JAMA Dermatology Clinicopathological Challenge

Erythematous Papules and Vesicles on the Palms, Soles, and Oropharynx

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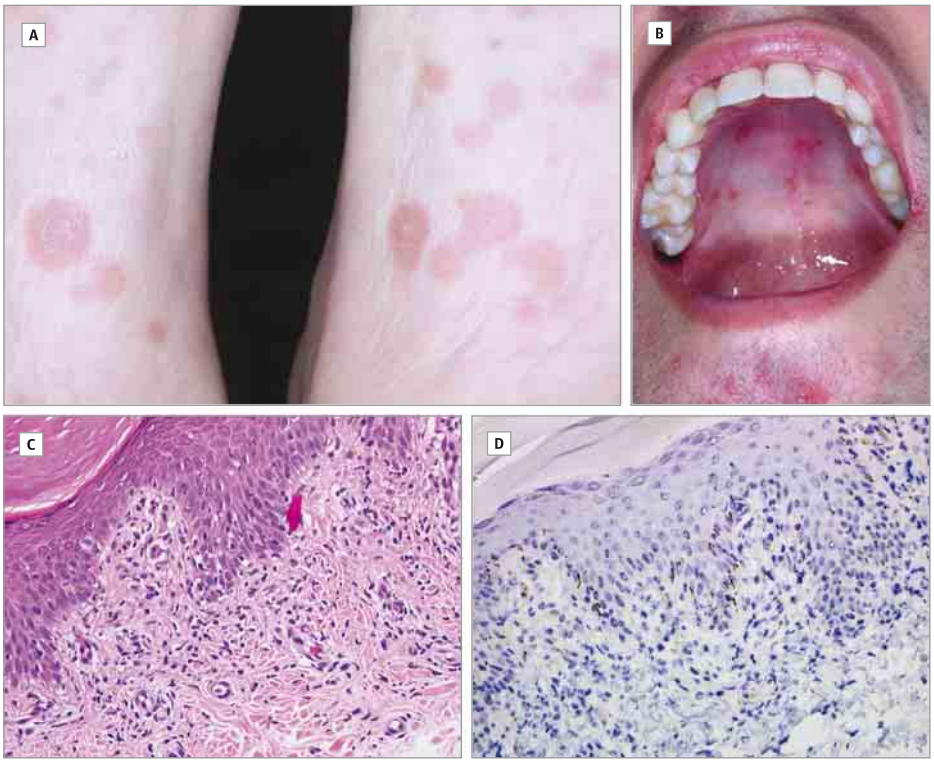

Figure. A, Patient's soles at presentation. B, Patient's palate at presentation. C, Hematoxylin-eosin–stained section of the biopsy specimen (original magnification, ×20). D, Immunohistochemistry stain of biopsy specimen (anti–*Treponema pallidum* polyclonal antibody immunostain; original magnification, ×20).

A 23-year-old white man who has sex with men (MSM) presented with a 1-month history of skin lesions on the palms and soles as well as a 2-week history of lesions in his oropharynx. He reported that a fraction of the lesions had blistered earlier in the course of his illness. The patient also described myalgias and fatigue over the preceding month. He moved to Texas from the northeast a few months prior to his illness. He denied any exposure to sexually transmitted infections or a history of genital lesions. On examination, the patient had erythematous papules on bilateral palms and soles as well as eroded vesicles on the palate (**Figure**, A and B). Lymphadenopathy was not present. A biopsy specimen of a papule on the left sole was obtained for immunohistochemical staining (Figure, C and D). A serologic antibody test revealed an elevated coxsackievirus titer of 1:16 (reference range, <1:8; >1:32 indicative of infection).

Quiz at jamadermatology.com

WHAT IS YOUR DIAGNOSIS?

A. Rocky Mountain spotted fever

B. Secondary syphilis

C. Hand, foot, and mouth disease

D. Primary human immunodeficiency virus infection

Diagnosis

B. Secondary syphilis

Microscopic Finding and Clinical Course

Although the lesion characteristics of syphilis vary widely (hence its nickname "the great mimicker"), lesions on the palms and soles are always suggestive of syphilis. Thus, a vesiculopapular eruption in this distribution should prompt testing for syphilis despite negative biopsy findings. Although the typical histologic examination of syphilis is characterized by an intense plasma cell infiltrate, it is not present in every case. This point is especially important to remember given the increased rate of primary and secondary syphilis, especially among MSM, since 2001.[1] The patient was positive for rapid plasma regain (RPR) (titer, 1:256) and had spirochetes present on the immunohistochemistry stain (anti–*Treponema pallidum* polyclonal antibody immunostain) of the biopsy specimen (Figure, D). The confirmatory test, fluorescent treponemal antibody absorbed (FTA-abs), returned a positive result. The patient was given a single dose of intramuscular penicillin G benzathine and tested for human immunodeficiency virus (HIV), gonorrhea, chlamydia, or hepatitis B and C virus infection, all of which returned negative results.

Although rickettsial and coxsackievirus infections should be considered for a vesiculopapular eruption on the palms and soles, they are not the most likely diagnoses given this patient's age, lack of exposure, and absence of fever and headache. The mild elevation of coxsackievirus titer is likely indicative of past but not current infection.

Discussion

Syphilis is a chronic, multistage disease caused by *Treponema pallidum* that is acquired via sexual contact when active primary or secondary lesions are present. The incidence of primary and secondary syphilis has more than doubled recently (5.3 cases per 100 000 people in 2013 vs 2.1 in 2000).[2] The greatest increases were among Hispanics (53.4%), whites (38.1%), and MSM aged 25 to 29 years (53.2%).[2] The outbreak in the MSM population is attributed to increased unsafe sexual behavior, possibly due to improved antiretroviral therapy for HIV.[3]

Secondary syphilis occurs 2 to 8 weeks after the chancre of primary syphilis resolves. Secondary syphilis presents with fever, malaise, weight loss, headache, pharyngitis, cutaneous eruption, and lymphadenopathy. Secondary syphilis is associated with a generalized and indolent cutaneous eruption that most commonly affects the trunks and limbs. The palms and soles are affected in 50% to 80% cases.[4] Early secondary syphilis lesions can be macular, small papular, follicular, pseudovesicular, lichenoid, vesicular, or psoriasiform. Late secondary syphilis lesions can be large, papular, annular, pustular, or pigmented.[5] Condyloma latum, or excoriated papules or verrucous growths, may occur in intertriginous areas.[1,5] Gray mucosal patches may be present on the buccal mucosa, tongue, and inner labia. Finally, moth-eaten alopecia, with histopathological features of alopecia areata, can occur.[1,4]

The differential diagnosis for the variable cutaneous eruption of secondary syphilis includes primary HIV infection, HIV immune reconstitution syndrome, pityriasis rosea, psoriasis, erythema multiforme, tinea versicolor, lichen planus, drug-related cutaneous eruption, viral exanthema, scabies, and streptococcal pharyngitits.[6]

If syphilis is suspected, nontreponemal serological tests (RPR test or Venereal Disease Research Laboratory test) should be ordered. Of note, the RPR test result may be negative in patients with high titers (prozone phenomenon). If suspicion is high, RPR testing should be repeated with additional dilutions.[1] Positive nontreponemal tests should trigger treponemal-specific testing with *Treponema pallidum* particle agglutination or FTA-abs. Histopathologically, secondary syphilis is often characterized by psoriasiform and lichenoid inflammation with variable numbers of plasma cells. Finally, immunohistochemical staining is more sensitive in detecting *T pallidum* than the Warthin-Starry and Steiner stains.[7]

Secondary syphilis is treated with a single dose of 2.4 million units of intramuscular penicillin G benzathine.[4] In cases of penicillin allergy, oral doxycycline, 100 mg daily for 14 days, is recommended.[6] Patients diagnosed as having syphilis of all stages should be tested for other sexually transmitted infections, including gonorrhea, chlamydia, hepatitis B virus, hepatitis C virus, and HIV. Partners of infected patients should be evaluated clinically and serologically.[8]

ARTICLE INFORMATION

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