

Prozone phenomenon in secondary syphilis with HIV co-infection: Two cases

Praneet Awake, Kalpana Angadi¹, Sourav Sen¹, Prasad Bhadange

Departments of Dermatology, Venereology and Leprosy and ¹Microbiology, Symbiosis Medical College for Women, Symbiosis International University, Pune, Maharashtra, India

Address for correspondence:

Dr. Praneet Awake, Department of Dermatology, Venereology and Leprosy, Symbiosis Medical College for Women, Symbiosis International University, Lavale, Mulshi, Pune - 412 115, Maharashtra, India.

E-mail: praneet.awake@smcw.siu.edu.in

Abstract

Prozone phenomenon is defined as a false-negative response resulting from higher antibody titer which interferes with formation of antigen-antibody lattice, necessary to visualize a positive flocculation test. The prozone effect can be observed in syphilis testing with cases of very high antibody titers, such as secondary syphilis, or with human immunodeficiency virus (HIV) co-infection. We report two cases of prozone phenomenon in secondary syphilis with HIV co-infection who initially tested nonreactive for rapid plasma reagin test but tested positive with further higher dilution.

Key words: Human immunodeficiency virus, prozone phenomenon, rapid plasma reagin test, syphilis

Introduction

The prozone phenomenon refers to a false-negative response which occurs because of overwhelming antibody titers. The prozone effect is more frequently observed with secondary syphilis (SS), and it is relatively more common in syphilis with human immunodeficiency virus (HIV) co-infection and in pregnancy.^[1] The incidence of prozone phenomenon has been reported to be between 0.5% and 2%.^[2] This is believed to be higher with HIV co-infection.^[3] The incidence of the prozone phenomenon is attaining clinical significance due to increasing population at risk for sexually transmitted diseases, especially those who are HIV positive.^[3] We describe the occurrence of the prozone phenomenon in two patients with SS and HIV co-infection.

Case Reports

Case 1

A 20-year-old man presented to dermatology outpatient with an asymptomatic reddish-brown colored rash over the palms and left sole of 25 days' duration [Figure 1]. He was treated by the general practitioner for the same with topical steroids. He had little symptomatic relief and his rash was persistent. A thorough examination revealed the presence of an erosion on the glans penis and he also had a mucous patch over the hard palate [Figure 1]. Thus, clinically SS was strongly suspected. He denied a history of any sexual exposure. Another systemic physical examination was done for him, and it was found to be within normal limits. The patient was subjected to rapid plasma reagin (RPR) test. The RPR test was nonreactive. Furthermore, his complete blood count, chest radiograph, electrocardiogram (ECG), and other routine tests were all within normal limits. Therefore, we requested for repeat RPR test, with higher dilution, and it was reactive with 1:320 dilutions. Treponema pallidum hemagglutination assay test was done, which was found to be positive. The patient was subjected to HIV test and was found to be seropositive. He was given 2.4 MU of injection benzathine penicillin intramuscularly and was referred to the antiretroviral therapy (ART) center for further evaluation and initiation of ART. The patient is under regular follow-up.

Case 2

A 55-year-old man who was on anti-retroviral therapy for 2 years presented with a reddish-colored rash over the palms and soles [Figure 1] and over the face of 2 months' duration with no symptoms. A thorough examination revealed multiple papules over the face and forehead, multiple ham-colored papules over the palms, soles, and the presence of mucosal erosions over the hard palate [Figure 1]. He gave a history of sexual exposure. The rest of his physical examination was within normal limits. His complete blood count, chest radiograph, ECG, and other routine tests were all within normal limits. The patient was subjected to RPR test. The RPR test was nonreactive. Depending upon strong clinical suspicion of SS, we requested for repeat RPR test with higher dilution and it was reactive with 1:512 dilutions. The patient

was given 2.4 MU of injection benzathine penicillin intramuscularly. The patient is under regular follow-up.

Discussion

Syphilis can present with a wide variety of clinical manifestations and has been referred to as "the great imitator." The prozone phenomenon in syphilitic serologic testing may cause misleading results in syphilis diagnosis and management. The prozone phenomenon is related to factors such as pregnancy, the phase of syphilis, HIV co-infection, and neurosyphilis.^[3]

There is an increased risk of contracting HIV in patients with syphilis and vice versa.^[4] In patients with syphilis and HIV co-infection, excess antibody production occurs because of anomalous B-cell behavior which results in hyper-responsiveness to antigenic stimulation.^[5] Homosexuals have a higher risk for undetected clinical syphilis and HIV because of the painless and transient nature of the primary chancre.^[6] There is a possibility of a higher incidence of the prozone in them because of HIV-induced B-cell dysfunction which may in turn increase the possibility of syphilis being undiagnosed and thus untreated. The coexistence of HIV infection affects the clinical presentations of previously well-defined diseases and their natural history as well as the response to therapy.^[7,8] The various effects of HIV on the clinical and laboratory manifestations of syphilis were highlighted in a review by Musher *et al.*^[2] The clinical and laboratory abnormalities in syphilis and HIV co-infection are depicted in [Table 1]

Table 1: Clinical and laboratory abnormalities in syphilis and human immunodeficiency virus co-infection

Clinical abnormalities	Laboratory abnormalities
Primary and SS presenting at the same time, asymptomatic neurosyphilis ^[2]	Increased rate of negative serological tests in both primary and SS ^[2]
More than expected time for treatment and relapse of infection after treatment ^[2]	Increased false negative nontreponemal antibody test due to prozone phenomenon ^[8]
Rapid progression to secondary and neurosyphilis ^[6]	Seroreversion to negative of specific treponemal antibody tests following treatment ^[9]
More number of primary chancre and extensive and deeper ulcers ^[9,10]	Significant increase in plasma HIV viral load ^[10]
Atypical manifestations ^[10]	A significant decrease in CD4 cell counts ^[10]
Aggressive secondary syphilis ^[11]	High rate of serological failure to clear nontreponemal antibody test after treatment ^[11]
Systemic manifestations such as uveitis, syphilitic aortitis, encephalitis, arteritis, gastric syphilis, and syphilitic hepatitis. ^[11]	Increased risk of serological failure with late stage of syphilis and HIV infected patients ^[11]

HIV=Human immunodeficiency virus; SS=Secondary syphilis

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How to cite this article: Awake P, Angadi K, Sen S, Bhadange P. Prozone phenomenon in secondary syphilis with HIV co-infection: Two cases. Indian J Sex Transm Dis 2022;43:183-5.

Submitted: 20-Apr-2022

Revised: 21-Jul-2022

Accepted: 28-Sep-2022

Published: 17-Nov-2022

Access this article online	
Quick Response Code:	Website: www.ijstd.org
	DOI: 10.4103/ijstd.ijstd_43_22

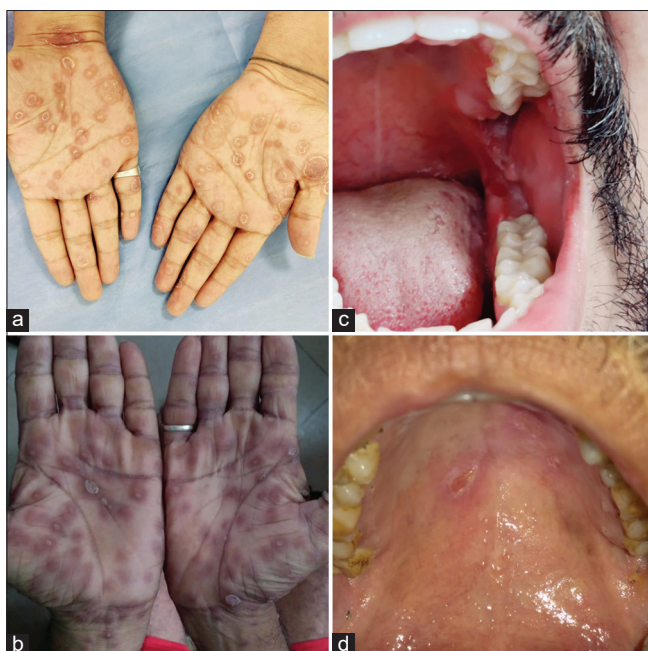


Figure 1: (a and b) Red-brown colored hyperkeratotic plaques over the palms and (c and d) mucous patch over the hard palate

The test for the prozone phenomenon is not done by many hospital laboratories routinely. This can be performed by diluting the patient's serum to bring the antibody concentration into the zone of equivalence. Therefore, it is important to notify the laboratory in this regard, whenever the clinical findings strongly suggest syphilis and when the nontreponemal serological test results are negative.^[10]

Conclusion

The purpose of this article is to focus attention on the prozone phenomenon in the serologic testing of syphilis with HIV co-infection, which may become more prevalent. Dermatologists need to be suspicious and familiar with the protean manifestations of syphilis to be able to exclude the prozone phenomenon.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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