DIFFERENTIAL DIAGNOSIS CHALLENGES IN A CASE OF SECONDARY SYPHILIS WITH NODULAR LESIONS

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Summary

Syphilis is an infectious sexually transmitted disease in most cases, caused by Treponema Pallidum.

Case report

Female patient, age 58, from a rural area, hospitalized for a papulo-nodular eruption, with a diffuse spread on the body, with elements ranging in size from 0.5 to 3 cm, some with a red-purple coloring which easily disappears after vitropressure, covered with fine scales, while other lesions exhibit necrosis and ulcers on the surface. The lesions occurred 3 months before the time of hospitalization, initially in the lower limbs, later comprising the other topographical regions.

One month before reporting to our clinic, the patient was hospitalized in Italy, where a skin biopsy was performed, the suggested diagnosis being cutaneous lymphoma with plasmocytic differentiation.

We performed two skin biopsies (cutaneous lesions with different clinical aspects) to highlight the coexistence of the two diseases (syphilis/lymphoma). The HP exam and immunophenotyping, together with serological explorations, excluded the diagnosis of cutaneous lymphoma with plasmocytic differentiation, indicating the diagnosis of secondary syphilis with nodular lesions.

Discussions

Although nodular lesions are usually found in tertiary syphilis, in very rare cases they may also be present in secondary syphilis. In this situation, the differential diagnosis is made with lymphomas and pseudolymphomas, with deep fungal infections, tuberculosis, skin metastases and leukemides. In some situations, secondary syphilis may mimic a granulomatous disorder, such as lepromatous leprosy or sarcoidosis. The presence of granulomatous nodular lesions in secondary syphilis appears to be caused by a hypersensitivity reaction of the body to the treponema or to be a consequence of the long-term evolution of the infection leading to the tertiary stage.

Conclusions

Although extremely rare, secondary syphilis with nodular lesions poses multiple differential diagnosis problems. Confusion with cutaneous lymphoma with plasmocytic differentiation may have dramatic conse-quences for the patient if an anticancer treatment is administered.

Key words: *Syphilis, nodular lesions, cutaneous lymphoma.*

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Introduction

Syphilis is an infectious sexually transmitted disease in most cases, caused by Treponema Pallidum.

Syphilis can mimic a whole series of conditions, making it difficult to diagnose when the clinical panel is atypical, as is the case here.

Case report

Female patient, age 58, from a rural area, hospitalized for a papulo-nodular eruption, with a diffuse spread on the body, with elements ranging in size from 0.5 to 3 cm, some with a red-purple coloring which easily disappears after vitropressure, covered with fine scales, while other lesions exhibit necrosis and ulcers on the surface. (Fig. 1, 2, 3) The lesions occurred 3 months before the time of hospitalization, initially in the lower limbs, later comprising the other topographical regions. The patient presents pruritus of medium intensity, while the mucous membranes, hair and nails remained intact. One month before reporting to our clinic, the patient was hospitalized in Italy, where a skin biopsy was performed, the suggested diagnosis being cutaneous lymphoma with plasmocytic differentiation.

The patient's husband died several years ago, but she is currently living in cohabitation with a person of the opposite sex. The patient states that the last sexual intercourse occurred about 3 months before hospital admission.

APP: surgically treated ectopic pregnancy (1993), ovarian cyst surgery (1997), tibial fracture with osteosynthesis material mounting. (2017).

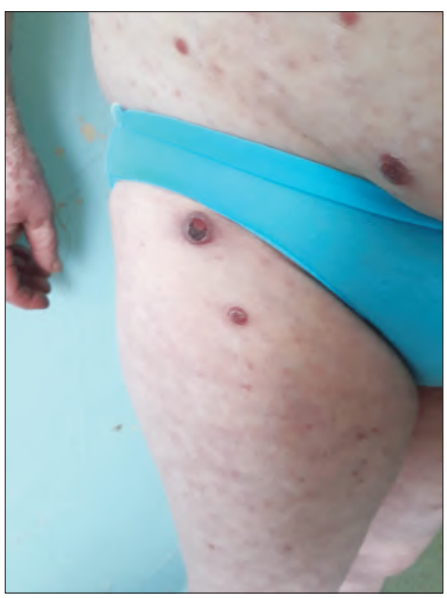

Fig. 1. Ulcerated nodular lesion with central necrosis

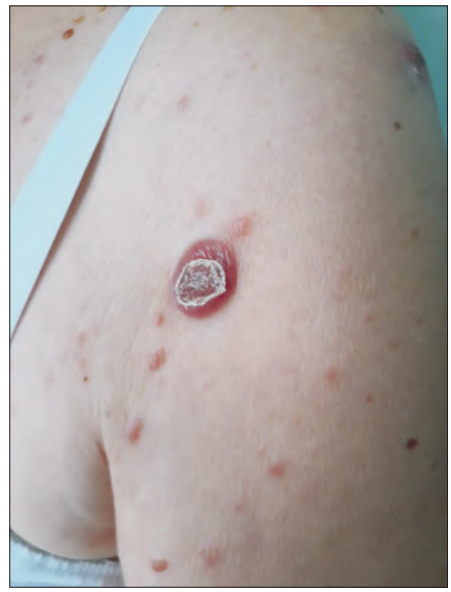

Fig. 2. Ulcerated nodular lesion, covered with scales. Multiple lenticular papules with a reddish-brown colour

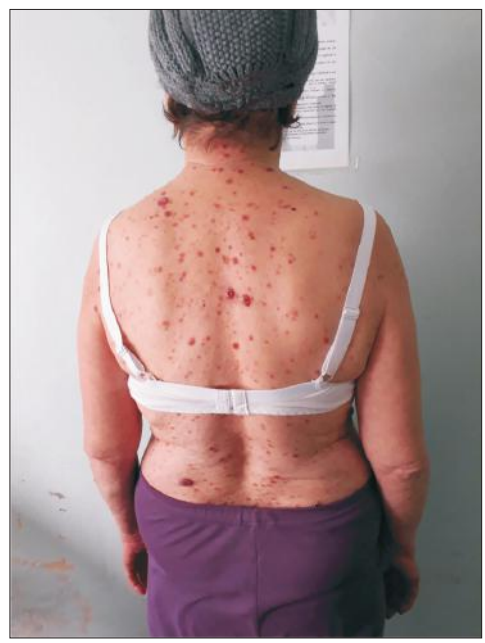

Fig. 3. Papulo-nodular eruption on the posterior thorax

Clinical Exam: Phototype III. Normal weight. Conjunctival hyperemia. Pain and crackles during the passive mobilization of large joints. Mild increase in abdomen volume through adipose panicle. Liver at 1-2 cm under the inferior costal margin. The rest of the clinical examination was within normal limits.

Laboratory Exam

IgA: 456,10 mg/dL; IgG: 2301, 36 mg/dL; IgM: 329,88 mg/dL; Urea: 17 md/dL; INR: 1,23; PT-RP: 13,30 sec; VSH: 105 mm/h; RPR (Rapid Plasma Reagine Test): 59,5 RU (negative <1 RU); TPLA (Treponema Pallidum Latex Agglutination): 266,9 TU (negative <10 TU). Investigations for HIV infection were negative.

Urinalysis: frequent flat epithelial cells and leucocytes, numerous bacterial flora and rare red blood cells.

Abdominal and pelvic ultrasound: within normal limits.

Pulmonary X-ray: No pathological process observed on the lungs of pleura. Moderate left ventricle hypertrophy. Uncoiled aorta.

Considering the previous diagnosis (Cutaneous Lymphoma of plasmocytic differentiation) and positive serology for the treponemic infection, we performed two skin biopsies (the lesions had different clinical aspects) to highlight the coexistence of the two diseases (syphillis/lymphoma).

The HP exam and immunophenotyping, together with serological explorations, excluded the diagnosis of cutaneous lymphoma with plasmocytic differentiation, indicating the diagnosis of secondary syphilis with nodular lesions.

During the hospitalization, the patient was treated with Penicillin 1,000,000 IU every 4 hours, for 4 days, followed by Benzatin Penicillin in ambulatory, according to the stage of the disease. Evolution was favorable (with symptomatology remittance and no new lesions).

Discussions

Syphilis was first described by Dr. Girolamo Fracastoro of Verona in 1530.

In 1905, Schaudinn and Hoffman described the association between Treponema pallidum and Syphilis, demonstrating the presence of Giemsa stained spirochetes in the serosity extracted from secondary syphilis lesions. In 1906, August von Wassermann discovered a serological reaction for the diagnosis of syphilis. In 1943, the first four cases of syphilis successfully treated with Penicillin have been reported, this remaining the treatment of choice even today. [1]

In Romania, the incidence of syphilis has experienced a period of growth between 1986-2002, from 7.1 per 100,000 inhabitants to 58.53 per 100,000 inhabitans; in 2003 the number of cases started to decline, reaching 4,83 cases per 100,000 inhabitants in 2016.

The disease does not have predominance for race or sex but is more common in the gay population. It does not have a specific onset age. Although decreasing, the incidence of congenital syphilis (4 cases in Romania in 2016) demonstrates a deficiency in the medical care of pregnant women.

The etiological factor of syphilis is Treponema pallidum, which is part of the Spirochetales order, the Spirochetaceae family, the Treponema genus. This includes four human pathogens and six nonpathogenic subtypes.

Secondary syphilis usually occurs after 45 days of primary infection. [2] [3] The lesions appear chronologically and are usually superficial macules or papules, rarely taking the appearance of pustular syphilis, lichenoid syphilides, pigmentary or ecthymatous syphilides. There have been described cases where the clinical panel manifested through nodules that can mimic a cutaneous lymphoma, as was the case with our patient.

Our patient was initially diagnosed with cutaneous lymphoma with plasmocytic differentiation due to the nodular appearance of the lesions and histopathological examination that revealed inflammatory infiltrate rich in plasma cells, aspect which can also be encountered in secondary syphilis.

Although nodular lesions are usually found in tertiary syphilis, in very rare cases they may also be present in secondary syphilis. In this

situation, the differential diagnosis is made with lymphomas and pseudolymphomas, with deep fungal infections, tuberculosis, skin metastases and leukemides. In some situations, secondary syphilis may mimic a granulomatous disorder, such as lepromatous leprosy or sarcoidosis. The presence of granulomatous nodular lesions in secondary syphilis appears to be caused by a hypersensitivity reaction of the body to the treponema or to be a consequence of the long-term evolution of the infection leading to the tertiary stage. [4]

The differential diagnosis between cutaneous lymphomas of plasmocytic differentiation and syphilis is based on histopathological aspects and immunophenotyping, a positive test result for syphilis and good results after the treatment with penicillin. [5]

From 1992 to 2013, approximately 20 cases of secondary syphilis with large nodular lesions were quoted. In most cases, the lesions were painless and non-pruritic, but a few patients described pruritus of low intensity as our patient. [3]

The syphilides are usually located on the trunk, scalp and extremities, especially palms and soles. In our patient, the lesions on the palms and soles were lacking, most of them being located on the trunk.

Generalized and small sized adenopathy is present in secondary syphilis but was absent in our patient. Other sexually transmitted diseases were also excluded following investigations.

The histopathological aspect in syphilis, just like the clinical appearance, can be varied and mimic various conditions. The most common aspect is perivascular plasma cells infiltrate, inflammatory infiltrate in the dermo-epidermal junction and epidermal hyperplasia. Several cases of secondary syphilis with atypical lesions and histopathological appearance that mimic a pseudolymphoma or even a lymphoma have been described. [6]

The diagnosis is generally based on positive serologic reactions and the presence of T. pallidum in the patients skin lesions.

In our patient's case, the histopathological exam and immunophenotyping excluded a cutaneous lymphoma, the serologic tests were positive for Treponema Pallidum, and the skin lesions disappeared after penicillin administration. All these represented arguments for sustaining the diagnosis of **secondary syphilis with nodular lesions**, a form rarely encountered in the dermatological practice.

Differentiation between secondary and tertiary syphilis is difficult, especially when the time of primary infection is unknown, and skin lesions have nodular appearance. It pleads for secondary syphilis the symmetrical aspect of the lesions, the absence of important tissue destruction and distribution of lesions on the trunk, limbs and scalp. In our patient's case, the lesions were disposed on the trunk, scalp and limbs, symmetrically, the lesions being approximately at the same stage of development, features that are specific for secondary syphilis. [7]

Conclusions

Although extremely rare, secondary syphilis with nodular lesions poses multiple differential diagnosis problems. Confusion with cutaneous lymphoma with plasmocytic differentiation may have dramatic consequences for the patient if an anticancer treatment is administered.

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Conflict of interest
NONE DECLARED

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