the great epidemic? an historical review. *Arch Intern Med*. 1967;119(4):411-418.

9. Sezer E, Luzar B, Calonje E. Secondary syphilis with an interstitial granuloma annulare-like histopathologic pattern. *J Cutan Pathol*. 2011;38(5):439-442.