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Secondary syphilis presenting as pseudolymphoma of the skin

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Secondary syphilis most commonly presents with a papulosquamous eruption that involves the palms, soles, and mucous membranes. The papulonodular variant has only been described 11 times in the literature. We describe a case of papulonodular secondary syphilis presenting as an atypical lymphoid hyperplasia suggestive of cutaneous lymphoma. (J Am Acad Dermatol 2003;49:S174-6.)

The last epidemic of syphilis in the United States occurred in 1990 with 50,578 cases of primary and secondary syphilis reported that year.[1] In 1998, there were 6993 cases reported, representing an 86% decrease.[1] In a report recently published by the Centers for Disease Control and Prevention,[2] it is stated that the national goal is to reduce cases of primary and secondary syphilis to less than 1000. Although a syphilis epidemic is unlikely in the new millennium, the case presented here is evidence that syphilis is still among us and is still "the great imitator."[3] We present a case of secondary syphilis in a 37-year-old man that simulated cutaneous lymphoma clinically and histologically.

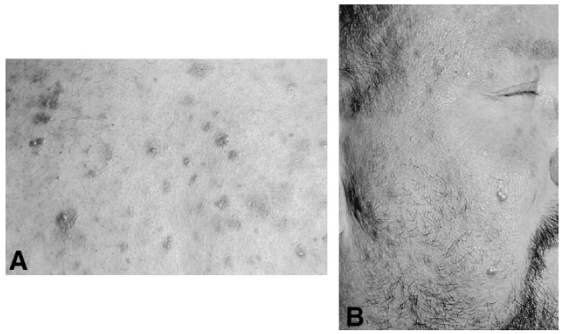

Fig 1. Papulonodular lesions on upper trunk (**A**) and face (**B**).

CASE REPORT

A 37-year-old white man was referred to our division of cutaneous lymphoma program for evaluation of a nonpruritic erythematous eruption present on his eyelids, cheeks, chest, and upper aspect of the back (Fig 1) for 4 months because the initial skin biopsy specimen was interpreted as an atypical lymphoid infiltrate. He denied any systemic symptoms, and had been treated previously with a 2-week course of prednisone without success. His medical history was significant for hypertension, and his only current medication was loratadine.

Physical examination revealed numerous erythematous macules, thin plaques and papules, and papulonodules, often centered at follicular orifices, without significant scaling disseminated over the upper aspect of the trunk with smaller lesions on the cheeks and upper portion of the eyelids. There was no enlargement of lymph nodes, liver, or spleen. Chest radiography revealed normal findings.

Two biopsy specimens were obtained from the back and showed 2 different histologic patterns. The first specimen showed a mild lymphoplasmacytoid infiltrate with a superficial, mid, deep, periadnexal, and interstitial pattern. The second specimen revealed a dense, wedge-shaped infiltrate containing many medium-sized lymphocytes with oval or cerebriform nuclei, occasional large transformed cells with nuclei containing prominent nucleoli, numerous plasma cells, and eosinophils (Figs 2 and 3). Lymphocytes were aligned along the dermoepidermal junction with single-cell epidermotropism, and one hair follicle showed extensive folliculotropism without follicular mucinosis. Cell-marker studies showed the dense lymphoid infiltrate to be composed of nearly equal proportions of T and B cells. The T-cell component showed a mixture of CD4 and $CD8^+$ cells in a ratio of about 2:1 with diminished expression of CD7 (Leu 9), CD62L (Leu 8), and mildly depressed CD5. A few $CD4^+$ cells were seen in the epidermis and the follicular epithelium. The B-cell component showed equal expression of κ and λ light chains and no germinal centers were seen. About 40% to 50% of the dermal infiltrate expressed BCL-2, mostly by the smaller mononuclear cells, and approximately 5% to 10% of the cells were $CD30^+$ (Ki-1). A definitive diagnosis of B-cell lymphoma could not be made because of the absence of monotypic light chain expression. Chronic inflammation versus the possibility of cutaneous T-cell lymphoma were included in the differential diagnosis of the immunohistochemical findings because of decreased expression of CD7, CD62L, and CD5. Polymerase chain reaction amplification of the immunoglobulin heavy chain gene and T-cell receptor γ gene failed to detect a B- or T-cell monoclonal population.

Initial laboratory studies revealed a normal complete blood cell and differential count; absence of Sézary cells on smears; normal flow immunotyping of blood lymphocyte subsets; increased serum uric acid (9.1 mg/dL; normal, 3.9-7.8 mg/dL); diffuse hypergammaglobulinemia by serum protein electropheresis; an increased serum IgE (143 U/mL; normal, 14-122

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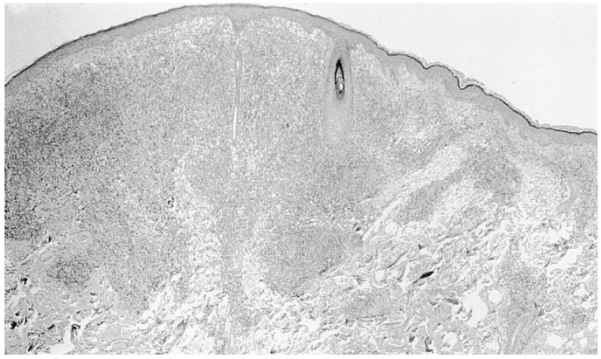

Fig 2. Dense wedge-shaped lymphoid infiltrate with focal epidermotropism. (Hematoxylin-eosin stain; original magnification ×10.)

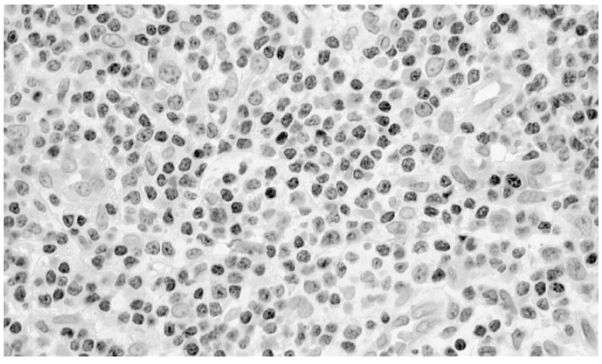

Fig 3. Dense, diffuse, infiltrate composed of medium-sized lymphocytes with oval or cerebriform nuclei, occasional large transformed cells with nuclei containing prominent nucleoli, numerous plasma cells, and eosinophils. (Hematoxylin-eosin stain; original magnification ×40.)

U/mL); a negative antihuman T-lymphotrophic virus–I; and a borderline positive Lyme IgG/IgM titer (0.80). Additional studies showed the rapid plasma reagin test to be reactive at a titer of 1:256, the microhemagglutination treponemal antibody test to be reactive, and the Lyme IgG/IgM antibody Western blot to be negative. The patient was given a diagnosis of secondary syphilis with a serologic cross-reaction producing the borderline positive Lyme disease titer.

The patient was initially treated with 100 mg of doxycycline twice daily for about 1 month for suspected lymphoid hyperplasia secondary to Lyme disease with improvement, but then was given 3 doses of intramuscular benzathine penicillin when the diagnosis of syphilis was established. The eruption cleared promptly.

DISCUSSION

Secondary syphilis presents 2 to 6 months after inoculation with the spirochete *Treponema pallidum*.[4] The classic presentation is that of a generalized papulosquamous eruption of the skin and mucous membranes accompanied by a flu-like prodrome with lymphadenopathy.[3] Discrete, copper-red, nonpruritic, annular macules, with rare peripheral scaling, are characteristically bilateral, symmetric, more prominent on the upper extremities and, in the early stages, on the palms and soles.[3] Other cutaneous manifestations include macular, papular, and pustular lesions. The characteristic histologic features of secondary syphilis include endarteritis, a superficial and deep perivascular plasma cell infiltrate, inflammatory cell infiltrate obscuring the dermoepidermal junction, and epidermal hyperplasia (lichenoid-psoriasiform).[5] Extensive studies comparing the histologic features of secondary syphilis, however, have noted a wide range of patterns.[5,6]

In all, 8 cases of secondary syphilis have been reported to histologically mimic a malignant neoplasm (J. Leyden, MD, oral communication, July 2000).[7-10] The histologic findings in the case reported by Hodak et al[7] were a dense infiltrate in the mid and reticular dermis composed mainly of lymphocytes and histiocytes with some concentration around the follicles. Endarteritis was not present. The initial histologic diagnosis was lymphocytoma cutis. The 3 cases reported by Cochran et al[8] describe a dense perivascular infiltrate composed of histiocytes, mononuclear cells, plasma cells, rare polymorphonuclear cells, and scattered monocytes with hyperchromatic nuclei and prominent nucleoli. Mitotic figures were appreciated in each of the 3 cases. Two cases possessed epidermal hyperkeratosis and mild acanthosis, and one demonstrated focal microabscesses. In 2 of the cases the infiltrate extended into the fat and surrounded the adenexal structures.[8] Goffinet et al[9] described 2 cases, one of which was interpreted histologically as giant-cell follicular lymphoma and the biopsy specimen of the second case was diagnosed as consistent with Hodgkin's disease. Gollnick et al[10] reported a case of syphilis with a nodular and papulosquamous component that mimicked cutaneous T-cell lymphoma clinically and histologically in which the patient was co-infected with human T-lymphotrophic virus–1. Leyden (oral communication, July 2000) reported a case of nodular secondary syphilis in which the initial biopsy specimen was consistent with cutaneous T-cell lymphoma, however, the presence of plasma cells in subsequent biopsy specimens suggested secondary syphilis.

In the 11 cases of nodular secondary syphilis described to date, the clinical presentation is that of generalized red-purple nodules and plaques with all but 1 case sparing the palms, soles, and mucous membranes (J. Leyden, MD, oral communication, July 2000).[3,7,10-15] One case exhibited extensive pruritus and generalized lymphadenopathy.[7] Another case exhibited lymphadenopathy, anorexia, and a 20-lb weight loss (J. Leyden, MD, oral communication, July 2000). Two cases were accompanied by a fever, and one of these demonstrated lymphadenopathy as well.[11,12] The histologic features were notable for dense diffuse dermal infiltrates composed of lymphocytes, plasma cells, multinucleated giant cells, eosinophils, and histiocytes. In 5 cases, a perivascular infiltrate of these inflammatory cells was described.[3,10,12,13] Of these cases, 3 showed epidermal hyperkeratosis.[12-15] One described a bandlike infiltrate of plasma cells, neutrophils, and some eosinophils.[3] Among the differential diagnoses were lymphoma, reticulohistiocytoma, Hodgkin's disease, sarcoidosis, lymphomatoid papulosis, pseudolymphoma, deep fungus infection, cutaneous tuberculosis, leprosy, foreign body granuloma, diffuse Kaposi's sarcoma, malignant lymphoreticular disease, and halodermia (J. Leyden, MD, oral communication, July 2000).[3,7,10-15]

The case we present here was equally confounding both clinically and histologically. The duration of the eruption, the absence of systemic symptoms, and the clinical and histologic appearance were suggestive of a lymphoreticular malignancy. Our initial clinical differential diagnosis included a peripheral T- or B-cell lymphoma and a pseudolymphoma, possibly induced by a drug or by Lyme borrelliosis. As in Leyden's case (oral communication, July 2000), it was because the infiltrate con-

tained plasma cells that secondary syphilis was also proposed in the differential diagnosis.

Although syphilis is notorious for having a myriad of clinical presentations and histologic features, a case such as is presented here has been infrequently described. We suggest that this case demonstrates the importance of keeping syphilis among the differential diagnoses for both papulosquamous and papulonodular eruptions even as the incidence and prevalence of the disease are decreasing in the United States.

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