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Skin and mucosal lesions in the course of HIV infection

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Abstract

Introduction:

Dermatological conditions are prevalent expressions of HIV and AIDS, often aiding in initial diagnoses due to their visibility on the skin and mucous membranes. Given HIV's primary transmission through sexual contact, dermatologists play a crucial role in identifying and managing these infections. Understanding the range of skin and mucosal lesions occurring throughout the course of the disease is vital, particularly as these symptoms can manifest in atypical ways or even precede other signs of immune deficiency. While most associated skin disorders can be treated in outpatient settings, some severe conditions significantly impact health outcomes.

Aim of the study:

The study aims to consolidate knowledge on the typical manifestations of HIV on the skin and mucous membranes, providing a comprehensive overview of these disease entities. The most common skin and mucosal symptoms associated with HIV infection are summarized and described.

Materials and methods:
The literature available in the PubMed database was reviewed using the following keywords: “HIV”, “AIDS”, “Skin lesions”, “Mucosal lesions”.
Conclusions:
Skin conditions are widespread in HIV-infected individuals, often displaying heightened severity compared to the general population. While many of these dermatological issues aren't unique to this group, their manifestations can be more pronounced. HIV-related skin problems vary widely, including specific eruptions linked to AIDS, opportunistic infections, and AIDS-related cancers. Although some HIV-associated skin diseases have decreased due to antiretroviral therapy, there's been a noticeable increase in drug reactions and other non-infectious skin conditions.
Key words: HIV; Skin Diseases

Introduction

Dermatological conditions rank as one of the most common expressions of HIV infection and acquired immunodeficiency syndrome (AIDS). The primary route of spread of HIV infection is through sexual contact, hence dermatologists play a key role in combating these infections. Knowledge of the skin and mucosal lesions that occur in the course of HIV infection and AIDS is of great practical importance, as many patients are initially diagnosed on the basis of clinical symptoms. This is true both in the early stages of infection, when lesions are uncharacteristic, and in later stages, when clinical lesions are the first sign suggestive of cellular immune disorders, especially when rare dermatoses are found, and skin and mucosal diseases have an unusual clinical picture and course. The majority of skin disorders associated with HIV/AIDS can be effectively treated in outpatient settings. Nevertheless, certain conditions contribute substantially to illness and death[1][2].

The purpose of the study is to summarize the available knowledge about typical cutaneous and mucosal manifestations of HIV infection. The disease entities were described and summarized.

Epidemiology

Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) affects a significant number of individuals - it can be called a global pandemic. As per the 2018 Global HIV & AIDS statistics, around 36.9 million people are currently living with HIV worldwide. Since the onset of the epidemic, approximately 77.3 million [59.9 million–100 million] individuals have contracted HIV, with 35.4 million [25.0–49.9 million] succumbing to AIDS-related illnesses. In the year 2017 alone, 940,000 [670,000–1.3 million] people lost their lives to AIDS-related illnesses[2]. The significant reduction in the number of patients with AIDS deaths in recent years(by as much as 48% compared to 2005) is primarily related to the increasing use of antiretroviral therapies.

The most common skin and mucosal lesions in the course of HIV/AIDS

Pruritus - the prevailing skin-related symptom mentioned by individuals with HIV[3][4]. Papular pruritic eruption (PPE), the most common dermatologic symptom in individuals with HIV, is distinguished by persistent symmetric papular eruptions on the limbs, trunk, and occasionally the face. Although the precise cause of PPE remains unknown, studies have revealed a connection between lower CD4 cell counts, heightened pruritus, and increased severity of the rash[5].

Bacterial infections - Even with enhanced management of the disease, infections remain a significant source of morbidity in individuals living with HIV. Several infections that are widespread in the general population seem to exhibit increased resistance or persistence among patients with HIV. The most common bacterial diseases found in HIV-positive patients are:

Bacillary angiomatosis - caused by Bartonella quintata and B.henselae. Bartonella henselae typically results in superficial skin lesions, whereas B. quintana is more prone to trigger subcutaneous, deep, and lytic bone lesions. The lesions are red papules, nodules and infiltrative lesions ulcerating or penetrating deep into tissues.

Cutaneous tuberculosis - caused by Mycobacterium tuberculosis. Manifestations of the condition encompass various forms, such as papulonecrotic tuberculid, lupus vulgaris,

tuberculous chancre, tuberculosis verrucosa cutis, scrofuloderma, orificial tuberculosis, lichen scrofulosorum, nodular granulomatous phlebitis, erythema induratum of Bazin, miliary tuberculosis, and metastatic tuberculosis abscess. Timely identification and treatment of cutaneous tuberculosis are especially crucial in widespread miliary tuberculosis, as this condition is associated with an unfavorable prognosis[6].

Nontuberculous mycobacteria (NTM) - documented to trigger skin lesions in individuals with HIV encompass Mycobacterium avium complex, M. kansasii, M.haemophilum, M.colombiense, M.shigaense, and M.malmoense. Clinical characteristics of NTM-related skin issues involve panniculitis, lesions resembling ecthyma gangrenosum, recurrent cellulitis, as well as erythematous papules, plaques, or nodules, and manifestations similar to Buruli ulcer[7].

Syphilis - may have a different clinical picture in HIV-infected patients, and serological reactions may be inadequately low or high compared to syphilis in the general population. Its course is usually more rapid and aggressive. In first-episode syphilis, primary giant, gangrenous and multiple ulcers are often found. In second-period syphilis, primary symptom persistence is observed until recurrent lesions develop. Central nervous system involvement is also more common.

Viral infections

Herpes simplex virus (HSV) - long-lasting skin lesions caused by HSV lasting more than a month, causing ulceration, meet the criteria for a Category C diagnosis of AIDS. In people who participate in passive anal sexual activity, herpes often appears in the anal area, anal canal and rectum. Such symptoms can cause rectal bleeding and discharge of a mucous-bloody substance. They are usually accompanied by significant discomfort, pain in the sacral area and high fever. HSV-induced lesions in the mouth can also progress aggressively, causing extensive erosions or even esophageal involvement [8].

Human papillomavirus (HPV) - HPV-associated cervical precancerous lesions (CIN2/3) are classified as Category B symptoms for HIV/AIDS diagnosis, while invasive cervical cancer falls under Category C. HIV-infected women are more likely to experience

high-grade dysplasia lesions on the cervix (CIN2/3), vulva (VIN2/3), vagina (VaIN2/3), anus (AIN2/3), penis (PIN2/3), as well as invasive cancers in these areas. People with HIV can develop large and persistent genital warts, which can grow to resemble giant Buschke-Löwenstein condylomas. The recurrent occurrence of HPV-induced lesions is also a problem [9].

Molluscum contagiosum virus (MCV) - in people with HIV, infectious mollusks can reach much larger diameters (as much as 2-3 cm) than in the general population, and can also occur in large numbers. Although in adults without HIV, infectious molluscum appears mainly in the genital area, in people with HIV/AIDS, lesions can also appear on the face, scalp, neck and chest, and can even recur despite treatment [10].

Chickenpox virus infections - chickenpox in people with HIV is more severe, and complications can include involvement of internal organs, which is often associated with a poorer prognosis, especially in children. Hemiplegia in people with HIV can be recurrent and differs from the form seen in the general population by involvement of two or more dermatomes or the diffuse nature of the lesions (chickenpox-like symptoms all over the body). Often the lesions are deeper, cause large ulcerations and lead to significant necrosis, leaving scars after healing [11].

Cytomegalovirus (CMV) - in people with HIV, cytomegalovirus-related skin lesions are less common, usually as macular rashes. Organ manifestations may include pneumonia, gastric ulcers, hepatitis, encephalitis, retinitis and choroiditis [12].

Hairy leukoplakia - leukoplakia manifests as white, raised papules that occur most often on the sides of the tongue, but can also appear in other areas of the mouth. They differ from yeast plaques in that they cannot be wiped off the surface of the tongue. Their formation is associated with excessive growth of all layers of the epithelium. Epstein-Barr virus (HHV-4) plays a role in the development of these lesions [13].

Other common dermatoses - certain common skin conditions, like seborrheic dermatitis, are documented more frequently in individuals with HIV compared to the general population.

Seborrheic dermatitis(SD) - SD associated with HIV may exhibit increased severity and resistance to typical treatments, such as mild topical corticosteroids and topical azoles, leading to more frequent relapses. Additionally, the scales are often thicker and more yellowish, and erythroderma tends to occur more frequently in HIV-related seborrheic dermatitis[14]. Nevertheless, the majority of instances of seborrheic dermatitis linked to HIV show improvement with antiretroviral therapy (ART); hence, prompt identification of HIV infection can enhance the overall prognosis[15].

Atopic dermatitis - a dermatitis resembling atopic condition is prevalent among individuals with HIV, particularly in pediatric cases. This occurrence is more frequent in individuals with a family history of atopy. It is important to note that in situations involving adult-onset or widespread eczematous skin conditions accompanied by lymphadenopathy and constitutional symptoms, HIV infection should be ruled out[16].

Psoriasis - a systemic inflammatory condition with physical and psychological implications, can serve as an initial indicator of HIV infection. Among individuals with HIV, psoriasis is inclined to be more intense, exhibit unconventional manifestations, and display elevated rates of treatment failure with conventional prescribed therapies. Nails involvement is more prevalent and conspicuous in psoriasis associated with HIV. Additionally, it may be accompanied by pruritis and arthritis in patients with this condition. Immune dysregulation associated with HIV may be accountable for the development of psoriasis in individuals with this infection[17].

Fungal infections - various fungal infections manifest at varying levels of immune compromise in individuals with HIV. Typical presentations like tinea (affecting any part of the body), onychomycosis, and candidal infections may emerge early but are more prone to be severe, exhibit atypical characteristics, and show reduced responsiveness to treatment.

Sporotrichosis - fungal infection primarily characterized by cutaneous lesions in individuals with a healthy immune system. Nevertheless, immunocompromised patients, including those with HIV, often experience disseminated cutaneous or systemic involvement[18].

Candidiasis - usually aggravated among HIV-positive patients, most infections are caused by Candida albicans. In the Polish population and in many European countries, HIV-infected people very quickly develop symptoms of chronic candidiasis[19].

Pityrosporum folliculitis and **pityriasis versicolor** - two conditions resulting from Malassezia yeasts, which are typically present in the normal skin microflora. Pityrosporum folliculitis leads to an inflammation resembling acne around the hair follicles, while pityriasis versicolor induces hyper- or hypo-pigmented lesions on the skin. In the course of HIV infection, pityriasis versicolor can occupy not only the neck and upper chest, but also the skin on the abdomen, in the groin and even the popliteal fossae[20].

Talaromyces marneffei - formerly known as Penicillium marneffei, is a systemic fungal infection typically documented in individuals with compromised immune system, particularly those with AIDS. However, it is predominantly observed in endemic regions, such as China and Southeast Asia. This opportunistic infection is characterized by the prevalent appearance of generalized papular lesions resembling molluscum contagiosum, which can pose a challenge in distinguishing it from cryptococcosis and histoplasmosis[21].

Parasitic infections

Scabies - often associated with inadequate hygiene. Papular, erythematous, erythematous-exfoliative lesions are disseminated and, in addition to their typical location in the interdigital spaces of the hands, can occupy the trunk, palms and soles, limbs and scalp. The disseminated variety of scabies, which also occurs in other immunosuppressed states, is called Norwegian scabies. The lesions are prone to recurrence. Due to the highly contagious nature of crusted scabies and the possibility of achieving a full cure through suitable therapy, there should be a strong suspicion of this condition in AIDS patients, even in cases where the lesions do not exhibit the typical appearance[22].

Demodicosis - caused by a parasite of the genus Demodex, which inhabits hair follicles and causes inflammation in them. Typical symptoms involve the loss of hair, itching, and inflammation. Additionally, there has been an observed connection with pityriasis folliculorum[23]. Demodex folliculorum infection also causes eosinophilic folliculitis, which is a rare but very characteristic symptom of HIV infection and AIDS[24].

Cutaneous leishmaniasis(CL) - resulting from the protozoa of the Leishmania species, is not inherently an opportunistic infection. However, its reactivation or exacerbation is more prevalent in immunosuppressed individuals. In the context of HIV-positive patients, visceral leishmaniasis can also disseminate and give rise to skin lesions[25].

Kaposi's sarcoma - historically, before the development of highly active antiretroviral therapy (HAART), 30% of patients developed Kaposi's sarcoma during the course of AIDS. There are four clinical epidemiological categories: epidemic-acquired immunodeficiency syndrome (AIDS)-related KS, iatrogenic KS, classic sporadic KS and endemic KS[26]. The HIV/AIDS-related course differs significantly from the course and clinical picture of classic and endemic KS. Primary skin lesions usually involve the face and are very small macules or papules that quickly enlarge into nodules and tumors. The skin lesions spread, mainly occupying the trunk and upper extremities, as well as the genital area. Often the first symptom is mucosal lesions taking the form of macules and submucosal nodules located most often on the palate. It can make eating and speech difficult[27].

Conclusions

Dermatologic conditions are prevalent among individuals infected with HIV. While many of these skin diseases are not exclusive to this population, their presentation can be more severe. The cutaneous expressions of HIV are diverse, encompassing AIDS-specific skin eruptions, opportunistic infections(among which we can divide bacterial, viral, fungal and parasitic etiology), and AIDS-related malignancies, such as Kaposi's sarcoma. Despite the decrease in certain HIV-associated skin diseases with the advent of antiretroviral therapy, there has been a rise in drug reactions and other non-infectious skin conditions.

Supplementary materials

Not applicable

Author's contribution

Conceptualization, Wiktoria Jakubowska and Daniel Ślusarczyk; methodology, Wiktoria Jakubowska and Daniel Ślusarczyk; software, Filip Pactwa and Aleksandra Kiełkowicz; check, Piotr Pisera and Aleksandra Kiełkowicz; formal analysis, Zuzanna Popińska and Piotr

Pisera; investigation, Bartłomiej Żmuda and Michał Żuberek; resources, Michał Żuberek and Wiktoria Jakubowska; data curation, Bartłomiej Żmuda and Zuzanna Popińska; writing - rough preparation, Wiktoria Jakubowska; writing - review and editing, Wiktoria Jakubowska and Bartłomiej Żmuda; visualization, Daniel Ślusarczyk and Filip Pactwa; supervision, Michał Żuberek and Filip Pactwa; project administration, Wiktoria Jakubowska. All authors have read and agreed with the published version of the manuscript.

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