Onycho-mucocutaneous syndrome secondary to human immunodeficiency virus disease

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Abstract

Cutaneous, mucosal, and nail examination is the key to unveiling a plethora of systemic diseases. Mucocutaneous lesions directly related to human immunodeficiency virus (HIV) infection usually present as initial manifestations of immune deficiency, of which few lesions act as predictors of an immunocompromised state. Here, we report two cases who presented with onycho-mucocutaneous symptoms which raised the suspicion of and invariably led to the diagnosis of an underlying immunosuppression secondary to HIV infection.

Key words: Extensive dermatophytosis, human immunodeficiency virus, onycho-mucocutaneous syndrome, oral hairy leukoplakia, proximal subungual onychomycosis

INTRODUCTION

Skin, hair, and nail are an index to underlying systemic disease. Mucocutaneous lesions directly related to Human Immunodeficiency Virus (HIV) infection usually present as initial manifestations of immune deficiency. More than 90% of HIV-infected individuals show cutaneous manifestations of HIV during their disease course.[1] The diagnosis of these dermatoses might pose a challenge since these patients present with atypical manifestations. Here, we report two cases who presented with onycho-mucocutaneous symptoms which aided in clinching the diagnosis of HIV infection and early initiation of antiretroviral therapy (ART).

CASE REPORTS

Case 1

A 50-year-old male, forest security personnel, presented with generalized pruritic rashes since 1 year. Lesions initially began over the lower abdomen and later became generalized. He had used multiple topical and oral steroids for the same. For the past 1 month, he developed fever, breathlessness, and chest pain for which he sought medical attention.

Cutaneous examination revealed multiple confluent erythematous scaly plaques distributed symmetrically over the trunk and extremities, with few areas having well-defined margins. Multiple pearly white umbilicated papules were present over the forehead and bi-temporal areas. Oral mucosa showed whitish plaques on the dorsal aspect of tongue, which on rubbing revealed bleeding spots. Whitish

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discoloration with roughening was noticed at the proximal part of the right thumbnail [Figure 1].

Based on the clinical features, a provisional diagnosis of exfoliative dermatitis due to dermatophytosis with proximal subungual onychomycosis (PSO), extragenital molluscum contagiosum (MC), and chronic oral pseudomembranous candidiasis was made. Internal medicine work-up was carried out and a diagnosis of sepsis and bilateral tubercular pleural effusion was made. Ophthalmological examination revealed choroid tubercles, which were suggestive of intraocular tuberculosis.

Potassium hydroxide (KOH) mount from skin scrapings and nail clippings revealed multiple septate hyphae and fungal culture grew *Trichophyton mentagrophytes*, thus confirming dermatophytic infection [Figure 2].

The patient gave a history of high risk sexual behavior. Based on clinical suspicion and several dermatological indicators of HIV infection, serology for HIV was done. The patient was found to be HIV 1 positive with a CD4 count of 57cells/mm^3. Venereal disease research laboratory and HBsAg were nonreactive.

We treated the patient with topical luliconazole, ART (Tenofovir + Lamivudine + Efavirenz) and intravenous fluconazole. He was also started on Category 1 antitubercular therapy. Molluscum lesions were curetted and treated topically with retinoic acid (0.05%).

Case 2

A 32-year-old male presented with complaints of spontaneous grayish-white discoloration of the right thumbnail since 1 month and painful ulcers on the genitals since 2 weeks, which were initially fluid filled. History of unprotected sexual intercourse with multiple partners was present. There was no history of prior drug intake.

On cutaneous examination, multiple erythematous to hyperpigmented, annular and polycyclic, scaly plaques were distributed over the bilateral crural folds, thighs, and trunk.

Whitish corrugated plaques over the lateral aspect of the tongue, diagnostic of oral hairy leukoplakia (OHL) was present. He had multiple, well-defined, discrete, exudative erosions over the penile shaft and glans, suggestive of herpes genitalis. Grayish-white discoloration of the proximal and lateral aspect of left thumb nail plate was indicative of PSO [Figure 3].

Tzanck smear from the genital erosions showed multinucleated giant cells, confirming the diagnosis of herpes genitalis. Multiple branched hyphae were visualized in the KOH mount taken from skin scrapings and fungal culture grew *T. mentagrophytes*.

With this background of multifarious dermatoses, HIV co-infection was suspected. Serology for HIV 1 was found to be reactive.

The patient was treated with oral acyclovir and itraconazole. He reported good improvement with the same. He was further referred to integrate counseling and testing center for initiation of ART.

Figure 1: Case 1 showing: (a) Extensive dermatophytosis; (b) Extragenital molluscum contagiosum; (c) Oral pseudomembranous candidiasis; (d) Proximal subungual onychomycosis of right thumbnail

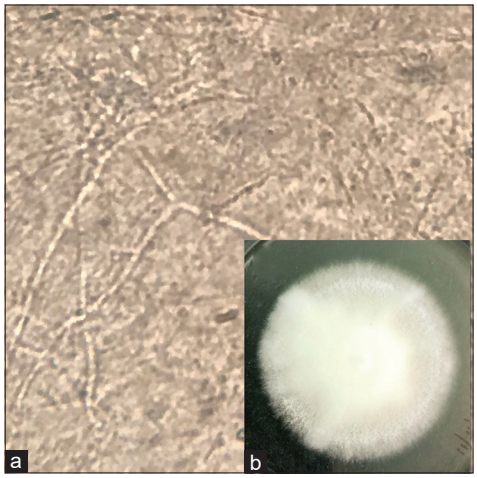

Figure 2: Skin scrapings showing: (a) Multiple septate hyphae on potassium hydroxide mount; (b) *Trichophyton mentagrophytes* growth on Sabouraud's dextrose agar

DISCUSSION

In a patient with HIV disease, oncho-mucocutaneous lesions often give inkling to the diagnosis. The diverse pattern of oncho-mucocutaneous infections seen in HIV is listed in Table 1. Dermatoses in HIV have unusual clinical presentations such as generalized involvement, aggressive clinical behavior, recalcitrance, resistance, recurrence, atypical presentation, isolation of unusual organisms, and chronicity.

HIV-related cutaneous manifestations serve as visual indicators of diagnosis and progression of the disease.[2] The prevalence of dermatophytosis is four times higher among HIV-infected population. Extensive dermatophytosis is a chronic fungal infection with the involvement of multiple body areas. *Trichophyton rubrum* and *T. mentagrophytes* are the most common dermatophytes isolated in HIV-infected patients.[3]

MC is usually self-limiting in immunocompetent individuals, but in HIV it behaves differently. Extragenital MC is frequently seen in adult patients with HIV, making it an indicator of an underlying immunocompromised state.[4]

Figure 3: Case 2 showing: (a) Herpes genitalis; (b) Oral hairy leukoplakia over lateral aspect of tongue; (c) Proximal subungual onychomycosis of left thumb nail plate

The prevalence of onychomycosis in HIV infection is 15%–40% and may be directly related to the degree of immunosuppression.[5] PSO is pathognomic of HIV infection. It is mostly caused by *T. rubrum*, but species like *T. mentagrophytes* have also been isolated. It is more frequently seen when the CD4 count falls <450 cells/mm^3.[6] The presence of PSO should always raise a suspicion of an underlying HIV infection.

Oral lesions are one of the earliest and important manifestations of HIV. They can be a predictor of disease progression into acquired immunodeficiency syndrome (AIDS). Pseudomembranous candidiasis is the most common fungal infection in HIV disease and is a marker of severity of infection. A fall in CD4 count or increase in HIV viral load leads to an increased frequency of oral candidiasis. OHL, caused by Epstein-Barr virus, is almost an exclusive disease of HIV, especially in untreated, undiagnosed patients. It is a hallmark of moderate to advanced immunosuppression.[7,8] The incidence of OHL has decreased considerably with the advent of ART.

Genital ulcer disease (GUD) is biological cofactor in the acquisition and transmission of HIV.[9] HSV-2 is a major cause of GUD. Chronic herpetic ulcers of >1 month duration are an AIDS defining illness.[10] Hence, genital examination is mandatory in every patient, suspected to have HIV infection.

CONCLUSION

We coined the term "oncho-mucocutaneous" syndrome in HIV disease to signify the increased chances of simultaneous involvement of the skin, mucosa, and nail in an HIV infected individual. We recommend that the presence of an oncho-mucocutaneous syndrome should alert a clinician to habitually investigate for a probable milieu of immunocompromised due to HIV infection.

Table 1: Oncho-mucocutaneous infections in human immunodeficiency virus disease[1-5]

Cutaneous	Mucosa	Nails
Herpes simplex virus infection	Oral hairy leukoplakia	Proximal subungual onychomycosis
Herpes zoster	Oro-esophageal candidiasis	Persistent necrotic digits secondary to HSV infection
Extragenital/giant mollusca	Genital and oral herpes simplex	Paronychia
Recurrent pyodermas	Gangrenous stomatitis	Yellow nail syndrome
Extensive dermatophytosis	Mucosal lesions of systemic mycoses	
Kaposi sarcoma	Kaposi sarcoma	
Viral warts	Acute necrotizing ulcerative	
Cutaneous lesions of systemic mycoses	stomatitis, gingivitis or periodontitis	
Extrapulmonary (cutaneous) tuberculosis		

HSV=Herpes simplex virus

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.

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Conflicts of interest

There are no conflicts of interest.

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