

Infiltrated plaques on the face and back

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A 31 year-old woman, previously healthy, presented a four-month history of enlarging plaques on the face and back without any constitutional complaints. She referred to one unprotected heterosexual contact but denied any past history of sexually transmitted infections. Physical examination revealed multiple, tumid, nontender erythemat-violaceous, slightly scaly, flat-topped plaques, distributed over her forehead [Figure - 1], left cheek, right oral commissure and back [Figure - 2]. Palms, soles, oral and genital mucosa were all free of lesions. There was no enlargement of lymph nodes, liver or spleen and the remaining physical examination was normal. Routine blood tests revealed an erythrocyte sedimentation rate of 84 mm at the end of one hour. Serological tests were negative for syphilis, hepatitis B and C and human immunodeficiency virus (HIV). Skin biopsy showed hyperkeratosis, focal parakeratosis and irregular acanthosis of the epidermis. There was a dense cellular infiltrate, grossly nodular, in the entire dermis [Figure - 3], [Figure - 4]. The results of the periodic acid-Schiff, Ziehl-Neelsen and Warthin-Starry stains were all negative. Cell-marker studies showed a heterogeneous population of cells without any phenotypic changes.

Diagnosis: Late secondary syphilis

Two weeks after the first observation, the serological test for syphilis was repeated. It was then reactive with a titre of 1/32 for VDRL (Venereal Disease Research Laboratory) and 1/512 for TPHA (*Treponema pallidum* hemagglutination). Skin biopsy revealed dense infiltrate consisting of multiple plasma cells and lymphocytes [Figure - 4].

Discussion

The secondary stage of syphilis referred to as "the great imitator", can present a myriad of clinical and histological features. Lesions called syphilids develop in 80-95% of the cases, usually 3-12 weeks after the appearance of a chancre which may be unnoticed, especially in women. The most characteristic is a maculopapular rash symmetrically distributed, involving the palms and soles that can be attributed to flu-like prodrome with lymphadenopathy. Papular syphilids observed in approximately 12% of the cases can be classified as papulosquamous, follicular, lenticular, corymbose, nodular or annular. ^[1] In our patient, the main differential diagnoses included lymphoma, deep fungal infections and sarcoidosis.

The most characteristic, but not pathognomonic, histopathologic features of secondary syphilis include epidermal hyperplasia, inflammatory cell infiltrate obscuring the dermoepidermal junction, and a dermal perivascular plasma cell infiltrate. Silver staining using the Warthin-Starry technique detects spirochetes in up to 71% of cases. ^[2] The DNA polymerase chain reaction (PCR) technique has been used to identify *T. pallidum* but is not readily available for routine clinical use. ^[3] The negative results obtained with the different techniques used did not allow a definite diagnosis in our case.


Serological testing remains the mainstay for the diagnosis of syphilis. Nontreponemal tests used for screening include Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR). The VDRL test is quantitative, reflects disease activity and therefore the response of the disease / patient to treatment. These tests are limited by their lack of sensitivity in early and late syphilis and by false-positive reactions due to preexisting conditions. Reactive results should be confirmed by a specific treponemal test such as the TPHA test or the fluorescent treponemal antibody absorbed (FTA-ABS) test. The disadvantages of the treponemal tests are that it remain positive for life despite treatment.

The presence of a risk factor, the absence of pain and pruritus and most importantly, the prominent presence of plasma cells made us repeat the serological test, which became positive for syphilis. It is often stated that, as in this case, some patients may have false-negative results of VDRL and TPHA tests. This is known as the prozone phenomenon, which occurs due to a high amount of antibody in the tested serum, preventing the flocculation reaction required for a positive result. Serum dilution is required to make the correct diagnosis. The incidence of the prozone phenomenon was found to be higher in patients co-infected with HIV. In this particular population, a delay of the response can also be expected, ^[4] therefore, a false-negative syphilis serology may occur. The patient presented had no HIV infection, which was confirmed after six months.

Such unusual clinical presentation has been correlated with a long duration of disease or

an exaggerated hypersensitivity to treponemal antigens. ^[5] The patient was treated with two doses of benzathine penicillin G (2.4 million units per week) by intramuscular injection, resulting in a rapid and complete resolution of the lesions. Six months after the treatment, there was a four-fold decrease of the VDRL titre and HIV serology remained negative. This case illustrates that recognition of the unusual manifestations of syphilis is crucial for its correct diagnosis and treatment.

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