The Challenge of Evaluating and Treating HIV Related Cutaneous Disease

Cutaneous infections often signal HIV disease progression.

It was the unusual appearance of Kaposi sarcoma in the skin of young homosexual males and the coexistence of pneumocystis pneumonia that led to the description of AIDS in the early 1980s. Since then, protean manifestations of cutaneous disease are recognised. The presence of skin disease can sometimes be the first indicator of HIV infection. Furthermore, the appearance of some cutaneous infections can serve as a marker of HIV disease progression. Many of the diseases are either exaggerated examples of inflammatory or infectious disorders and can be difficult to diagnose. Others, such as bacillary angiomatosis and Epstein Barr related oral hairy leukoplakia were first described in a HIV setting. The relative ease of examination and access to biopsy of the skin has proven invaluable.

In this review the various cutaneous manifestations are discussed with specific reference to the ever changing situation as patients now have almost undetectable viral levels and are treated with a plethora of drugs.

Cutaneous Manifestations

Seroconversion Rash: During the seroconversion period between exposure to the virus and development of a significant viral load the patient can manifest a “flu-like illness” with lymphadenopathy and a significant viral load. The patient can manifest a “flu-like illness” with lymphadenopathy and a significant viral load.

Infections:

(a) Viral

Varicella Zoster: The varicella zoster virus is a frequent cause of infection, with not only dermal involvement but multiperipheral involvement. Chronic crusted lesions can appear. Treatment with valcylovir until all the crusts have cleared is essential. Culture of the virus is difficult but a rapid Tzanck smear which reveals the multinucleated giant cells can be helpful.

Herpes Simplex: A particular problem in immune suppressed HIV infected patients are chronic ulcerative crusted lesions caused by the herpes simplex virus, usually found at mucocutaneous borders (Fig 1). Tzanck smears are not always helpful, thus biopsy may be necessary. Prolonged treatment with acyclovir or valcylovir is required.

Molluscum Contagiosum: Crops of these classic flesh coloured umbilicated papules are commonly seen as the Figure 2 multiple molluscum contagiosum CD4 count declines. The lesions may be large and distressing to the patient (Fig 2). They can appear similar to skin tumours and other infectious conditions such as Cryptococcus neoformans.

Epstein Barr Virus: The appearance of oral hairy leukoplakia manifesting as adherent linear white hairy streaks along the sides of the tongue is characteristic and denotes immunosuppression with reactivation of latent Epstein Barr virus (Fig 3).

(b) Bacterial

Staphlococcus aureus: Individuals become colonised with Staphlococcus aureus leading to a variety of manifestations including impetigo, ecthyma, cellulitis and abscesses. This colonisation can cause devastating systemic infections via indwelling catheters and central lines.

Bacillary angiomatosis: caused by a rickettsia like organism that manifests as lesions on the oral mucosa and skin that resembles Kaposi sarcoma and histologically as granulomatous vascular proliferations. The clusters of gram-negative rods stain with the Warthin-Starkey silver stain. Treatment is with erythromycin or doxycycline.

Syphilis: Lues magna is a form of secondary syphilis which manifests as ulcers, papules and nodules with prominent facial involvement.

Mycobacterial tuberculosis: both typical and atypical are not uncommon manifestations of HIV-1 disease. Diagnosis can be difficult.

(c) Fungal Disease

Superficial candidal infections affecting the mouth, the oesophagus and vulvovaginal area are common and often early indicators of HIV-1 disease. Involvement of flexures results in troublesome intertrigo.

Dermatophyte infections follow typical patterns but can be extensive. Nails, both finger and toe can be infected with T. rubrum. Proximal white subungual onychomycosis is characteristic.

Deep disseminated fungal infections can manifest as mucocutaneous rashes. Where endemic, coccidiomycosis and histoplasmosis manifest as nodular and ulcerative skin lesions. Fungal stains on tissue biopsies help establish the diagnosis. Cryptococcus skin lesions occur worldwide and can masquerade as molluscum like papules or as nodules and ulcers.

Infestations

Classical scabies as seen in the general population is common. However, due to immunosuppression crusted scabies can manifest as hyperkeratotic plaques in unusual sites such as the scalp. Eradication can be difficult. Recently oral ivermectin has been used as an additional agent.

Skin Malignancy

Kaposi sarcoma was noted to be commoner in homosexuals and thus it was suspected that it might be caused by an infectious agent. The recent discovery of the KS herpes virus supports this concept. KS can manifest as subtle erythematous macules on scars or acral tissue to gross peripheral oedema and fungating tumours.

Inflammatory Dermatoses

Psoriasis which is very inflammatory can indicate HIV infection. A frequent clinical pattern seen is similar to Reiter’s syndrome, with thick hyperkeratotic and pustular lesions developing on the extremities particularly around the nails with an associated psorias
arthriti (fig 4). Systemic agents such as methotrexate and cyclosporin, though sometimes employed, pose further immunosuppressive fears. Retinoids with or without ultraviolet light can be helpful. Phototherapy is well tolerated.

Seborrhoeic Dermatitis was one of the earliest hallmarks of HIV infection. It is seen in greater frequency than in the general population. Frequent use of ketoconazole shampoos and application of topical antifungal creams such as clotrimazole, terbinafine and ketoconazole has enhanced management of what can be a distressing rash for the patient.

Miscellaneous Dermatoses:

There are various skin disorders which have been reported to occur with greater frequency in HIV infected patients (Table 1).

<table>
<thead>
<tr>
<th>Table 1: Miscellaneous Dermatoses associated with HIV</th>
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<tbody>
<tr>
<td>Pityriasis rubra pilaris</td>
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<tr>
<td>Granuloma annulare</td>
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<td>Yellow nail syndrome</td>
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<td>Lichen myxedematous</td>
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<td>Bullous pemphigoid</td>
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<td>Pemphigus herpetiformis</td>
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<td>Erythema elevatum diutinum</td>
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As the newer antiviral drugs are introduced, some unusual cutaneous side effects have been noted. Zidovudine can cause a peculiar pigmentation of the nails. Accumulation of adipose tissue in the dorsocervical area, commonly known as a 'buffalo hump' and visceral abdominal region would appear to be caused by protease inhibitor treatment. Some of the drugs share a retinoid acid binding protein and have been noted to cause side effects seen frequently with retinoid treatment such as alopecia, chelitis, paronychia and granulation tissue formation.

Pruritus and Folliculitis:

There are many different causes of itch which can be intractable (Table 2).

Folliculitis can be due to infective causes such as bacteria, Pityro-sporum or Demodex. A superficial skin culture may not be sufficient to make a diagnosis, demonstration by means of Haematoxylin/Eosin with PAS or Gram stain will show the causative organism. Appropriate systemic/topical treatments generally give relief.

Eosinophilic folliculitis is a unique HIV related disorder. Multiple urticaria! follicular papules are seen on the head and neck, trunk and proximal portions of the extremities (fig 5). Culture is negative, there is an associated peripheral eosinophilia and raised serum IgE. The histological features include a perifollicular and perivascular infiltrate with eosinophils. Eosinophilic folliculitis can denote advancing immunosuppress-ion with low CD4 counts of less than 250 cells per cubic millimetre. Treatment with antihistamines, potent topical steroids, dapsone, UVB phototherapy and isotretinoin have all been shown to help.

The majority of skin disorders are straightforward to diagnose and treat. For the patient these relatively minor ailments can be of major significance to their well-being. Not uncommonly one is presented with a patient who has atypical cutaneous skin lesions which prove to be a diagnostic challenge. These lesions may be keratotic plaques, ulcerating nodules or erythematous papules. When there is doubt regarding the diagnosis it is vital to do several biopsies, not just for H&E but also for tissue culture and to liaise carefully with the laboratory.

In the past few years the treatment and management of patients with HIV infection has dramatically changed. With the advent of highly active antiretroviral treatment (HAART) patients can now expect to lead fairly normal lives. With these combinations of agents that inhibit replication of HIV in vivo, a new era has been reached whereby undetectable plasma viral loads and possible eventual eradication of the virus is discussed. Sadly, this prospect is not currently accessible to those living in developing countries. The pattern of skin disease seen has also changed. One rarely sees the florid manifestations of HIV cutaneous disease in patients who are well controlled on multiple antiretroviral medications. The restoration of the immune response in HIV infected patients can however be associated with a paradoxical reactivation of an infection or inflammatory disorder.

References: