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■ Diagnostic Utility of the Skin Biopsy in HIV Infection and AIDS

Diagnostic Utility of the Skin Biopsy in HIV Infection and AIDS

An estimated 38.6 million people worldwide are living with human immunodeficiency virus (HIV) infection or the acquired immunodeficiency syndrome (AIDS) according to the 2006 UNAIDS survey. Sub-Saharan Africa continues to represent the global epicentre of this pandemic. This places an enormous burden on financial and health resources in countries (which include South Africa) most severely affected by the disease.

Skin disease is often the first presenting feature of HIV infection or AIDS. More than 90% of patients with HIV/AIDS will develop one or more skin diseases during the course of their illness. The skin disease picture and skin disease spectrum may vary in the face of a declining CD4 count.

A skin biopsy may provide the first opportunity to diagnose an unsuspected and potentially life-threatening opportunistic infection, especially in patients who have not had access to highly active anti-retroviral therapy (HAART).

All medical practitioners working in regions of the world where HIV/AIDS is prevalent ideally should be familiar with the spectrum of cutaneous manifestations of HIV/AIDS. These include a range of non-infective dermatoses, infectious diseases (often opportunistic) caused by viruses, bacteria, fungi, protozoa and even arthropods, and neoplastic conditions such as Kaposi's sarcoma (KS) and B-cell non-Hodgkin lymphoma (NHL). The non-infective dermatoses may be classified as follows:

- Dermatoses peculiar to HIV infection (eg HIV exanthem, papular pruritic eruption of HIV infection).
- Common dermatoses occurring with greater frequency or modified by HIV/AIDS (eg seborrhoeic dermatitis, psoriasis).
- Less common conditions that have been reported in association with AIDS (eg pityriasis rubra pilaris, Reiter's disease).

The risk for adverse skin reactions to certain drugs is also greatly increased. Although the introduction of HAART has resulted in a dramatic decrease in opportunistic infections, several of these drugs may result in adverse reactions in the skin.

The spectrum of potential adverse drug reactions in patients receiving HAART is large, and includes exanthematous (morbilliform) drug eruptions, drug hypersensitivity ("DRESS"), Steven's-Johnson syndrome, toxic epidermal necrolysis, mucocutaneous pigmentation, leucocytoclastic vasculitis, lipodystrophy syndromes, etc.

Careful clinico-pathological correlation is of paramount importance. Although most skin biopsies will be obtained from patients who are known to be infected with HIV, it is wise to always maintain a high index of suspicion for undiagnosed HIV/AIDS when the clinical history indicates that a common dermatosis has displayed unusual/atypical clinical features, pursued an abnormal clinical course, exhibited greater clinical severity than anticipated, or failed to respond satisfactorily to standard therapy. Histopathologists are aware that biopsy material should always be examined carefully to exclude dual pathology. The diagnosis may need to be confirmed with histochemical and immunohistochemical stains, and/or molecular studies. Where indicated, additional biopsies for microbiological culture may be required.

Skin biopsies play a vital diagnostic role in the setting of HIV infection, when diverse diseases present with remarkably similar clinical features, eg giant molluscum contagiosum, cryptococcosis and bacillary angiomatosis (BA), where there are multiple cutaneous nodules, sometimes with umbilication (central depression within the cutaneous lesion, figures A, B and C).

An erroneous clinical diagnosis and failure to perform a confirmatory skin biopsy will inevitably result in delayed treatment or the institution of inappropriate therapy, with potentially fatal consequences (eg cryptococcosis). Certain conditions may also manifest diverse clinical features in the setting of AIDS (eg histoplasmosis).

Diagnostic Utility of the Skin Biopsy in HIV Infection and AIDS (...continued)



Multiple nodular facial cutaneous lesions in three patients with AIDS. A. Molluscum contagiosum. B. Bacillary angiomatosis. C. Cryptococcosis. Note the considerable clinical overlap between these three conditions.

Superficial shave biopsies should be discouraged, as they are often not sufficiently representative of the lesion. This is especially true for HIV-associated vascular proliferations and dermal nodules of NHL. In verrucous or ulcerated KS, for example, the KS lesion is either not included in the specimen or there is only scant representation of the most superficial and often non-diagnostic aspect thereof. In extensively ulcerated lesions, most of the shave biopsy is occupied by inflamed granulation tissue in response to the exudate. Both KS and granulation tissue represent spindle cell proliferations with vascular differentiation, and may thus resemble one another. The uppermost portion of an ulcerated KS lesion covered by granulation tissue may be easily overlooked when the KS component merges with the overlying granulation tissue if a superficial shave biopsy instead of an adequate punch biopsy or incisional biopsy is performed.

It is hoped that this brief overview has given the reader some insight into the diagnostic utility of the skin biopsy in this important clinical context.

Dr. Wayne Grayson
MBChB(UFS) PhD(Witwatersrand) FCPATH(SA)
Former Associate Professor of Pathology at the University of the Witwatersrand
Histology, Metal Box, AMPATH

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