HIV and Skin Disorders

HIV infection and its fulminant form AIDS are associated with immune deficiency, especially of the thymus-dependent system. This can lead to opportunistic infections or infections that are more rampant than normal and these infections may involve the skin. In HIV-positive children, low CD counts have been associated with infectious skin eruptions, whereas high CD counts are associated with skin disease associated with hypersensitivity reactions. A knowledge of the cutaneous manifestations of HIV can thus help to indicate the patient’s immune status.

Immune surveillance has long been postulated as a mechanism for the early detection and eradication of malignancy. There are some malignancies that are more common in this condition and some that are more aggressive.

Some cutaneous manifestations of HIV are so classical that they may lead to suspicion of the disease and early diagnosis with a greater chance of a successful outcome. If a doctor has reason to suspect HIV and believes that a blood test is indicated, this should be made clear to the patient.

Epidemiology

In 2013, a total of 6,000 persons (4,500 men and 1,500 women) were newly diagnosed with HIV in the UK. The number of newly diagnosed heterosexual men and women has dropped over the years from 4,890 in 2004 to 2,490 in 2013 due to fewer diagnoses among people born in sub-Saharan Africa. 76% of infections in men who had sex with men (MSM) were acquired in the UK.

See separate article Human Immunodeficiency Virus (HIV) for more details.

Presentation

- Acute primary HIV infection may lead to a transient, generalised, morbilliform eruption that is most common on the trunk and occasionally on the face, arms scalp or thighs. This appears as pink macules and papules of up to 1 cm in size. Acute HIV syndrome occurs in 50-70% of recently infected patients and it occurs 3-6 weeks after exposure. There may be systemic symptoms and fever, with the rash appearing two or three days later.
- In the early asymptomatic stage of HIV disease, no signs of infection other than lymphadenopathy are present. This stage may last for 10 years or longer.
- As immunosuppression occurs, nonspecific skin changes occur in which common disorders have atypical features. Recurrent shingles, numerous hyperkeratotic warts, treatment-resistant seborrhoeic dermatitis and oral hairy leukoplakia are examples. The last is very highly suggestive of HIV infection and may be associated with Epstein-Barr virus (EBV).
- In the later stages of HIV disease, chronic herpes simplex infection, molluscum contagiosum and cytomegalovirus (CMV) appear.
- Mycobacterial infections and mucocutaneous candidiasis occur.
- Kaposi’s sarcoma (KS) can occur before the onset of immunosuppression.
- Condylomata acuminata and verrucae appear early, without an increase in occurrence after the disease progresses, whereas herpes simplex infections, molluscum contagiosum and oral hairy leukoplakia increase as the disease advances.
- Verrucous herpes infection, condyloma-like molluscum contagiosum and AIDS-associated pigmented or nonpigmented erythoderma may be seen.
- Leishmaniasis and miliary tuberculosis (TB) are also reported.

Kaposi’s sarcoma

This was the first reported malignancy associated with HIV infection. It begins as pink macules that disseminate and become palpable. Three types have been identified - patch, plaque or nodular grade. Mucosal involvement is common but visceral disease is uncommon (affecting about 10% at diagnosis) and investigation for such involvement is not necessary in the absence of symptoms.

The clinical progression in patients infected with HIV is more aggressive than in those who have the sarcoma without immune suppression. The advent of antiretroviral therapy (ART) has complicated the prognostic relevance of KS but it is considered that having KS as the first AIDS-defining illness combined with an increasing CD4 cell count improves prognosis, whereas having KS at >50 years conveys a poorer prognosis.

Other malignancies

HIV increases the risk of various malignancies, including primary lymphoma of the central nervous system (CNS), undifferentiated non-Hodgkin’s lymphoma, squamous cell carcinoma, anorectal carcinoma and cutaneous malignancies. AIDS-defining cancers (Kaposi’s sarcoma, non-Hodgkin’s lymphoma and cervical cancer) with strong links to immunosuppression have reduced in incidence with the increased use of ART. The overall risk of cancer remains higher than the general population. Some of these are associated with viruses such as EBV and human papillomavirus (HPV).
B-cell non-Hodgkin's lymphomas may cause skin nodules. Anal carcinoma and cervical intraepithelial neoplasia are associated with HPV. They tend to be more progressive and aggressive.

An increase in squamous cell carcinoma of the anal mucosa has been reported, especially in young men who have sex with men with HIV infection.

Intraoral or multiple squamous cell carcinomas, Bowen's disease and metastatic basal cell carcinoma (BCC) have occasionally been reported in patients with HIV. The usual dictum about BCC is that it does not metastasise. However, 'eruptive' BCC has been reported, in which multiple BCCs have developed following the appearance of a single lesion in a patient with HIV.

Malignant melanoma in patients with HIV appears to be more aggressive.

Children with AIDS have a higher risk of developing leiomyosarcoma. The overall incidence is low but an American study reported that it has become the second most frequent malignancy in children with HIV infection or other immunodeficiency diseases.

Viral infections

Various herpes viruses can be a problem. There may be chronic perianal and perioral herpetic ulcers caused by HSV, recurrent typical dermatomal zoster caused by herpes zoster virus (HZV) and disseminated CMV infection.

- Recurrent oral and anogenital HSV are common in patients with HIV and may lead to chronic ulcerations. In children, herpes simplex stomatitis is more common than varicella-zoster virus (VZV) and may become chronic and ulcerative.
- Acute disseminated varicella-zoster infection with atypical manifestations may occur. They include hyperkeratotic papules, folliculitis, verrucous lesions, chronic ulcerations, disseminated ecchyma lesions and chronic varicella-zoster infection mimicking BCC. Varicella causes few problems in most children with HIV but occasionally it can cause fulminant chickenpox, pneumonitis, hepatitis, shingles and encephalitis.
- EBV has been implicated in the pathogenesis of oral hairy leukoplakia. It produces filiform white papules on the sides of the tongue. It is not pre-malignant but it may be the initial sign of progressive immunosuppression. White plaques may be confused with oral candidiasis, lichen planus and geographic tongue.
- CMV produces ulcers in the perineal region. CMV infection has a poor prognosis with HIV.
- Widespread or recalcitrant warts may occur on the oral mucosa, the face, the perianal region and the female genital tract. The perianal and cervical lesions may be difficult to treat. Large plantar warts are caused by HPV-66.
- The molluscum contagiosum virus produces small papules with central umbilication. In HIV infection, lesions may be widespread and atypical. The lesions may present on unusual sites (such as the face, neck and scalp) and the lesions may be of unusual morphology and size. Such unusual forms include solitary, endophytic, aggregated, inflamed and giant molluscum.
Fungal infections\textsuperscript{[13, 14]}

They may be superficial or deep.

- Recurrent and persistent mucocutaneous candidiasis is common with HIV infection. In the USA, recurrent vaginal candidiasis is the most common presentation of HIV infection in women. Perhaps after excluding diabetes, HIV should be considered.
- In adults, generalised dermatophytosis or tinea capitis, which is typically caused by \textit{Trichophyton rubrum}, may suggest HIV infection.
- Pityriasis versicolor may be persistent and recurrent.
- Deep fungal infections such as coccidiomycosis, may also produce lesions on the skin.

Bacterial infection

- Impetigo and folliculitis may be recurrent and persistent, especially in children.
- Disseminated furunculosis, gingivitis, gangrenous stomatitis and abscess formation may occur.
- Tuberculosis is more common in HIV infection. There may well be miliary TB and this can involve the skin. Mycobacterium infection is not just TB but, in endemic areas, leprosy may appear, probably in the lepromatous form as TB leprosy infers an immunological response.
- Bacillary angiomatosis, which is caused by \textit{Bartonella henselae} and rarely by \textit{Bartonella quintana}, usually produces red papules and nodules.
- Infection may occur with unusual species of mycobacterium such as \textit{Mycobacterium avium}.
- Syphilis is not confined to history but occurs more frequently in patients who have same sex partners, are bisexual or in those who use illicit drugs. Patients with syphilis have a high prevalence of HIV that may reflect multiple sexual partners and lifestyle. The ulcers of syphilis may facilitate the transmission of HIV. Patients with HIV infection with primary syphilis tend to have multiple ulcers compared with patients who are not infected with HIV. Rapid progression of secondary syphilis to tertiary syphilis occurs with HIV.\textsuperscript{[16]} Seroconversion may be delayed and standard serological tests for syphilis may be unreliable.

Infestation\textsuperscript{[17]}

Atypical or Norwegian scabies is characterised by widespread hyperkeratotic, scaly maculopapular eruptions or crusted plaques. It tends to be associated with alcoholic tramps with very poor hygiene and possibly some immune inadequacy but it is also seen with HIV.

Other skin diseases\textsuperscript{[19]}

- Seborrhoeic dermatitis or eruptions like it are seen in many patients with AIDS. Seborrhoeic dermatitis may even be the presenting feature of HIV. The eruption has widespread inflammatory and hyperkeratotic lesions and may progress to erythroderma in some patients. The incidence may be higher in patients with AIDS-related dementia or CNS disease.
- Psoriasis and reactive arthritis are more common. In some cases, existing psoriasis may become more severe with disseminated plaques and pustules (psoriatic pustulosis).
- The typical skin lesions of pityriasis rosea may be seen.
- Acquired ichthyosis may begin on the lower extremities and spread in advanced disease.
- Pruritic papular eruption (PPE) is a common cutaneous manifestation with HIV. There are small, itchy, red or skin-coloured papules on the head, neck and upper part of the trunk. It is highly indicative of advanced immunosuppression.\textsuperscript{[20]}
- Aphthous ulcers may be severe.
- Thrombocytopenic purpura, vitiligo, alopecia areata, sicca syndrome, pemphigoid and other autoimmune blistering diseases have been reported with HIV disease.
- Atopic disease may be reactivated. Atopic eczema can be severe in children.
- Urticaria may occur primarily or as a drug eruption. Cold urticaria has also been associated with HIV disease.
- Cutaneous vasculitis has been reported.
- Photosensitivity is more prominent. Photo-induced lichenoid drug reactions may be seen, especially on dark skin.

Hair and nails\textsuperscript{[21]}

- Diffuse alopecia or alopecia areata may be inflammatory and permanent.
- Generalised alopecia can occur after treatment with indinavir, an antiretroviral agent.\textsuperscript{[22]}
- Elongation of the eyelashes and softening and straightening of the scalp hair may be seen.
- Beau's lines, telogen effluvium and pallor of the nail beds may accompany any chronic illness.\textsuperscript{[23]}
- Zidovudine may produce longitudinal, transverse, or diffuse melanin pigmentation of the nails but nail pigmentation has also been observed in patients with HIV who have never received the drug.\textsuperscript{[24]}
- Proximal subungual onychomycosis is highly suggestive of HIV disease.\textsuperscript{[25]}

Drug reactions\textsuperscript{[26]}

- Morbilliform drug eruptions occur in around two thirds of patients who are treated with co-trimoxazole. Nowadays this is rarely used in British general practice but it is the drug of choice for \textit{Pneumocystis jirovecii} pneumonia, which is an opportunistic infection that is typical of AIDS. Reddish macules and papules can become permanent after the treatment is stopped.
- Toxic epidermal necrolysis has been reported with antibiotics, fluconazole, clindamycin and phenobarbital in patients with HIV.
- Drug eruptions are the most common cause of erythroderma in patients with HIV.
Management

Management is as for the particular skin condition plus specific treatment for the HIV. Treatment may have to be more prolonged and aggressive than normal. Immunomodulatory therapy may be very useful in the treatment of viral infections associated with HIV.[27] Imiquimod is useful for treating anogenital warts in HIV-positive patients and may help to prevent progression to anal cancer.[28] It is also useful in controlling molluscum contagiosum. In KS, treatment options include ART, local radiotherapy or intralesional vinblastine for symptomatic or cosmetic improvement in early stages and chemotherapy in the advanced stage.[29]

Further reading & references


14. Hay R, Bendek SE, Chen S, et al; Skin Diseases - Disease Control Priorities in Developing Countries
17. Schwartz RA, et al; Cutaneous Manifestations of HIV. Medscape, April 2014

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