RESIDENT’S FORUM

Diffuse papulosquamous eruptions in an HIV patient presenting with negative rapid plasma reagin test

Case report

A 35-year-old homosexual man presented to our dermatology clinic with a three-week history of skin rashes, on a background of current human immunodeficiency virus (HIV) infection and a negative testing result for syphilis infection. He was regularly followed-up in the infection out-patient department for the past two years. On physical examination, numerous pinkish to reddish oval maculopapules, with diameters ranging from 2 to 10 mm, and overlying fine scales and crusts were seen on the neck, chest wall, back and proximal limbs (Figure 1). Involvements of palm or sole were not noted. The patient also complained of intermittent mild itching of the lesions. Serial laboratory tests were arranged and were found to have a negative testing of rapid plasma reagin (RPR). The lymphocyte count was 1580 cells/mL, CD4⁺ cell count was 483 cells/mL, HIV viral load was 17088 copies/mL. Skin sections exhibited dense lymphohistiocytic infiltration in the dermo-epidermal junction, and the upper dermis demonstrated perivascular infiltration. Vacuolar degeneration in the basal layer was observed and the dermis displayed some lymphocytic exocytosis and scattered plasma cells. (Figure 2) Most lymphoid cells were positive for CD3, with some found to be CD20(+) lymphocytes. The CD30 stain was negative. Ten days post-examination, the patient manifested generalized erythematous to dark-brown scaly maculopapules on the scalp, face, trunk and limbs. In addition, some oval reddish to brownish macules scattered over both palms and soles were also present (Figure 3).

Figure 1 Numerous 2-mm to 10-mm pinkish to reddish oval maculopapules scattered on the (A) chest wall and (B) back and buttocks. Overlying fine scales and crust were also noted.

Figure 2 (A) Dense infiltration was noted on the upper dermis and superficial perivascular area (hematoxylin and eosin; original magnification, 20×). (B) Spongiosis, basal vacuolar degeneration, and exocytosis of lymphocytes were noted. Lymphohistiocyte infiltration and some plasma cells were noted too (hematoxylin and eosin; original magnification, 200×).
Syphilis was highly suspected albeit previous negative testing results, therefore *Treponema pallidum* hemagglutination assay (TPHA) was tested and patient's previous serum was rechecked with serial dilutions for RPR test. TPHA was positive at 1:5120 and the RPR was negative at 1:2 and 1:4. However, it became positive when diluted at 1:8 and remained positive to 1:256. Our RPR test result illustrated the prozone phenomenon and the patient consequently received an intramuscular injection of 2.4 million units of penicillin-G. At the outpatient follow-ups, gradual resolution of skin lesions in the 1 month period was observed and the RPR titer at the 6th month was 1:4.

Syphilis is a sexually transmitted disease caused by the spirochete, *Treponema pallidum*. It is often described as “the great imitator” due to its variable manifestations. Infection must be identified by either direct visualization of the organism in patients’ specimens, or, more commonly, by serologic testing. There are two types of serologic tests, one being nontreponemal tests which include venereal disease research laboratory and RPR. The other being treponemal tests which include TPHA and fluorescent treponemal antibody absorption. Nontreponemal test was used for screening and followed by treponemal test for diagnostic confirmation.

The “prozone phenomenon” is defined as a false negative test due to very high titers or concentration of either antigen or antibody. RPR is a test that looks for antibody-antigen agglutination. An agglutination reaction would be positive when the optimal ratio of antigen to antibody yields an insoluble precipitate that is visible. An overabundance of antibodies interferes with the clumping of antigen-antibody complexes. When such specimen is diluted, sufficient agglutination can be seen and the true sample reactivity becomes apparent.

The prozone phenomenon can be seen in the following settings: secondary syphilis, syphilis and HIV co-infection, and syphilis during pregnancy. Serologic testing is an indirect method of diagnosis since it relies upon a humoral immune response to infection. As such, it has some inherent limitations, particularly in the HIV-infected patient. In prozone phenomenon, dysfunctional B-cells can lead to an overpopulation of antibody in response to an antigen. The excess antibody produced in response to a new infection may then lead to inhibition of flocculation on the RPR test. Smith and Holman reported a case with positive HIV-1 serology and a negative RPR at 1:2. The patient’s RPR became positive when diluted at 1:4 and remained positive to 1:2056. Genç and Ledger stated that by diluting the serum prior to testing, the antibody concentration was decreased and subsequently the prozone phenomenon could be prevented. However, routine serial dilutions were not cost effective due to the low rate (1%) of prozone phenomenon. The incidence of prozone phenomenon reported by el-Zaatari et al was 0.3%. In this study, 4,328 patients were screened. Only one out of 313 syphilis infected patients had a false negative result.

In Taiwan, the HIV-infected patients had increased nearly four-folds and the number of syphilis infection had doubled during the past 10 years. Therefore, notwithstanding the low occurrence, physicians and technicians should still keep in mind the possibility of false negative RPR test due to prozone effect in patients with co-infection of HIV and syphilis. We recommend serum dilution or direct treponemal tests for patients with known HIV-infection, who are suspected to have syphilis, despite previous negative RPR test result.

**References**


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