Case report

Tertiary syphilis

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Case 1 A 42-year-old married man reported heterosexual behavior with multiple partners, chronic alcoholism, and a previous history of urethritis. He presented with a 1-year history of two asymptomatic, erythematous to violaceous, annular or polycyclic plaques, involving the anterior aspect of the left thigh. The lesions had raised, well-defined, infiltrated borders, with irregular crusted ulcers at the periphery, and there was central healing with atrophy (Fig. 1). Histologic examination of a skin biopsy specimen showed lymphocytes and plasma cells infiltrating the superficial and deep dermis, and epithelioid granulomas. Warthin–Starry stain for spirochetes was negative. Venereal Disease Research Laboratory (VDRL) test was reactive (1 : 64) and *Treponema pallidum* hemagglutination assay (TPHA) was positive. Tests for hepatitis B, hepatitis C, human immunodeficiency virus-1 (HIV-1), and HIV-2 were negative. Neurologic examination revealed changes attributable to chronic alcoholism. VDRL test and TPHA of cerebrospinal fluid were negative. Echocardiogram showed moderate dilatation of the ascending aorta, thickening of the aortic valves, and moderate aortic insufficiency. The patient received 2.4 million units of benzathine penicillin G, intramuscularly, once per week for three consecutive weeks, with rapid resolution of the lesions. His wife had a nonreactive VDRL test and positive TPHA, and was treated with the same regimen.

Case 2 A 32-year-old married woman of rural background and residence presented with a 1-year history of occasionally pruritic, papulonodular lesions, involving the presternal (Fig. 2) and left eyebrow (Fig. 3) regions, papules in a polycyclic configuration, and clusters of erythematous, infiltrated nodules, some of which showed ulceration with a surface crust. There was central atrophy and noncontractile scarring. Her husband had been treated for primary syphilis approximately 5 years earlier with benzathine penicillin G; however, the wife was not notified and therefore was not treated. Histologic examination of a presternal lesion revealed erosion and acanthosis with irregular papillomatosis of the epidermis, a dense superficial dermal infiltrate of lymphocytes, plasma cells, and epithelioid cells, and granulomas with multinucleated giant cells. Warthin–Starry stain was negative. VDRL test was reactive (1 : 128) and TPHA was positive. Serology for hepatitis B and C and for HIV-1 and HIV-2 was negative. VDRL and TPHA analyses of the cerebrospinal fluid were negative. The patient was treated with 2.4 million units of benzathine penicillin G, intramuscularly, once per week for 3 weeks, with rapid resolution of the lesions. One year after treatment, there was slight central, noncontractile atrophy and peripheral hyperpigmentation (Fig. 4).

Case 3 Accompanied by a social worker, this single, mentally retarded, indigent 42-year-old man presented with a greater than 1-year history of two fetid, erythematous to violaceous, exudative plaques with ulcerated bases and circinate, ulcerated borders, involving the inner aspects of both thighs (Fig. 5). Histologic examination showed marked pseudoepitheliomatous hyperplasia of the epidermis and marked inflammation of the papillary and reticular dermis, mainly with plasma cells (Fig. 6). Warthin–Starry stain was negative. VDRL test was reactive (1 : 8) and TPHA was positive. Serologic tests for hepatitis B and C and for HIV-1 and HIV-2 were negative. Neurologic examination revealed profound memory impairment and abnormal balance. Computed tomography scan of the head and evaluation of the cerebrospinal fluid were unremarkable. The patient was treated with three intramuscular injections of benzathine penicillin G, 2.4 million units, over three consecutive weeks. The lesions responded rapidly to treatment, with evolution to peripheral hyperpigmentation and central, noncontractile atrophy.

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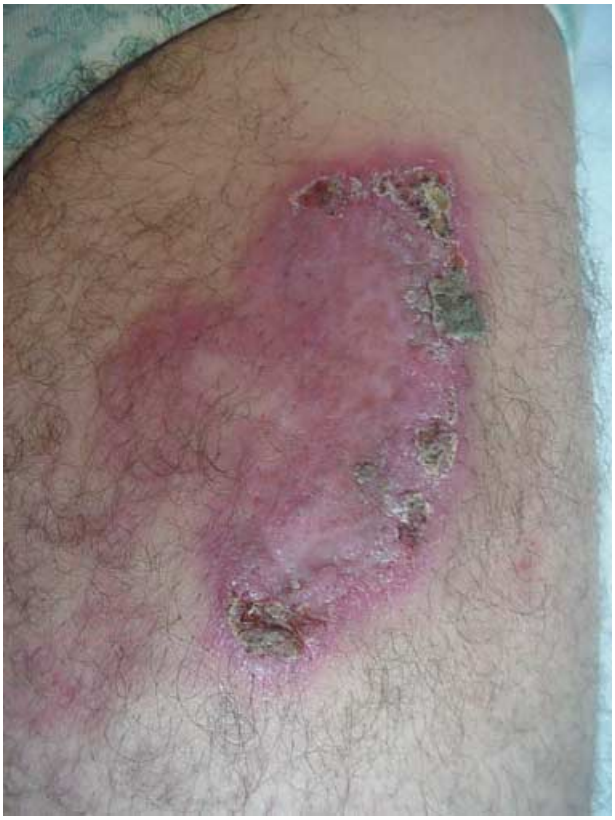

Figure 1 Erythematous to violaceous plaque, with crusted and ulcerated border, on the left thigh

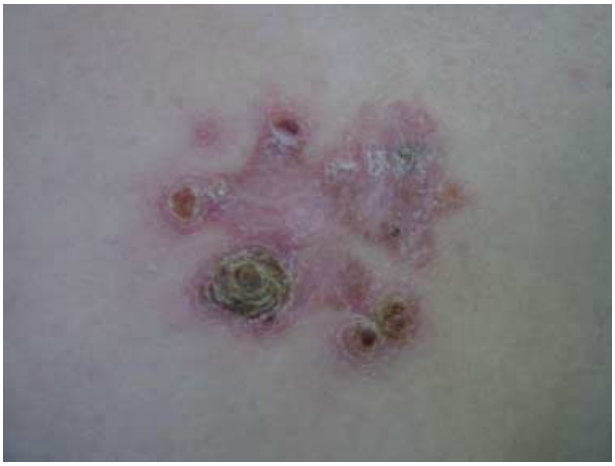

Figure 2 Clustered, infiltrated nodules, with crusted surfaces and central atrophic scarring, in the presternal region

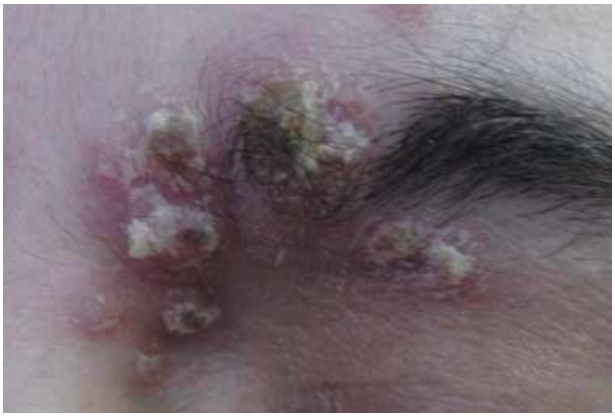

Figure 3 Infiltrated nodules with crusted surfaces on the left eyebrow

Discussion

Tertiary syphilis is a rare systemic disease that may present with mucocutaneous, cardiac, ophthalmologic, neurologic, or osseous abnormalities.[1] Physicians in Western Europe and the USA may therefore fail to recognize its clinical features. To highlight this problem, we have presented the clinical, histologic, and serologic features of three patients with a recent diagnosis of tertiary syphilis.

The incidence of tertiary syphilis has decreased drastically with the use of penicillin for the treatment of primary and secondary stages. Over the past 20 years, however, cases have been reported sporadically,[2–7] particularly in patients with poor access to healthcare[4] and in those who prefer homeopathic medicine.[5] Initial diagnosis may be delayed when serology is negative,[6] and some patients have been treated for the wrong disease, particularly discoid lupus erythematosus.[7] The clinical morphology of the skin lesions varies depending on whether involvement is hypodermal (syphilitic gumma) or dermal (granulomatous nodules or psoriasiform granulomatous plaques).[1] Tertiary syphilis may mimic diseases such as granuloma annulare[2] or pyoderma gangrenosum.[3] Our three patients had papulonodular lesions. Cases 1 and 3 had plaques with circinate, ulcerated borders, whereas Case 2 presented with clusters of infiltrated nodules, with crusted surfaces and polycyclic borders. Presentation with papulonodular lesions is rare, and lesions are usually disseminated, but occasionally localized to sites such as the face, mucosa, and palms or soles.[1] The clinical and histologic presentation of secondary and tertiary syphilis may overlap.[8] Papulonodular lesions may occur in secondary syphilis.[9] There may be desquamation of lesions in secondary syphilis, but not ulceration. Lesions of tertiary syphilis may heal with atrophic, noncontractile scars, with peripheral hyperpigmentation. By contrast, secondary syphilis improves within weeks, without scarring, with or without treatment.[1] Constitutional abnormalities, such as fever, anorexia, weight loss, and lymphadenitis, are features of secondary syphilis and seldom occur in tertiary syphilis.[1]

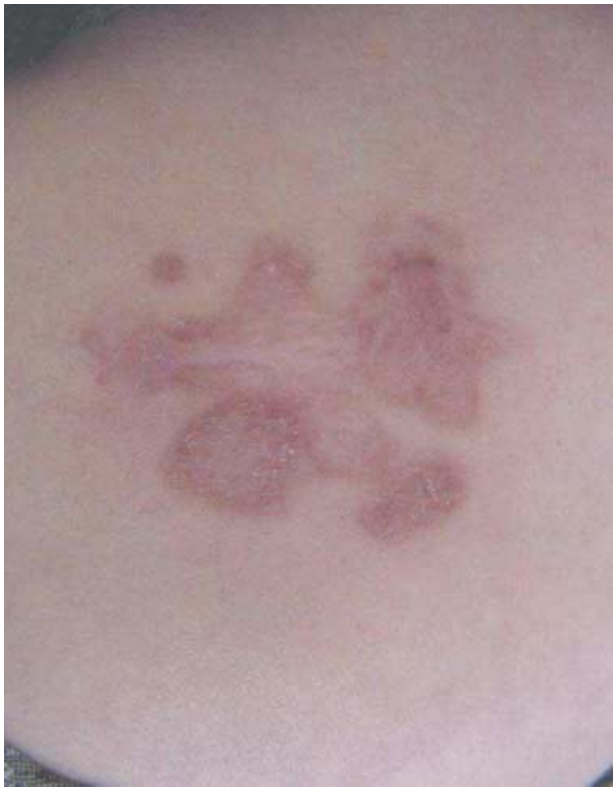

Figure 4 Presternal lesions, 1 year after treatment

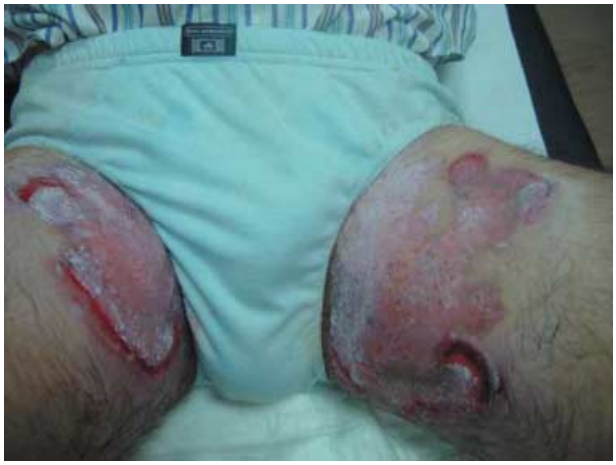

Figure 5 Ulcerated plaques involving the inner aspect of both thighs

In the lesions in all three of our patients, the histologic pattern was a dense inflammatory infiltrate of lymphocytes and numerous plasma cells, and two of the three had granulomas with multinucleated giant cells. These findings are characteristic of tertiary syphilis, but may be seen in secondary syphilis.[10] Lesions of tertiary syphilis may contain minimal plasma cell infiltration, which contributes to the difficulty in diagnosis.[11]

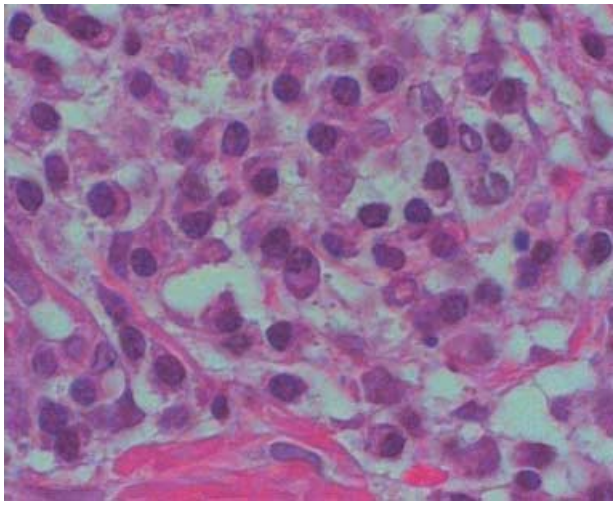

Figure 6 Inflammatory infiltrate with predominance of plasma cells (hematoxylin and eosin, ×1000)

The serology was positive in our three patients, with a high Venereal Disease Research Laboratory (VDRL) titer in the second case (VDRL = 1 : 128). In untreated latent syphilis, titers tend to decline, reaching low values in the late latent stage (VDRL < 1 : 4).[12] Approximately one-fourth of untreated patients become nonreactive.[13] Conversely, in active benign tertiary syphilis, serologic tests are always reactive, often with a high titer.[14] The serology is usually positive in patients with gumma,[15] but may be negative in those with localized lesions, such as osseous gumma.[16] Nonreactive VDRL may contribute to a delay in diagnosis.[6,7] Neurologic and cardiac involvement must be excluded in patients with tertiary syphilis. Our patients had negative cerebrospinal fluid evaluation. None had cardiovascular complaints, but the findings of moderate dilatation of the ascending aorta and thickening with moderate insufficiency of the aortic valves, detected in Case 1, are the most common cardiovascular complications of tertiary syphilis.[1]

The incidence of primary syphilis has increased in many European countries and the USA, in association with HIV infection, drug abuse, and high-risk sexual behavior,[12,17,18] with a dramatic rise in the number of cases of congenital syphilis.[12] Syphilis is more common in individuals of lower socioeconomic status and in those who have limited access to healthcare. Hence, there is a continuing need for routine serologic testing. Our three patients with tertiary syphilis emphasize the importance of maintaining clinical suspicion and expertise in order to recognize and diagnosis tertiary syphilis.

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