Papulonodular secondary syphilis in a 52-year-old non-HIV heterosexual patient

V. Breznik, M. Potočnik, and J. Miljković

SUMMARY

There has been a recent increase in the incidence of syphilis in Slovenia, similar to other countries. Secondary syphilis can manifest with various clinical and histopathological presentations. We report the case of a 52-year-old patient that presented with nonpruritic nodular lesions on the face, trunk, and insteps that clinically mimicked lymphoma or sarcoidosis. Histopathological findings showed granulomatous inflammation. The serology revealed positive non-treponemal and treponemal tests. Treatment with benzathine penicillin G was successful.

KEY WORDS

syphilis, secondary, papular, nodular, Slovenia, MSM

Introduction

In recent years we have seen an increase in the incidence of early as well as late syphilis in our department. According to the Slovenian Institute of Public Health, there was a 50% increase in registered early syphilis incidence in 2007 compared to 2006. Thus the incidence of registered early syphilis rose from 0.7/100,000 in 2006 to 1.4/100,000 in 2007 (1). Slovenia has a relatively low incidence of this disease compared to other developed countries, but we have seen the same trend of a rising incidence of syphilis, especially among men having sex with men (MSM), in the last decade. This population has high rate of human immunodefficiency virus (HIV) coinfection in addition to often practicing unsafe sex (1–3).

We present an interesting case of secondary syphilis presenting with uncommon clinical and histopathological features resembling lymphoma or sarcoidosis.

Case report

A 52-year-old man (a gardener by profession) presented with a 3-month history of generalized nonpruritic erythematous eruption on his face, chest, upper back, and insteps. He denied any mucosal lesions and systemic symptoms. He had been unsuccessfully treated with mometasone furoate and ketoconazole cream. His medical history was significant for head injury a long time ago and hypertension. His current medications were enalapril and nimesulide. He did not report any allergies.

Physical examination revealed numerous symmetrical circular red-brown to purple papules and nodules with slight scaling, located on the face, upper trunk, and insteps (Figs. 1, 2). There were also smaller erythematous macules on the soles, but his palms were unmarked. No mucosal lesions, alopecia, or lymphadenopathy were found. Initial diagnostic

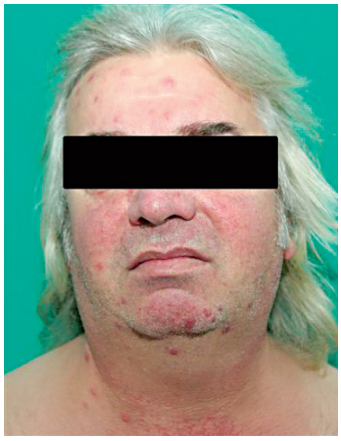

Figure 1. Secondary syphilis: red to purple papules and nodules located on the face.

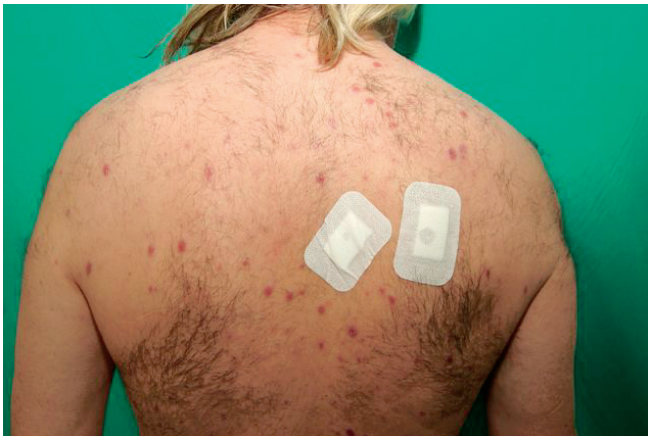

Figure 2. Secondary syphilis: papules and nodules located on the upper trunk.

considerations were lymphoma, sarcoidosis, or secondary syphilis.

Two biopsy specimens taken from the trunk showed a similar histopathological pattern. Moderate atrophy and orthokeratosis were present in the epidermis. A dense diffuse infiltrate extended through entire dermis and comprised mostly plasma cells, lymphocytes, and rare neutrophils as well as many small granulomas and some giant cells (Fig. 3). The histopathological features were consistent with secondary syphilis.

Subsequently the patient admitted unprotected heterosexual contact 7 months earlier, but he denied ulceration on his genitalia or elsewhere.

Initial laboratory tests showed normal erythrocyte sedimentation rate, complete blood count, liver and kidney tests, serum glucose, proteins, antinuclear antibody (ANA), and complement (C3 and C4). Chest X-ray was within normal rates. Laboratory results showed elevated levels of angiotensin converting enzyme (2.17 ukat/l), rheumatoid factor (95 U/ml), circulating immune complex (4.7), and IgE (534 KE/l).

Screening serum tests for syphilis were highly reactive: a Venereal Diseases Research Laboratory (VDRL) titer of 1:1024 and *Treponema pallidum* Hemagglutination Assay (TPHA) titer of 1:40960. Confirmatory tests showed an IgG Fluorescent Treponemal Antibody-Absorption (IgG FTA-ABS) titer of 1:40960, a 19S IgM FTA-ABS titer of 1:512, and a positive LIA (Line Immuno Assay) test. Hepatitis and HIV serology were negative. Neurological and ophthalmological examinations were within normal limits.

A diagnosis of secondary syphilis was made and the patient was treated with benzathine penicillin G 2.4 million units by intramuscular injection once a week for 3 consecutive weeks. He received pretreatment with dexamethasone 8 mg intramuscularly. The skin lesions slowly regressed within 2 months and regular follow-up was carried out. Serological tests 3 months after treatment showed a VDRL titer of 1:8, 19 S IgM FTA ABS was negative, an IgG FTA-ABS titer of 1:2560, a TPHA titre of 1:1280, and a positive LIA test.

Discussion

Secondary syphilis presents 2 to 6 months after inoculation with the spirochete *Treponema pallidum* (4) and 5 to 7 weeks after resolution of primary chancre, although in approximately 30% of cases the primary chancre still persists (5). The classic presentation is with cutaneous lesions (occurring in approximately 75% of patients), mucosal lesions, and systemic symptoms such as malaise, headache, low-grade fever, weight loss, and lymphadenopathy (6). The most common cutaneous presentation of secondary syphilis is a generalized nonpruritic symmetrical maculous eruption that is purple, pink, or coppery-brown in color. The involvement of the palms and soles is an important distinguishing feature of secondary syphilis (7). In our case, only plantar involvement was seen. A few typical papules were accompanied by diffuse nodules with no mucous involvement. Secondary syphilis may rarely present as nodules and plaques (6, 8). According to a study by Kumar et al., nodular secondary syphilis occurred in approximately 4% of patients that were also HIV seropositive (9).

The characteristic histological features of secondary syphilis include a superficial and deep perivascular lymphohistiocytic infiltrate containing a variable proportion of plasma cells, dilated blood vessels with thickened endothelial cells, and frequently involved

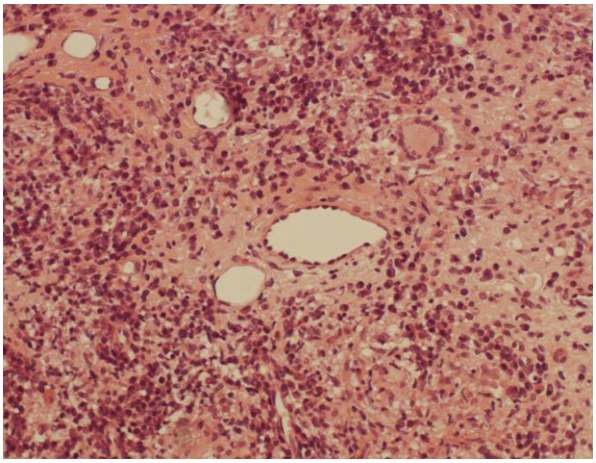

Figure 3. Secondary syphilis: diffuse infiltrate through the entire dermis composed of plasma cells, lymphocytes, some small granulomas, and giant cells (hematoxylin-eosin, ×400).

epidermis (exocytosis, spongiosis, parakeratosis, and acanthosis; 10). Studies comparing the histological features of secondary syphilis have shown considerable variation in histological pattern. These studies suggested that formation of dermal granulomatous foci, which were also present in our patient, correlated with duration of the eruption. In eruptions of 2 to 4 months' duration, granulomatous foci were common, and they were consistently present in older untreated lesions (10, 11). Cases of nodular syphilis presenting with granulomatous inflammation have already been reported (5, 12, 13).

In our case, ACE levels were elevated, but chest X-ray did not show bilateral hilar lymphadenopathy, which would suggest pulmonary sarcoidosis in connection with clinically suspicious cutaneous sarcoidosis. ACE levels are usually elevated in 60 to 80% of patients with sarcoidosis, especially those with pulmonary involvement. However, elevated levels may also be seen in a wide variety of disorders, including other forms of chronic interstitial lung diseases, malignancies, autoimmune diseases, and infections. Thus, one cannot rely on ACE levels to establish a diagnosis of sarcoidosis (14).

In addition, we found elevated levels of RF, which could have been a false-positive result because the patient did not report any symptoms of rheumatologic or connective tissue disease. Positive RF results may also be seen in healthy patients and in patients with conditions such as endocarditis, tuberculosis, syphilis, viral infection, cancer, or diseases of the liver, lungs, or kidneys. The frequency of false-positive RF results also increases with age (15).

The diagnosis of secondary syphilis in our unusual case was accomplished by the histopathological findings and positive screening and confirmatory serological tests. Serologic testing is the mainstay of laboratory diagnosis due to the inability to culture *Treponema pallidum* and the unreliability and difficulty of dark field microscopy (3). At this stage of the disease, non-specific and specific treponemal tests should be reactive. The exception is the prozone phenomenon, which occurs when a very high titer of VDRL or rapid plasma reagin (RPR) gives a false-negative result that becomes positive with serum dilution (2). An alternative reliable method for diagnosis of syphilis is polymerase chain reaction (PCR).

In our patient, clinical response to penicillin therapy, which has remained a treatment of choice for syphilis since 1943 (2), proved the correct diagnosis together with the decrease in VDRL titers during regular follow-up. Our patient did not experience Jarisch-Herxheimer reaction, an acute febrile illness accompanied by malaise and exacerbation of cutaneous lesions, which occurs after treatment of various infectious diseases. It has been reported in 79 to 90% of patients treated with penicillin for secondary syphilis (6). Pretreatment with systemic corticosteroid (dexamethasone) might have prevented this adverse reaction in our patient.

Serological testing for HIV and hepatitis in our patient were negative. Testing for concurrent sexually transmitted infections (STIs) is recommended because they have a higher prevalence in patients with syphilis (9). Syphilis, in the presence of HIV, has a higher rate of atypical and severe presentations or asymptomatic course (16). Coinfection with HIV can cause false-negative or false-positive results in non-treponemal and treponemal tests (3).

The differential diagnosis of nodular syphilis should include atypical mycobacteriosis, deep fungal infections, leprosy, tuberculosis, leishmaniasis, sarcoidosis, lymphoma, Kaposi's sarcoma, lymphomatoid papulosis, halogenoderma, foreign body granuloma, and drug eruptions (7, 8). There are also several case reports of atypical presentations of secondary syphilis clinically mimicking pseudolymphoma (4), lichen planus (17), and Sweet's syndrome (18).

In conclusion, syphilis has once again become a major health problem in the last decade, especially among MSM. Although cutaneous exanthema and lymphadenopathy are the most common manifestations of secondary syphilis, atypical presentations such as nodular syphilis are frequently seen and may cause diagnostic problems. It is important that we be aware of various presentations of this disease as well as other STIs in order to treat them properly and to avoid serious consequences of misdiagnosis.

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AUTHORS' ADDRESSES

Vesna Breznik, Department of Dermatology, Maribor University Clinical Center, Maribor, Slovenia

Marko Potočnik, Department of Dermatology, Ljubljana University Medical Center, Ljubljana, Slovenia

Jovan Miljković, MD, PhD, Specialist in Dermatology, Department of Dermatology, Maribor University Clinical Center, Ljubljanska 5, 2000 Maribor, Slovenia, corresponding author, E-mail: miljkovic.j@ukc-mb.si