INVITED ARTICLE

EARLY CLINICAL MANIFESTATIONS OF HIV INFECTION

R K W Chan

ABSTRACT

HIV infection produces a spectrum of illness from totally asymptomatic infection to AIDS. In between these two extremes, infected persons may manifest a variety of signs and symptoms. These include an acute infectious mononucleosis-like illness, progressive generalised lymphadenopathy, and numerous cutaneous and oral lesions. Whilst most of these conditions are not pathognomonic for HIV infection, certain features may indicate the possibility of an underlying HIV infection. Clinicians should be aware of these tell-tale signs.

Keywords : HIV infection, clinical manifestations

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INTRODUCTION

Infection by the Human Immunodeficiency Virus (HIV) is lifelong and incurable. The virus infects and integrates its genetic material into a variety of cells; these include CD4 (helper) lymphocytes, macrophages, monocytes, glial cells of the brain, Langerhan's cells in the skin and chromaffin cells in the gut[1].

After infection occurs, in the majority of cases, the virus either remains dormant or multiplies at a very low rate. With time however there is an increase in the rate of viral replication and spread of the infection to other uninfected cells. The exact mechanisms whereby this occurs is unclear at present but involves the activity of a number of regulatory genes in the HIV genome[2].

With progression of the infection there is a slow but steady destruction of the immune system. It is estimated that the absolute number of CD4 lymphocytes falls from a normal level of 800-900/cu mm by 60-100 per year[3]. This is manifested clinically by the appearance of infections and malignant complications. In addition to these complications, HIV infection is also accompanied by other signs and symptoms which cannot be so easily explained by immune deficiency alone. It is postulated that immune dysregulation and dysfunction and the infection of non-immunologic cells may account for some of these features[4].

The rate of progress of HIV infection to AIDS is variable from patient to patient. Present estimates are 0-2% progression at 2 years, 5-10% progression at 4 years, 10-25% at 6 years and 30-40% at 8 years. The average incubation period to AIDS as estimated from a number of cohort studies is between 7-10 years[3].

The Centres for Disease Control (CDC) introduced in May 1986[5], a system to classify the clinical manifestations of HIV infection according to the stage of the infection and when they occur (Table I). The groups are mutually exclusive and hierachical, that is, persons classified in a particular group should not be reclassified into a preceding group if clinical findings resolve, since clinical improvement may not accurately reflect changes in the severity of the underlying disease.

Table I
Classification System for HIV Infection

Group I	– Acute Infection
Group II	– Asymptomatic Infection
Group III	– Persistent Generalised Lymphadenopathy
Group IV	– Other Disease
Subgroup A	– Constitutional disease
Subgroup B	– Neurologic disease
Subgroup C	– Secondary Infectious diseases
Category C1	– Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
Category C2	– other specified secondary infectious diseases
Subgroup D	– Secondary cancers
Subgroup E	– Other conditions

HIV-infected persons therefore may manifest signs and symptoms of infection for some time before acquiring the life-threatening infections and malignancies which qualify them to be diagnosed as having AIDS. Under the Revised Case Definition for AIDS, patients in Group IV except subgroup A, C2 and E qualify to be called AIDS[6]. Group IVA broadly represents the AIDS related complex.

National Skin Centre
1 Mandalay Road
Singapore 1130

R K W Chan, MBBS, MRCP
Consultant

In this article, I shall attempt to describe the more common early clinical manifestations of HIV infection before the onset of AIDS.

1 Acute HIV infection (Group I)

This is an acute febrile illness occurring soon after infection by HIV. It is associated with seroconversion and lasts for up to 2 weeks[7]. Clinical manifestations may include fever, generalised lymphadenopathy, sore throat, a macular erythematous truncal rash, lethargy, anorexia, nausea, myalgia, arthralgia, headaches, diarrhoea and neurological signs. The illness resembles infectious mononucleosis, but is often mild and therefore missed. The actual incidence of this primary HIV infection is not known. Some studies have estimated that 50-90% of adults experience this acute symdrome. Complete recovery occurs, although enlarged lymph nodes may persist.

2 Progressive Generalised Lymphadenopathy (Group III)

This is defined as palpable lymphadenopathy of 1 cm or greater at 2 or more extrainguinal sites persisting for more than 3 months. There must be an absence of any concurrent illness other than HIV infection to explain the findings. The lymphadenopathy is usually symmetrical, painless, mobile and firm, affecting most commonly the anterior and posterior cervical chains, axillary and submandibular nodes. Histology usually demonstrates a non-specific follicular hyperplasia which is followed by involution. It has been observed that the presence or absence of PGL is not an independent predictor for developing AIDS. However, the loss of adenopathy or a decrease in lymph node size may predate the development of AIDS[18].

3 Cutaneous Manifestations of HIV Disease

HIV infection is associated with numerous cutaneous manifestations even before the onset of immunologic dysfunction and AIDS[8-11]. They can be broadly categorised into:

a) infectious manifestions
b) papulosquamous manifestations
c) others

a) Infectious Manifestations:

i) Herpes simplex lesions in HIV patients usually represent reactivation of previous infections. They present as severe, chronic, recurrent or non-healing ulcers in the ano-genital areas, in and around the mouth and also on the skin. Perirectal lesions are often mistaken for boils and may lead to intractable erosive ulcers. Response to acyclovir therapy is usually satisfactory, but continuous treatment may be required.

ii) Herpes zoster has been reported in greater frequency in HIV infected persons. It is an early indicator of impaired immunity and is an early marker of progression to AIDS. Severity of the lesions, degress of pain and zoster of the cranial or cervical dermatomes were all associated with a poor outcome in one study[12].

iii) Molluscum contagiosum is a skin infection by a pox virus. In HIV disease, it frequently occurs on the face and may be widespread. Individual lesions are small pearly white papules with a central umbilication. Treatment is by topical application of phenol or tri-chloroacetic acid with a sharpened orange stick, cryotherapy or electrosurgery.

iv) Fungal skin infections are common in HIV patients. Dermatophyte infections of the skin and nails are often chronic and recurrent. Candidal intertrigo and pityriasis versicolor are also seen.

v) Bacterial skin infections are extremely common in persons infected by HIV. They may present as neck and beard impetigo, ecthyma, superficial abcesses, perianal fistulae and sinuses and cellulitis. Responsible organisms include staphylococci, streptococci, H. influenza and Pseudomonas spp.

b) Papulosquamous Manifestations:

i) Seborrhoeic dermatitis in HIV disease is often severe and extensive, involving the scalp, face trunk and even limbs. Lesions are red papules with white or yellow waxy scales. It is believed that the Pityrosporon yeasts have an important role in the pathogenesis. Response to topical steroids and antifungals is usually satisfactory.

ii) Psoriasis has been described to develop in HIV disease in persons with no prior history of psoriasis. Other reports have documented exacerbation of pre-existing psoriasis and the development of severe erythrodermic psoriasis. These are usually late manifestations of HIV disease. Severe psoriasis is a poor prognostic sign. Response to Etretinate and Azidothymidine has been described.

c) Others:

i) Xeroderma (dry skin) is a common sign in symptomatic HIV disease and almost universal in AIDS patients. Emollients are useful to relieve the pruritus.

ii) Itchy folliculitis probably related to pityrosporon infection is also a common finding in HIV disease. Lesions usually occur on the upper trunk but may be found anywhere. The eruption is very pruritic and consists of tiny non-inflamed papules and pustules. Treatment is symptomatic with topical steroids and antifungal creams and antihistamines.

iii) Allergic reactions to drugs are seen frequently in HIV infected patients.

iv) Alopecia of a diffuse pattern is seen in most patients with AIDS and ARC.

4 Oral Manifestations of HIV Disease[13]

i) Oral candidiasis is often the inital clinical manifestation of HIV infection. It is present in the vast majority of cases of ARC and AIDS. The presence of unexplained oral thrush in a person from a high-risk group strongly suggests HIV infection[14]. It occurs usually later than herpes zoster but is a significant predictor of progression. Treatment is with topical or oral antifungal preparations.

ii) Oral hairy leukoplakia is a condition unique to HIV infection. It develops on the sides of the tongue and occasionally on the buccal mucosa, appearing as raised white areas with a corrugated or "hairy" appearance. These lesions are adherent and cannot be scraped off with a spatula, unlike thrush. The aetiology of the condition is believed to be EB virus and/or human papillomavirus infection. Treatment with topical acyclovir and Tretinoin has been tried. Oral hairy leukoplakia is also a significant predictor of disease progression[15].

ii) Gingivitis in HIV infection is often severe, recurrent and difficult to resolve. Acute necrotising gingivitis (Vincent's infection) is also seen. Comprehensive oral hygiene and the use of antiseptics and antibiotics are required for treatment.

iv) Severe recurrent oral aphthous ulceration is a less common finding.

5 Constitutional Disease (Group IVA)

The constitutional symptoms of HIV infection include fever persisting more than 1 month, involuntary weight loss of greater than 10% of baseline, diarrhoea persisting more than 1 month, fatigue that reduces physical activity and night sweats. Attempts to identify an AIDS-defining illness should always be made before arriving at this diagnosis. Before the discovery of HIV, these constitutional symptoms together with oral candidiasis were designated as the AIDS related complex or ARC. This term is now out-dated. Constitutional symptoms are strong predictors for the development of AIDS[16-18].

CONCLUSION

With the exception of oral hairy leukoplakia, the early clinical manifestations of HIV infection may be seen in uninfected individuals. The conditions are however much more severe and intractable in HIV-infected persons. These features should alert the attending clinician to the possibility of an underlying HIV infection. Appropriate history-taking to determine high-risk behaviour may then indicate the need for HIV antibody testing after providing pre-test counselling and obtaining informed consent.

Oral candidiasis, oral hairy leukoplakia, constitutional disease and to a lesser degree, herpes zoster are clinical markers of immune deficiency and significant predictors of HIV disease progression.

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