MANAGEMENT OF EARLY HIV INFECTION

Vesicles of varicella zoster.

Most patients infected with the human immunodeficiency virus (HIV) do not have the acquired immune deficiency syndrome (AIDS). Indeed many are perfectly fit, having been diagnosed as having the virus only as a result of a blood test. The range of infection, from asymptomatic seroconversion to AIDS, was covered last week. Many doctors in all walks of medicine will increasingly be looking after patients who are anti-HIV positive at all stages in their illness and will have to take decisions about appropriate investigations and management.

Acute infection

Glandular fever like illness
Encephalopathy
Meningitis
Myelopathy
Neuropathy

The clinical manifestations of acute HIV seroconversion include a glandular fever like illness, encephalopathy, meningitis, myelopathy, or neuropathy. HIV infections are still largely confined to high risk groups, and should be considered only once a detailed sexual and drug history has established that the patient is at risk. As blood donors are currently being screened to exclude HIV, it is unlikely that a patient receiving blood or blood products from a UK source will be infected. If HIV is suspected an acute phase serum sample should be stored and tested together with a convalescent serum sample. HIV antibodies may be detected as early as two weeks or as late as three months after the illness. Before the samples are tested for HIV antibodies the possible diagnosis should be discussed with the patient and the implications of a positive result outlined.

Many conditions can cause a glandular fever like syndrome, so acute seroconversion illnesses associated with HIV are only rarely recognised. The differential diagnosis in patients presenting with a glandular fever like illness is vast. Tests which may help to make the diagnosis include a white cell count and film (atypical lymphocytes may be seen with all the viral causes of the mononucleosis syndrome including HIV, as well as toxoplasmosis), serological tests, a throat swab for bacterial culture and to exclude herpes simplex infection, and, if indicated, a bone marrow aspirate.

When a patient presents with an encephalopathy the clinical features may suggest a central nervous system infection or space occupying lesion, and investigations to exclude these (including computed tomography and examination of the cerebrospinal fluid) may be required. Other neurological manifestations of acute seroconversion, including meningitis, neuropathy, or myelopathy, occur extremely rarely and are described in a forthcoming chapter.

The immediate outlook of patients with acute seroconversion illness is excellent, but the subsequent risk of progression remains unknown, although it is likely to be similar to that occurring in asymptomatic individuals.

Differential diagnosis of glandular fever like illness

Condition	Test
Infectious mononucleosis	Paul-Bunnell
Cytomegalovirus infection	Serology
Rubella	Serology
Herpes simplex stomatitis	HSV culture
Adenovirus infection	Serology
Acute HIV seroconversion	HIV antibodies
Toxoplasmosis	Serology
Streptococcal pharyngitis	Bacterial culture
Leukaemia/lymphoma	Full blood count/ bone marrow

Persistent generalised lymphadenopathy (PGL)

Common causes of generalised lymphadenopathy

Condition	Tests
Infections	
Bacterial	
Syphilis	Serological tests (Venereal Diseases Research Laboratory, <i>Treponema pallidum</i> haemagglutination, and fluorescent treponemal antibody tests)
Brucellosis	Serological tests
Viral	
Infectious mononucleosis (Epstein-Barr virus)	Paul-Bunnell
Cytomegalovirus	CMV cultures or antibodies
Hepatitis B	Serology
Hepatitis A	Serology
Rubella	Serology
Parasites	
Toxoplasma	Toxoplasma serology
Tumours	
Lymphomas	Full blood count and lymph node biopsy
Leukaemias	
Others	
Miscellaneous	
Sarcoidosis	Clinical features Kviem test

One of the common presentations of chronic HIV infection is lymphadenopathy, the definition and clinical features of which were covered last week. There are, however, many causes of generalised lymphadenopathy, so the problem is one of differential diagnosis. Nevertheless, most of the alternative causes can be excluded clinically or with the appropriate tests (see box); and these other causes should first be excluded when a patient presents with lymphadenopathy.

If the enlarged lymph nodes persist for three months or longer the possibility of doing an HIV antibody test should be considered and discussed with the patient. A question which is often asked is when does one recommend a lymph node biopsy? When the nodes are of typical distribution, the patient is HIV antibody positive, and the other causes have been excluded the yield from biopsies will be limited, showing merely a non-specific reactive hyperplasia. However, several clinical features have been found to be helpful in making the decision. These include asymmetrical or painful enlargement of nodes, sudden increase in size, constitutional symptoms such as fevers, night sweats, or weight loss, and hilar lymphadenopathy. One could also add to the list reassurance of the patient and the doctor.

History and examination

Typical PGL (symmetrical, firm, discrete and non-tender; neck, axillary, inguinal epitrochlear/retroperitoneal)

Asymmetrical or painful nodes

Tests to exclude 'other' causes

Follow for 3 months

? HIV antibody test

No change?

Continue to follow every 3 months

Consider lymph node biopsy

Sudden increase in lymph node size

Indications for lymph node biopsy

- (1) Constitutional symptoms
- (2) Painful nodes
- (3) Asymmetrical enlargement
- (4) Sudden increase in size
- (5) Hilar lymphadenopathy

Constitutional symptoms

- Fever lasting at least 1 month
- Weight loss <10% baseline
- Diarrhoea lasting at least 1 month

The constitutional symptoms associated with HIV infection include malaise, fevers, night sweats, weight loss, and diarrhoea. These symptoms probably occur intermittently in many infected people. The time to take more notice is when the fever or diarrhoea has persisted for more than a month or the weight loss reaches 10% of the baseline. Attempts should always be made to discover if some other organism is responsible. Many patients find these symptoms very worrying and debilitating, and when no cause is found treatment with antipyretics and antidiarrhoeal preparations is often helpful. Before the discovery of HIV as the specific cause of AIDS these constitutional symptoms together with oral candidosis were often pooled under the heading of the AIDS related complex. This category has become less useful since the advent of antibody tests.

Skin and mouth problems

Hairy leukoplakia.

Skin problems

- Fungal**—Tinea — cruris
— pedis
— other
— Candida — genital
— perianal
— other
— Pityriasis — vesicolor
- Bacterial**—Impetigo
Acneform folliculitis
- Viral**—Herpes simplex (type 1 and 2)
— oral
— genital
— perianal
— other
- Varicella zoster
Human papilloma virus
Molluscum contagiosum

Miscellaneous—Seborrhoeic dermatitis

Mouth problems

Dental caries/abscesses

Ulceration—aphthous

- herpetic
- bacterial

Candidosis

Hairy leukoplakia

Various minor skin problems occur in patients infected with the virus. Sometimes these are exacerbations of previous skin disease, but more often they are new. Seborrhoeic dermatitis is one of the commonest. It usually presents as a red scaly rash affecting the face and scalp, although the whole body may be covered. Other common problems include tinea cruris and pedis, candidiasis (particularly affecting the penis and perianal area), impetigo, and shingles. Recurrent perianal or genital herpes often becomes more troublesome, with recurrences lasting longer and occurring more often than previously. Diagnosis and treatment of these complaints are often difficult, and expert help should be sought early. Treatment is usually successful but these conditions often recur.

Mouth problems are also common. Oral candida can often be managed with topical antifungal preparations, but if these are unsuccessful systemic ketoconazole is indicated.

Hairy leukoplakia is apparently unique to patients infected with HIV. It consists of white warty like projections occurring particularly on the lateral aspects of the tongue and the cheeks. Its cause is unknown, but electron microscopic studies suggest that a virus (possibly Epstein-Barr or the human papilloma virus) may be implicated. Although it is usually painless, its unsightliness worries many patients. Acyclovir may be of some benefit. Other mouth infections, including dental abscesses, oral ulceration (herpetic or bacterial), and progressive dental caries, also occur. As with the skin problems, these conditions may be difficult to diagnose and treat. Maintenance of good oral hygiene is obviously important.

Haematological problems

- Lymphopenia
- Neutropenia
- Thrombocytopenia
- Anaemia

Haematological problems include depression of the lymphocytes, neutrophils, and thrombocytes as well as anaemia. Depression of the lymphocytes probably contributes to the increased susceptibility to infection; the neutropenia is usually only moderate and does not. Thrombocytopenia is due to a variety of autoimmune mechanisms. Most have only a moderate (and often transient) fall in platelets, but a few drop their platelet counts to below $20 \times 10^9/l$. These patients may bleed spontaneously with catastrophic consequences. A variety of treatments have been used, including short term platelet infusions, gammaglobulin, steroids (of limited use because of the increased risk of infection), and splenectomy.

The anaemia is usually mild, but sometimes the haemoglobin concentration may be very low. Transfusions and haematinics are of limited value, and the exact cause of the anaemia has not been fully elucidated.

Top left: oral candida; top right: mouth ulcer; middle left: tinea cruris; middle right: varicella zoster; bottom left: extensive seborrhoeic dermatitis; bottom right: perianal herpes.

Prognostic markers

Clinical	
Constitutional symptoms	Hairy leukoplakia
Herpes zoster	Oral candidosis
Laboratory	
Anaemia	Reduced interferon
Cytopenias	Reduced mitogenic response to pokeweed mitogen
Raised erythrocyte sedimentation rate	?Reduced HIV specific-cellular response to HIV
Depletion of CD4 lymphocytes	
Raised CD8 lymphocytes	Reduced anti-p24
Raised IgA	Raised p24

One of the hardest problems confronting the physician dealing with a patient with HIV antibodies is the difficulty of predicting which patients will progress to AIDS. But there are both clinical features and laboratory markers which may help.

The clinical features of a poor prognosis are oral candidosis, herpes zoster, hairy leukoplakia, and the presence of fever, malaise, diarrhoea, or weight loss (as defined previously). Useful laboratory markers include lymphopenia, neutropenia, thrombocytopenia, anaemia, a raised erythrocyte sedimentation rate, and a variety of immunological markers, in particular low T4 (helper lymphocytes) and low B₂ microglobulin values. Recent studies have shown that a low or falling level of a specific viral antibody called anti-gag (anti-p24) is a very good predictor of subsequent progression to AIDS.

There has been much speculation on the role of cofactors—for example, sexually transmitted diseases or the use of recreational drugs—in the progression of early HIV infection, but no convincing evidence implicates any cofactor. The most important “cofactor” may well be time. The longer one has HIV the greater the chance of progressing to AIDS.

General management of the HIV antibody positive patient

- Protect confidentiality
- Medical issues
- Psychological support (patient, family, friends)
- Avoidance of transmission
- Other issues (eg dental treatment, insurance, work or school, etc)

One of the most important aspects of dealing with any antibody positive patient is confidentiality. Maintaining confidentiality might be complicated: for example, the patient's family or friends may not know his diagnosis or indeed his sexual orientation; people at work (or school) may seek medical information (especially if the patient is having time off work); or the patient may fear that information may inadvertently be given to third parties. Special precautions may be required, firstly, to reassure the patient that confidentiality is protected and, secondly, to limit any unwarranted dissemination of confidential information.

The routine medical management of these patients is usually straightforward. Patients should be seen regularly—for example every two to three months. At each visit the patient's weight should be recorded and special attention given to mouth or skin problems. If necessary the patient should be referred to the appropriate specialist. Repeating a full blood count and measuring the erythrocyte sedimentation rate at each visit is often helpful. Patients should be advised to reattend if they develop signs or symptoms suggestive of Kaposi's sarcoma or opportunistic infection—purplish lesions of the skin, shortness of breath, cough, dysphagia, diarrhoea, weight loss, fever, headaches, fitting, or altered consciousness.

Patients should also be advised about reducing the risk of transmission. Psychological and emotional support of the patient, the family, and friends are a vital aspect of management and will be covered in detail in a later article. The physician may also be asked to advise about dental treatment, insurance, and work. Patients should be advised to tell their dentists about the infection, and it may sometimes be necessary to refer them to a dental unit with an interest in HIV and related problems. People with antibodies will often have considerable difficulty in obtaining life insurance. Some insurance companies are asking specific questions about the virus and refusing to insure those who are positive. Finally, patients should be told that being positive is no bar to employment. Because of widespread misconceptions about infectivity, however, information about the patient's condition should not be divulged to employers.

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