A case of primary and secondary syphilis presenting together as immune reconstitution inflammatory syndrome

Debdeep Mitra, Gautam Kumar Singh, Barnali Mitra[1], Krishna Talukdar[2], Amen Dhillon, Tegveer Singh
Departments of Dermatology and [1]Pediatrics, Base Hospital Delhi, Base Hospital Delhi Cantt, New Delhi,
[2]Department of Dermatology Jorhat Medical College and Hospital, Jorhat, Assam, India

Address for correspondence:
Dr. Debdeep Mitra, Base Hospital Delhi Cantt, New Delhi - 110 010, India.
E-mail: debdeep7@gmail.com

Abstract

Immune reconstitution inflammatory syndrome (IRIS) is a condition during the clinical course of HIV infection in which there is paradoxical worsening and/or new onset of opportunistic infections in a HIV-positive patient who has recently been started on anti-retroviral therapy (ART). We present a case of AIDS with CD4 count of 20 cells/μl who presented within 6 weeks of starting ART with a CD4 count of 160 cells/μl and a painless solitary genital ulcer along with annular dark-colored plaques over soles. His screening test for syphilis was negative both during baseline evaluation, prior to initiation of ART, and during his clinical presentation. His disease was confirmed based on a positive treponema pallidum hemagglutination test report and a suggestive skin biopsy. He responded well to three doses of Benzathine Penicillin and continuation of ART. There are very few case reports of syphilis presenting as IRIS and this case is all the more unique as he had features of both primary and secondary syphilis occurring together within 6 weeks of starting ART. This report would reiterate the fact that syphilis and HIV co-infection can alter the natural course of both the diseases and a high index of suspicion is required for treating them.

Key words: HIV, immune reconstitution inflammatory syndrome, syphilis

INTRODUCTION

Immune reconstitution inflammatory syndrome (IRIS) is a condition during the clinical course of HIV infection in which there is paradoxical worsening and/or new onset of opportunistic infections in a HIV-positive patient who has recently been started on anti-retroviral therapy (ART).[1,2] The other prerequisites are a low CD4 count and a high viral load at the onset of ART. This condition is also noted in patients who have been shifted to a more potent ART regimen and there is an improvement of CD4 count with a paradoxical appearance of new onset opportunistic infections. Although IRIS has been associated with many opportunistic infections including various sexually transmitted infections, recurrence of syphilis has been rarely reported. Here, we report a case of IRIS associated with primary and secondary syphilis in an HIV-positive patient after initiation of antiretrovirals.

CASE REPORT

Our patient is a 48-year-old male, diagnosed with AIDS about 8 weeks back when he was being evaluated for chronic diarrhea, presented with a painless solitary genital ulcer and multiple coin-shaped annular plaques over soles. He denied

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history of any recent high risk sexual behavior. He did not complain of any fever, joint pain, or oral ulcer and had good drug compliance.

At the time of his diagnosis, about 8 weeks back, his HIV viral load was 300,000 copies/ml and CD4 count was 20 cells/µl. He was started on ART 6 weeks back based on his diagnosis of AIDS. His VDRL test and screening tests for other opportunistic infections including tuberculosis, cryptococcosis, and toxoplasma were negative during the initial workup and he did not have any genital ulcer or any skin lesion. He was started on Tenofovir/Lamivudine/Efavirenz therapy along with azithromycin and trimethoprim/sulfamethoxazole prophylaxis. Six weeks after initiation of therapy, the patient returned with complaints of an insidious onset painless solitary genital ulcer and skin lesions [Figure 1]. Repeat VDRL test again was negative during this visit. His CD4 count had increased to 160 cells/µl and his viral load was not detectable. However, due to strong suspicion of syphilis presenting in HIV setting, a skin biopsy was performed and treponema pallidum hemagglutination (TPHA) with titers was ordered. The other differential which was considered was a drug rash including a fixed drug eruption, but the medicines were continued as the rash was not severe and not symptomatic. The skin biopsy demonstrated lichenoid granulomatous infiltrate with swollen endothelial capillary walls and a dense plasma cell infiltrate wit obliterative endarteritis [Figure 2]. His TPHA test was positive with titers of 1:1024. Cerebrospinal fluid examination was negative for neurosyphilis and he did not have any other feature of tertiary syphilis. He was managed with three weekly doses of injection benzathine penicillin 1.2 Mega unit in each buttock intramuscular after penicillin sensitivity testing. His ART was continued and his skin lesions resolved completely 2 weeks' posttherapy. He is current under monthly follow-up for the recurrence of any other opportunistic infection or any other feature of syphilis as treatment failure is known in HIV and syphilis co-infection.

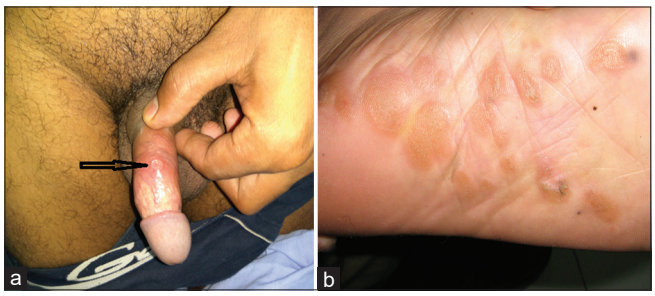

Figure 1: (a) solitary punched on indurated genital ulcer. (b) Annular copper-colored plaques on soles

DISCUSSION

As per literature, the incidence of IRIS varies between 7% and 24% of HIV patients within first 3 months following the initiation of ART.[3,4] The biggest risk factor for developing IRIS is ART naïve patients with low CD4 cunts and a high viral RNA load at the initiation of therapy.[5] Although various infections have been mentioned as manifestations of IRIS, syphilis has very rarely been mentioned in this regard. Neurosyphilis occurring as IRIS has been mentioned in one previous report.[6] Two cases of eye involvement in syphilis occurring as probably a manifestation of IRIS has also been reported before.[6] There are just two case reports mentioning syphilis as IRIS and this seems like the first report wherein the patient had both primary and secondary lesions of syphilis presenting as IRIS.[6-8] This concept of telescoping or occurrence of one phase of syphilis before its natural time of progression, that is, occurrence of primary and secondary stages together has been mentioned in literature in 1933.[9] This phenomenon of telescoping of stages of syphilis was described way beyond the discovery of HIV or penicillin. This case also shows this phenomenon wherein the primary and secondary stages of syphilis have presented together.

The exact pathogenesis of IRIS and reactivation of opportunistic infections despite an improving CD4 count is still not fully understood. Studies have shown a positive correlation between the severity of IRIS and the degree of immune recovery during ignition of ART.[10] Patients prone to develop IRIS are likely to have impairment in their innate immune system impairment that causes their T-cells to produce a cytokine storm in the form of large amount of pro-inflammatory cytokines with exuberant immunological responses to antigenic stimuli.

Co-infection with syphilis and HIV can result in unusual manifestations of syphilis and change the natural course and clinical presentation including

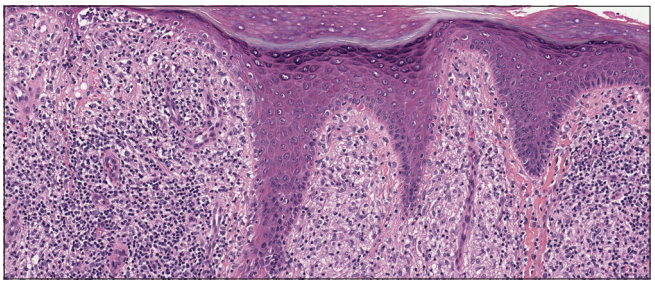

Figure 2: Histopathology picture of skin biopsy on H and E stain showing lichenoid granulomatous infiltrate with swollen endothelial capillary walls suggestive of secondary syphilis lesion; ×100

the laboratory findings of classical syphilis.[11] The negative VDRL report could have been due to hook effect or prozone phenomenon in which an antigen excess had caused a false-negative result. The hook effect or the prozone effect is an immunologic phenomenon whereby the effectiveness of antibodies to form immune complexes is sometimes impaired when concentrations of an antibody or an antigen are very high. The formation of immune complexes stops increasing with greater concentrations and then decreases with extremely high concentrations, producing a hook shape on a graph of measurements.

There are no universally accepted criteria for IRIS, however, the paradoxical appearance of opportunistic infection in HIV-positive patients with low CD4 counts prior to initiation of ART and the temporal profile of appearance of infection after ART therapy and improvement of CD4 counts is considered as IRIS. The possibility of bacterial super infection, drug-resistant infection, or drug reaction should essentially be ruled out before considering an IRIS.

CONCLUSION

Our case adds up one more case of secondary syphilis presenting as IRIS but what was unique in this case was the occurrence of primary and secondary stages of syphilis together along with telescoping of secondary syphilis before the natural timeline of syphilis. IRIS-associated syphilis should be considered in cases of typical genital lesion and skin manifestations of secondary syphilis. The high index of suspicion leads to conducting definitive tests for syphilis despite a negative screening test. Long-term follow-up is vital in syphilis and HIV confection considering treatment failure and latent neurosyphilis is a real time possibility. The presence of an IRIS response does not predict overall HIV or OI treatment responses, and discontinuation of ART is not generally recommended, as the benefits of treating HIV infection outweigh the risk associated with IRIS. Our patient responded successfully to syphilis therapy and was continued on ART with regular follow-ups.

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 initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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