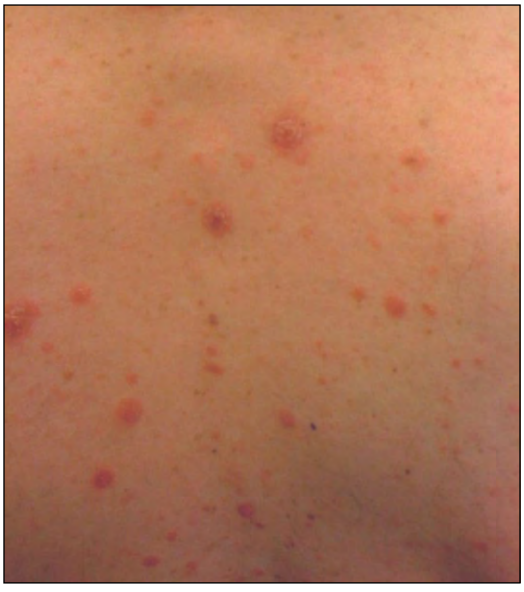
What Is Your Diagnosis?



A 44-year-old man who was human immunodeficiency virus positive presented with a generalized pruritic eruption of 1 week's duration. He denied prodromal symptoms such as fever, chills, headache, or meningismus. The current viral load was undetectable. A rapid plasma reagin test conducted 3 months prior to the cutaneous eruption was negative. Physical examination revealed multiple erythematous papules and thin scaly plaques involving the face, trunk, and proximal extremities, with sparing of the palms and soles. There were no genital, oral, or ocular lesions.

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The authors report no conflict of interest.
The views expressed in this article are those of the authors and do not reflect the official policy or position of the US Department of the Navy, US Department of Defense, or the US Government.
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The Diagnosis: Secondary Syphilis

Histologic examination of a biopsy specimen from the erythematous papules and thin scaly plaques on the trunk (Figure 1) revealed psoriasiform hyperplasia of the epidermis surmounted by confluent parakeratosis that contained focal collections of neutrophils. The dermis was marked by a dense, bandlike, lymphoplasmacytic infiltrate in the superficial dermis with perivascular and periadnexal distribution in the mid to deep dermis (Figure 2). Grocott-Gomori methenamine-silver and periodic acid–Schiff stains with appropriate controls did not reveal fungal organisms. Although no organisms were appreciated on Warthin-Starry silver stain, multiple spirochetes were seen within the epidermis and along the dermoepidermal junction on immunohistochemical staining with polyclonal antibodies directed against *Treponema pallidum* (Figure 3). Subsequent laboratory tests revealed a positive rapid plasma reagin test and fluorescent treponemal antibody absorption test, thus confirming a diagnosis of secondary syphilis. The patient was treated with intramuscular penicillin G benzathine (2,400,000 U weekly) for 3 weeks.

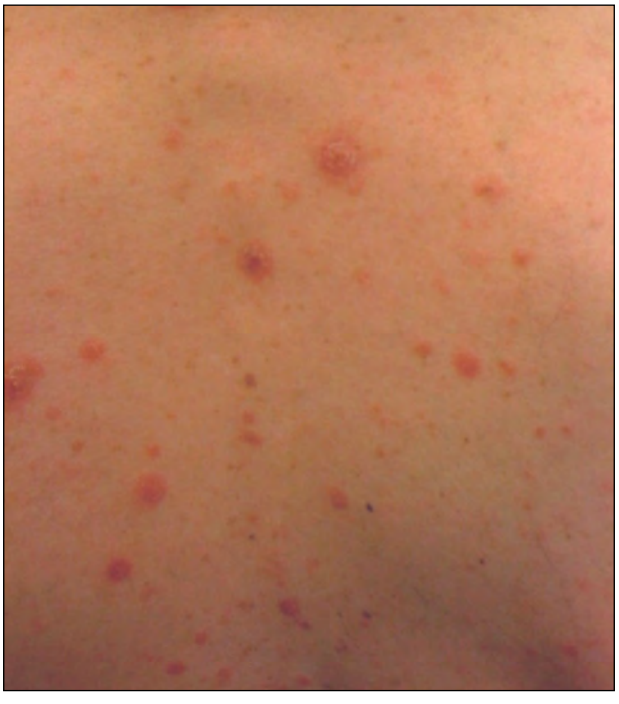

Figure 1. Diffuse erythematous scaly plaques and papules on the trunk.

The incidence rate of syphilis in the United States reached its nadir in 2000 but has steadily increased, particularly among human immunodeficiency virus–positive patients.[1] A presumptive diagnosis can be made with the use of nontreponemal tests (eg, rapid plasma reagin test, VDRL test) and treponemal tests (eg, *T pallidum* hemagglutination test, *T pallidum* particle agglutination assay); however, use of nontreponemal

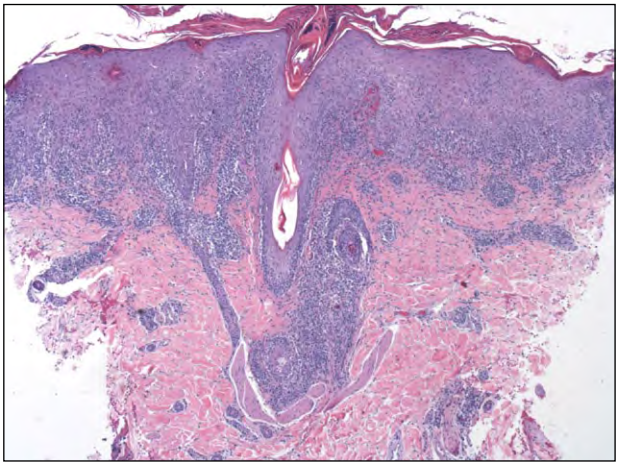

Figure 2. Dense, bandlike, lymphoplasmacytic infiltrate in the superficial dermis with perivascular and periadnexal distribution in the mid to deep dermis (H&E, original magnification ×10).

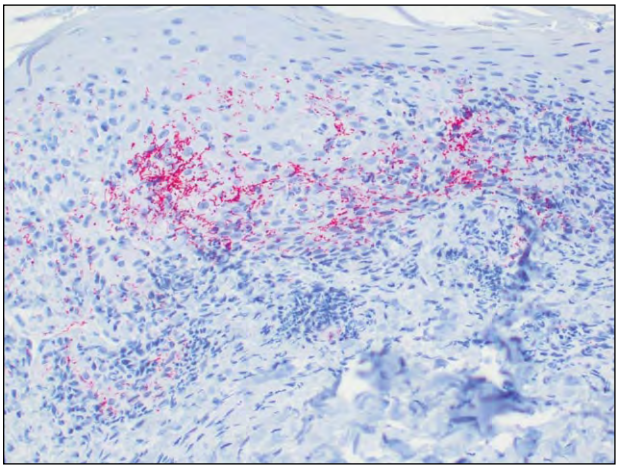

Figure 3. Immunohistochemical staining with polyclonal antibodies to *Treponema pallidum* revealed multiple spirochetes in the epidermis and along the dermoepidermal junction (original magnification ×10).

tests alone can result in false-positive results, and some human immunodeficiency virus–positive patients have atypical serologies.[2] Therefore, alternative tests are needed, and a skin biopsy also may assist in the diagnosis.

The histopathologic findings of secondary syphilis are just as diverse as its myriad of clinical presentations. The density and distribution of the inflammatory infiltrate is highly variable. Most biopsies show a lymphoplasmacytic infiltrate associated with plump endothelial cells; nonetheless, plasma cells can be sparse to absent in 25% of biopsies, and vascular changes may be minimal.[3] The inflammatory infiltrate often is superficial and deep, surrounding blood vessels, nerves, and adnexa; however, a lichenoid infiltrate, pseudolymphoma, granulomatous dermatitis, or a combination of these patterns also may be seen.[4-6]

Neutrophilic spongiosis or psoriasiform hyperplasia frequently is present in the epidermis.[4] Although *T pallidum* can be identified in tissue sections using silver stains such as the Warthin-Starry silver, Steiner, or Dieterle stain, the organisms often are difficult to appreciate because of staining of background artifacts.[5] Furthermore, the sensitivity of silver staining has been reported to be as low as 33%,[6] and this type of stain is not specific to *T pallidum*,[7] hence illustrating the need for better detection methods. Immunohistochemical stains using polyclonal or monoclonal antibodies and polymerase chain reaction (PCR) protocols using a *T pallidum* 47 kDa protein hybridization probe offers improved sensitivity and specificity. One study showed a sensitivity of 91% (11/12) for immunohistochemical stains and 75% (9/12) for PCR.[7] The majority of organisms are located in the epidermis or superficial dermis with a perivascular distribution.[5,7] Immunohistochemical staining and PCR have improved sensitivity and specificity for detecting spirochetes compared to standard methods, thereby allowing for more expeditious diagnosis, which can eliminate long-term sequelae associated with untreated disease.

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