PROZONE PHENOMENON AND AN UNUSUAL PRESENTATION OF SECONDARY SYPHILIS – CASE REPORT

FENOMENUL DE PROZONĂ ŞI O MANIFESTARE ATIPICĂ DE SIFILIS SECUNDAR – PREZENTARE DE CAZ

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Abstract

The prozone phenomenon is a rare false negative response encountered in agglutination or precipitation reactions such as the non-treponemal tests. It is a result of high antibody titers which interfere with lattice formation, making it difficult to obtain a positive flocculation test. The prozone phenomenon is mostly associated with secondary syphilis, HIV infection and pregnancy. We present a case of atypical clinical presentation of secondary syphilis and prozone phenomenon. Clinicians must be aware of the existence of the prozone phenomenon, especially in cases of high clinical suspicion of syphilis and negative reagin test results and request testing with serum dilutions.

Keywords: prozone phenomenon, secondary syphilis

Rezumat

Fenomenul de prozonă este un răspuns fals negativ întâlnit relativ rar în reacții de aglutinare sau precipitare, cum ar fi testele non-treponemice. Acest fenomen este rezultatul unor titruri crescute de anticorpi care fac dificilă obținerea unui test de floculare pozitiv. Fenomenul de prozonă este în mod special asociat cu sifilisul secundar, infecția cu HIV și sarcina. Prezentăm un caz de manifestare atipică de sifilis secundar și fenomen de prozonă. Clinicienii trebuie să fie la curent cu existența fenomenului de prozonă, în special în cazuri cu un înalt nivel de suspicuiune clinică de sifilis și teste non-treponemice negative și să solicite testarea cu diluții succesive ale serului.
Introduction
The prozone phenomenon is a false negative response which appears in agglutination or precipitation reactions, being caused by high antibody concentrations, blocked antibodies or presence of nonspecific inhibitors in patients’ sera (1). This phenomenon has been documented most frequently with secondary syphilis associated with HIV infection and pregnancy. Recently, the prozone phenomenon has also been encountered in neurosyphilis, with lower RPR titers, ranging between 1:8 and 1:512 (2). The incidence of prozone phenomenon seems to be very low, with documented reports between 0.2 and 2%, with possible higher values in the presence of HIV infection (3).

Clinicians must be aware of the existence of prozone phenomenon in the context of typical syphilis manifestations, especially in HIV infected patients, and request non-treponemal testing with serum dilutions when RPR or VDRL tests are nonreactive (4).

We present the case of a male patient with atypical clinical presentation of secondary syphilis and prozone phenomenon.

Case report
A 28-year-old man was admitted to our service for nonspecific cutaneous lesions located on the penile shaft and scrotum. According to the history, he had an unprotected sexual contact four months before and requested consultation to another dermatologist two months after exposure because he started to develop transient skin lesions located on the penile shaft and scrotum. At that moment, he was tested for sexually transmitted diseases, including syphilis. The results were negative and the patient was reassured that he is negative for sexually transmitted diseases: hepatitis B and C, HIV and syphilis. He was prescribed a short course of local corticotherapy with remission of the lesions and later recurrence, also remitted with the same prescribed local treatment.

Clinical examination revealed multiple, firm, painful, flesh colored or pinkish, annular and arcuate papules and plaques located on the scrotum and penile shaft (Figure 1). We suspected that our patients had lichen planus and therefore we performed a biopsy.

Histologic findings showed a classical lichenoid psoriasiform pattern of secondary syphilis: psoriasiform hyperplasia of the epidermis with linear lichenoid infiltrate composed of lymphocytes, histiocytes and plenty of plasmacytes. The inflammatory reaction of secondary syphilis is histologically similar to that of the primary chancre but is less intense (Figure 2).

We performed again syphilis tests: treponemal and nontreponemal tests that were positive: VDRL (1:64) and TPHA. The patient was tested again for HIV and he was negative.

The patient was treated for secondary syphilis with penicillin according to the national guideline: Benzathine penicillin G 2,4 million units intramuscularly, administered as two doses of 2,4 million units IM each at one week interval with complete remission of the lesions.

Discussion
For syphilis screening, current European and US diagnosis and treatment guidelines recommend either non-treponemal, treponemal or the association of both non-treponemal and treponemal-based tests (5, 6). The latter variant is strongly recommended since a reactive non-treponemal test must be confirmed with a treponemal one. In addition, non-treponemal tests can reveal false-positive or false-negative results. Specific T. pallidum serology remains reactive for the rest of one’s life; therefore, the assessment of disease activity and syphilis re-infection relies on reagin (non-treponemal) antibody titers (4).

The prozone phenomenon is a false negative response most likely due to higher antibody titers. RPR or VDRL become positive, therefore forming lattice, depending on specific conditions that favor the optimal ratio of antigen-antibody complex, rendering an insoluble, visible precipitate. The optimal ratio is defined by the zone of equivalence. The zones with antigen excess (post zone) or with antibody excess (prozone) may yield false-negative results. The best way to test for prozone phenomenon is by diluting the serum until antibody concentration is brought into the equivalence zone (3).
The prozone phenomenon appears more frequently in cases of high antibody titers such as secondary syphilis or immunosuppression due to HIV infection or pregnancy.

The clinical manifestations were unspecific, with multiple erythematous patches located on the shaft of the penis, some of them with elevated papular margins, while others were ill defined. We therefore considered the following differential diagnosis: lichen planus, granuloma annulare, chronic eczema, psoriasis.

The final diagnosis was based on histopathological examination, which highlighted classical lichenoid psoriasiform pattern of secondary syphilis.

HIV screening in our patient yielded negative results.

Although rarely encountered, clinicians must be aware of this phenomenon, especially in the context of HIV infection.

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Bibliography