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Cutaneous manifestations associated with unknown HIV infection: a case report

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Abstract

Cutaneous manifestations are extremely common in people living with human immunodeficiency virus (PLHIV), and sometimes, these manifestations can help with the diagnosis. In the advanced stages of the infection, the impairment of the immune system can increase susceptibility to cutaneous infections. We present the case of a patient affected by an unknown advanced human immunodeficiency virus (HIV) infection whose diagnosis was made through skin manifestations.

Introduction

Cutaneous manifestations are extremely frequent in people living with human immunodeficiency virus (PLHIV). These may include specific skin eruptions (such as itch, acne, folliculitis, and acute retroviral syndrome rash), opportunistic infections, and malignancies.¹ Identification of typical skin manifestations or the presence of severe and recalcitrant dermatoses can ease early diagnosis of human immunodeficiency virus (HIV) infection. On the other hand, the development of neoplastic and/or opportunistic infections may alert the physician to the impairment of the immune system due to the virus (acquired immunodeficiency syndrome [AIDS]).²

We present the case of a male patient affected by an unknown advanced HIV infection (late presenter), whose diagnosis was made through skin manifestations.

Case Report

A 36-year-old Caucasian male patient was referred to our dermatological outpatient clinic for toenail alterations and psoriasiform dermatitis of the feet, both present for several months. The dermatological evaluation revealed the presence of erythematous, scaly, and itchy dermatitis, with severe xerosis, of both feet associated with dystrophic toenails (Figure 1 A,B). The patient had been previously treated with topical steroids with unsatisfactory results and worsening clinical manifestations. Moreover, a reddish, rapidly growing nodule of the plantar area of the left foot was found. (Figure 1C)

On suspicion of dermatomycosis, a microscopic examination was performed, showing the presence of *Trichophyton rubrum*. Moreover, the microscopy also revealed the presence of mites and eggs of *Sarcoptes scabiei* from scraping the cutaneous lesions, and a diagnosis of Norwegian scabies was made. Treatment with systemic ivermectin (200µg/kg/dose PO) and topical permethrin 5% cream was started, with rapid clinical improvement and reduction of pruritus. Treatment with systemic ivermectin was also repeated after 10 days.

Furthermore, a biopsy of the plantar nodule and histological examination established the diagnosis of Kaposi's sarcoma.

The presence of three different skin manifestations at the same time may indicate an immune system deficiency. An evaluation for infectious and venereal diseases was conducted, and serology revealed a positive HIV test, confirming a diagnosis of AIDS.

The patient was taken into care by the STI & HIV Unit of our Institute for the staging of HIV-related disease. At the baseline, blood tests revealed a CD4⁺ count of 14 cells/ μ L, and the HIV viral load was 2506128cp/mL. Moreover, the human herpes virus (HHV)-8 viral load was undetectable despite the positivity of HHV-8 antibodies. Given the severe immunodeficiency, it was necessary to exclude other opportunistic infections before starting antiretroviral therapy (ART) to avoid immune reconstitution syndrome (IRIS).³ *Fundus* examination was negative; QuantiFERON-TB Gold test was negative, and *Cryptococcus neoformans* antigen test was also negative. An abdominal ultrasound scan revealed numerous miliary nodular lesions in the liver and spleen. A liver biopsy was performed, and histological/microbiological examination revealed the presence of diffuse granulomatous lesions and *Mycobacterium avium complex* (MAC) disseminated infection; therefore, immediate antimycobacterial treatment was started with rifabutin, azithromycin, and ethambutol.

Esophagogastroduodenoscopy was negative. Nevertheless, the colonoscopy revealed 4 purple and nodular lesions in the descending colon and sigma. Endoscopic biopsies confirmed the diagnosis of visceral Kaposi's sarcoma, and the patient immediately underwent oncology care and chemotherapy with doxorubicin. Because of potential drug-drug interactions between antivirals, doxorubicin, and anti-MAC therapy, ART was initiated with an interaction-free regimen: dolutegravir plus emtricitabine and tenofovir disoproxil fumarate that has been well tolerated. After 9 months from the beginning of ART, the HIV viral load undetectability was obtained (HIV RNA<30cp/mL), since the patient had been fully compliant with the prescribed therapies. Nonetheless, within the first 3 months of ART, we documented a worsening of the known skin lesions, some of which took on an exophytic appearance, becoming larger. This phenomenon is well known in the literature and consists of a paradoxical IRIS on Kaposi's lesions (Figure 2).⁴ At the moment, after almost a year, the patient is adherently taking ART, and he is still on anti-MAC therapy and doxorubicin, with a good response to the therapies.

Discussion

In Italy, a gradual increase in the incidence of HIV diagnoses has been observed in recent years. During 2023, 2349 new HIV infections were recorded, with an incidence of 4.0 new diagnoses per 100,000 residents. In the same year, heterosexual transmission accounted for 47.7% of reported diagnoses, followed by sex between men and injecting drug use. However, the highest number of

diagnoses was recorded among men who have sex with men (MSM), due to risky sexual behavior, followed by men who have sex with women (MWW) and women who have sex with men (WSM). Unfortunately, the proportion of individuals with late-diagnosed HIV infection has been constantly increasing. In 2023, more than one-third of newly diagnosed cases have been diagnosed due to the presence of HIV-related symptoms, compared to only one-fifth due to risky sexual behavior. To date, HIV prevention and treatment programs need to be improved in order to ensure early diagnosis and the efficiency and quality of care. Late HIV diagnosis is associated with increased development of HIV morbidity and mortality (such as opportunistic infections and malignancies) and poor response to antiretroviral treatments, as well as increased risk of HIV transmission and high costs for society.⁵ Increased susceptibility to cutaneous infections is extremely common in PLHIV, especially in the context of AIDS, due to impairment of the immune system. Lower levels of CD4⁺ are associated with the development of opportunistic infections, including herpetic, cryptococcal, and mycobacterial infections.⁶

Kaposi's sarcoma is a low-grade vascular tumor that can be HIV-related (epidemic form), which can affect mucocutaneous areas and visceral organs. It typically reveals the advanced immunosuppression occurring in the late stages of HIV infection.

Conclusions

This case report underlines that many different skin disorders may be present in HIV-advanced naïve patients, ranging from deep fungal infections to parasitic infections such as scabies or viral reactivation of herpes viruses (HHV-8, HSV, VZV). Depending on the patient's immune status, these skin disorders may appear similar to those seen in immunocompetent patients or unusual and difficult to recognize. In any case, the skin represents the scenario where all kinds of diseases could manifest, and every medical professional who takes care of these persons must consider these cutaneous diseases as signs of serious underlying medical conditions, such as AIDS.

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Figure 1. A, B) Scaly and itchy dermatitis, associated with xerosis, of both feet associated with dystrophic toenails; C) a reddish rapidly growing nodule of the left foot.



Figure 2. Paradoxical IRIS on Kaposi's lesions: worsening of the skin lesion within the first 3 months of ART.