Secondary Syphilis in a HIV positive patient masquerading as Reiter's Syndrome

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Abstract
Co-infection of syphilis and HIV is common, however a few cases present with features of active syphilis. HIV infection may alter the manifestations of syphilis and may present with unusual manifestations. We present a case report of secondary rupeiod syphilis in a HIV infected patient mimicking Reiter's Syndrome. A 28 year-old male of African descent presented with urethritis, arthritis and keratoderma blenorrhagica as well as a symmetrical psoriasiform eruption and circinate balanitis. He was recently seropositive for HIV. The patient was accurately diagnosed by using a combination of clinical findings, serology and histopathology. He was successfully treated with Benzathine penicillin. The significance of accurate diagnosis and treatment of a potentially fatal disease is described.

INTRODUCTION
Syphilis and human immunodeficiency virus (HIV) infections are frequently encountered in sexually transmitted infections (STI) clinic. Co-infection is not uncommon due to the similarities in transmission of the infections. Syphilis is well known as a great mimic in clinical medicine. HIV-infected patients with secondary syphilis present with concomitant genitals ulcers more frequently. The presentation of Syphilis may be altered by the presence of HIV infection due to abnormalities of the immune status resulting in unusual presentations rendering accurate diagnosis a challenge. Reiter's syndrome typically presents as a triad of seronegative arthritis, nongonococcal urethritis and conjunctivitis associated with an antecedent genitourinary or gastrointestinal infection. Reiter's syndrome associated with HIV infection has also been reported. Syphilis masquerading as Reiter's syndrome in a HIV infected patients is rare and fewer than five case reports are noted in the literature thus far. The significance of this entity lies in the accurate diagnosis and institution of appropriate treatment.

CASE REPORT
A 28 yr old male of African descent presented at our STI clinic with skin rash, genital ulcers and urethritis. He was diagnosed as positive for HIV infection two weeks prior to the presentation. The skin rash first appeared as small itchy papules on his face and in a month the rash spread widely to the neck, arms, trunk and lower limbs. The skin rash appeared as polymorphic eruption covered with silvery white scales. Bilaterally symmetrical thick hyperkeratotic lesions were present on the sole of the feet typical of Keratoderma blenorrhagicum. Palms showed only few scattered papules. He also had dysuria and urethral mucopurulent discharge during the same period. The uncircumcised penis was partially phimosed. Genital ulcers measuring 0.5x0.5cms were present on the glans penis and coronal sulcus mimicking circinate balanitis. Erythema and scaling were also noted on the glans penis. Thick scrotal plaques with scaling and foci of oozing associated pain were present. Nails and scalp were distinctly spared. His right knee joint was swollen and painful. There was no evidence of ocular involvement. Split papules at the angles of the mouth were present. Physical examination revealed bilateral inguinal adenopathy, and reducible left indirect inguinal hernia. Oral cavity revealed poor hygiene but no ulcers or mucosal patches were noted. Cardiovascular, respiratory, abdominal and neurological examination was within normal limits. The patient reported multiple sex partners and was addicted to Marijuana. He had tried herbal medicines before he presented to our clinic. Routine investigations: CBC – Hb: 11.4gm/dl, white cell count – 4600/µl, Platelet count –165,000/µl and urinalysis was normal. Urethral smear showed many pus cells, hence patient was treated with ceftriaxone 250mg Stat intramuscularly after test dose. Later culture from urethral smear was positive for Neisseria Gonorrhoeae and treated with ceftriaxone 1g intramuscularly.
swab was negative for gonorrhea. CD4 count was 235 cells/µl. The viral load was 203,000 copies/ml. VDRL was positive at a titer of 1:256, and Microhemagglutination antibody test for Treponema pallidum (MHA-TP) was positive. Dark field examination was negative.

A skin biopsy was performed from a lesion on the upper arm after obtaining an informed consent. Histology revealed mild hyperplasia of epidermis with focal exocytosis. Epidermal dermal interface is altered with prominent upper dermal lympho-histiocytic infiltrates mixed with plasma cells. The inflammatory cell infiltrates were predominantly perivascular and periadnexal in location (Fig. 6). The histological features were consistent with secondary syphilis. The patient was finally diagnosed as having psoriasiform secondary syphilis mimicking Reiter's syndrome with CDC clinical category B - HIV infection. The patient was treated with two doses of Benzathine penicillin 2.4 MU intramuscularly after a test dose on consecutive weeks. One week following the penicillin there was marked improvement in the skin and genital lesions (Fig 2-5.) He was also referred for treatment of HIV infection. Four months later there were only post-inflammatory hyperpigmented healed lesions remaining. The symptoms of urethritis and arthritis had resolved and the VDRL was non-reactive.

Figure 1
Figure 1: Penile ulcers and Left inguinal hernia

Figure 2
Figure 2&3: Psoriasiform skin eruption – before and after treatment

Figure 3
Figure 4
Figure 4&5: Keratoderma of sole of the feet before and after treatment with penicillin

Figure 5

Figure 6
Figure 6: Histology of skin biopsy shows nodular collections of lympho-histiocytic infiltrates mixed with plasma cells around blood vessels and adnexa in the dermis. (H&E; 10x)

DISCUSSION
Arthrocutaneous disorders, which include Reiter's Syndrome, Psoriasis and chronic arthritis, are prevalent in association with HIV (Human Immunodeficiency Virus) infection. Prevalence of Syphilis along with HIV infection due to similarities of transmission is well documented. HIV infection may influence the clinical picture, course and therapy of concurrent syphilis. Syphilis is known to cause substantial morbidity and increase in risk of spread of HIV
infection. Rare manifestations of secondary syphilis mimicking arthrocutaneous disorders like Reiter's Syndrome have been reported. Our patient who was recently diagnosed of having HIV infection manifested with clinical features of uveitis, arthritis and keratoderma blenorrhagica suggesting Reiter's Syndrome. Nearly a third of the cases of Reiter's syndrome may not show the complete triad.

Patients with unusual manifestations of secondary syphilis may be misdiagnosed or the diagnosis delayed. A high index of clinical suspicion is required for an accurate diagnosis. Demonstration of aetiologic agent or culture in vitro is rarely accomplished. Hence the diagnosis was relied on clinical findings, serology and biopsy findings. Patients with HIV infection may have a high rate of false negative serology for syphilis and sometimes may have false positive reactions. They may also remain seropositive for non-treponemal antibody after therapy. Hence the serological results have to be interpreted with due care along with other findings. In our patient, high titer for VDRL (Venerale Disease Research Laboratory testing) and positive test for specific treponemal antibody (MHA-TP) in conjunction with histological findings confirmed the diagnosis of Syphilis.

It has been reported that as many as 70% of HIV infected patients have histories or serologic evidence of syphilis but only a few have described active syphilis. Patients who are seropositive for HIV more often present in the secondary stage and have more aggressive course. This may suggest that HIV infection may alter the humoral response to the second pathogen and in a few cases may present with atypical findings. Comparison of cases reported in the literature having features mimicking Reiter's syndrome indicates that this presentation has no predilection to any ethnicity or association with the CD4 count. The CD4 count in our case was 235cells/µl compared to 147cells/µl reported by Mitsumasa K et al.

Most reports have shown a favorable response to treatment with penicillin, although some patients were also prescribed prednisone at the same time. The dramatic response within three weeks to benzathine penicillin without steroids in our case demonstrates the therapeutic impact of accurate diagnosis. It also confirms the diagnosis of syphilis because other arthrocutaneous disorders like Reiter's syndrome do not respond to penicillin.

It is interesting to note that the cases reported thus far have overlapping features, which include: a) usually manifest in the 3rd – 4th decade of life, b) diagnosed as secondary syphilis, c) have keratoderma blenorrhagica with scaly psoriasiform symmetrical skin rash, d) associated with asymptomatic or early clinical stages of HIV infection, d) showed good response to penicillin despite immunosuppressed state. Considering that the above-mentioned features and more similar cases being reported in the literature could indicate a distinct manifestation of Syphilis in HIV infection. This type of psoriasiform secondary syphilis, which mimicks Reiter's Syndrome has also been called "rupeiod syphilis."

Summary: We report a case of unusual manifestation of syphilis in a HIV infected patient with features mimicking Reiter's Syndrome. The diagnosis was confirmed by a combination of clinical presentation, serology and histopathology followed by a remarkable clinical response to penicillin treatment. This report highlights the importance of recognition of unusual manifestations and the therapeutic implications of syphilis with HIV infection.

References
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