Case Report

Co-infection of syphilis and hepatitis B with carcinoma penis in a human immunodeficiency virus male

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Abstract

Human immunodeficiency virus (HIV) infections have a high probability of co-infections with Syphilis and hepatitis B virus since they share the common routes of transmission. We report a 41-year-old HIV male (on antiretroviral therapy for the past 6 years) admitted for a complaint of penile ulcer for 2 months. Serology for syphilis and hepatitis B were positive. Skin biopsy of the penile ulcer confirmed squamous cell carcinoma. Henceforth, the patient was referred to oncology department for further management. We present this rare combination of syphilis and hepatitis B with carcinoma penis in an HIV patient.

Key words: Co-infection, human immunodefiency virus, syphilis

INTRODUCTION

Currently, India is one of the countries with high number of people living with human immunodeficiency virus (HIV) in (21.17 lakhs in 2015) with national adult HIV prevalence at 0.26%. HIV, hepatitis B virus (HBV), and syphilis are sexually transmitted and share common risk factors. If a person is affected with more than one organism, it is called co-infection.[1] HIV alters the natural course of these sexually transmitted infections (STIs). For example, in syphilis co-infection; (i) secondary syphilis will be more aggressive and there is an increased chances of early neurological and ophthalmic involvement, (ii) possibility of false-negative serology is high, (iii) relapse is more common. In HBV co-infection, HBV escalates HIV replication by activating HIV long terminal repeat with X protein.[2] Hence, monitoring for syphilis, hepatitis B is mandatory in all HIV patients. Here, we report a rare co-infection of syphilis and hepatitis B with carcinoma penis in an HIV male.

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CASE REPORT

A 41-year-old HIV male was admitted to our department for the complaint of genital ulcer for the past 2 months. He was on antiretroviral therapy (ART) for the last 6 years, and his present CD4 count was 360 cells/mm^3. Two months back, he had a small papule in the distal shaft of the penis which gradually developed to an ulcer with intermittent foul smelling, moderate purulent discharge since 20 days. He never had genital ulcers before. There was no difficulty in micturition. History toward major surgeries, blood transfusions, and intravenous drug abuse was unremarkable. He was married since 19 years and lost his wife 7 years back due to carcinoma breast. HIV status of his wife is not known. He becomes promiscuous after his wife's demise. He was survived with his two children; first one male 12 years (HIV-nonreactive), second one-female, 8 years (HIV-reactive, on ART for 3 years).

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On examination, ulceroproliferative (cauliflower-like) growth of size measuring 5 cm × 3 cm was seen in the distal half of the penis obscuring the external urethral orifice. The surface of the lesion was lobulated; margins were well defined to ill-defined, raised edges and purulent discharge from multiple sites. Few areas of necrosis were also seen [Figure 1]. Both sides of the inguinal lymph nodes were enlarged, nontender, and freely mobile. With the above history and clinical features, the clinical working diagnosis was either carcinoma penis or atypical herpes genitalis. Donovanosis was not considered because of the inguinal lymphadenopathy. The patient was empirically started on tablet Acyclovir 400 mg thrice daily. Serology for venereal disease research laboratory (VDRL), hepatitis B and hepatitis C were done. Specific investigations for genito-ulcerative diseases such as Gram-stain, tzanck smear, tissue smear, wet mount, and dark field examination were done to rule out chancroid, herpes genitalis, donovanosis, and syphilis, respectively. Other investigations such as pus culture, chest X-ray, liver function test, renal function test, ultrasound abdomen, and electrocardiogram were also done. Skin biopsy from the edge of the ulcer was taken to rule out carcinoma penis. However, the results were reactive for syphilis (VDRL reactive 1 in 1 dilution); later confirmed with treponema heamagglutination test and hepatitis B (positive HBs antigen, done by enzyme-linked immunosorbant assay). The patient was not affordable for undergoing other HBV viral markers like HBe and HBc antigens. Ultimately, histopathology of the ulcer has confirmed the infiltrating, moderately differentiated squamous cell carcinoma [Figure 2]. Due to the lack of polymerase chain reaction facilities in our setup, human papillomavirus (HPV) could not be identified. For syphilis, the patient was given a single dose of intramuscular injection benzathine penicillin 24 lakh international units after test dose. Eventually, the patient was referred to hepatology and oncology departments for management of HBV and carcinoma penis, respectively.

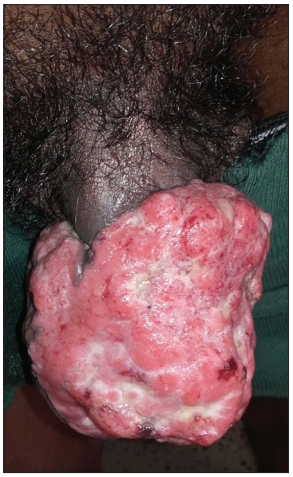

Figure 1: Photograph showing the ulceroproliferative growth in the distal half of the penis

DISCUSSION

Genito-ulcerative STI increases the HIV infection by 2–5 times and HIV, in turn, may augment the acquisition of other STI resulting in "epidemiologic synergy." Many studies have suggested the prevalence of co-infections of syphilis and hepatitis B with HIV. Antala and Joshi reported 27% of HIV patients were co-infected with either syphilis or HBV.[1] Furthermore, in studies by Silverman *et al*.,[3] and Segura *et al*.,[4] the rates of co-infection were 35.1%, 25% respectively. HPV, an oncogenic virus also co-infects HIV. Soares *et al*. stated the co-infection rates of HPV-16, HPV-18 as 60.9%, 46.3%, respectively.[5]

In our case, routine serological screening has picked up the co-infected *Treponema pallidum* and hepatitis B virus. In addition, skin biopsy has confirmed the presence of squamous cell carcinoma of penis, probably due to HPV. Prior infection with HPV-16, 18 is a definite a risk factor for penile cancer.[6] In a large number of case series, HPV identified in penile intraepithelial neoplasia, was between 70% and 100% of lesions and invasive penile cancer was around 40%–50%.[7] Co-infection of HIV-1 and HPV reduces cell-mediated immune response to HPV,[8] aberrantly express interleukin 6, and HIV-encoded Tat protein enhances the expression of HPV-induced E6 and E7 transforming proteins leading to penile cancer.[9] Even though HPV vaccination is 100% effective in preventing HPV-16/18-related vulval neoplasia, it is not useful in prevention penile cancers.[10] Hence, preventive strategies such as circumcision, avoidance of smoking, and unprotected sex are beneficial against penile cancer. Clinical experience alone is inadequate

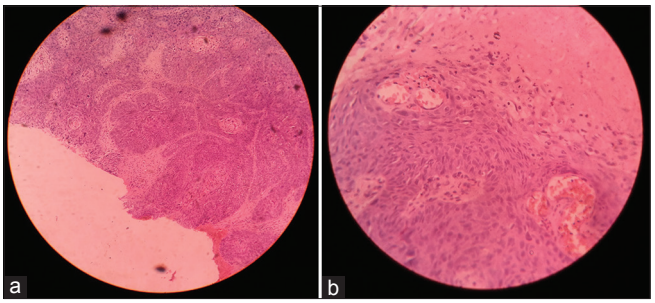

Figure 2: Skin biopsy from the ulcer shows (a) the nests of malignant squamous epithelial cells diffusely infiltrating the stroma and (b) individual cells are polygonal with eosinophilic cytoplasm and round to oval nuclei. Also, keratin pearls are seen

to identify the presence of co-infection in HIV scenario. Therefore, STI screening including HBV, HPV is important for averting the complications like hepatocellular-cariconoma and squamous cell carcinoma.

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Conflicts of interest
There are no conflicts of interest.

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History of syphilis

Syphilis is known since antiquity; perhaps no other disease has amazed and plagued mankind as much as this malady.Sir William Osler has aptly said "He, who knows syphilis, knows medicine."

ORIGIN OF SYPHILIS

It has been known by various names viz Great Pox, morbus gallicus, lues venereum, Polish disease, etc.

It is believed to have acquired its present name from the legend of mythical shepherd, Syphilis, in poem, “Syphilis SiveMorbusGallicus”, described by **Hieronymus Fracastorius** in 1530,who gave clinical description of syphilis and treatment with mercury and guaiacum (south American wood resin). He recounted the tale of a shepherd,Syphilis,who defended Apollo and was punished with foul disease.

Jarisch-Herxheimer reaction is described after **Adolf Jarisch** (1850-1902) an Austrian dermatologist and **Herxheimer** (1861-1942) a German dermatologist. Jarisch in 1895 and Herxheimer in 1902 observed this reaction after the use of mercury for syphilis.It isseen more frequently with the use of penicillins.

The father of modern pathology" **Rudolf Carl Virchow** (1821-1902)documented the range of systemic menifestations and observed that tongue often showed a smooth base in congenital syphilis. This is called as Virchow's sign.

SPECIFICITY OF SYPHILIS AND GONORRHEA

Hunter (1728-1793) was a Scottish surgeon who believed in the Unity or Monist Theory, that is, gonorrhea and syphilis were the same disease. To prove his observation, he conducted a famous experiment in 1767, in which he inoculated himself with matter from a patient who suffered gonorrhea. Ten days later he developed a chancre, followed by secondary syphilis, thus proving his point. It is now believed that the donor had both syphilis and gonorrhea. Since then primary chancre is known as Hunterian chancre or hard chancre. He was later proved wrong by Philippe Ricord in 1838.