Recognising acute HIV infection

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BACKGROUND Early diagnosis and appropriate management of acute or primary human immunodeficiency virus (HIV) infection may significantly alter the long term course of the disease and help reduce further transmission.

OBJECTIVE General practitioners are the doctors most likely to see a person with acute or primary HIV infection. This article aims to assist GPs in the early diagnosis and management of these patients.

DISCUSSION The symptoms of acute HIV infection include headache, fever, malaise and rash. Good history taking including assessing possible HIV transmission risk and careful examination can alert GPs to the illness. Appropriate investigations require knowledge of the time course of serological and virological markers and expert laboratory advice may be needed. Management may include general supportive measures for physical, psychological and social issues and some clinicians advocate the use of antiretrovirals. Postexposure prophylaxis is becoming more widely available in Australia. Most patients can be cared for by their own GP with the support and advice of a more HIV experienced colleague.

General practitioners are the first doctors likely to see someone with a primary human immunodeficiency virus (HIV) infection. The symptoms of headache, fever, malaise and rash may mimic many other flu-like illnesses but there are distinguishing features that can be discovered with good history taking and relevant clinical examination. Knowing what to ask as much as knowing what to look for remains the key to diagnosis.

If patients are diagnosed early with primary HIV infection, early treatment with antiretrovirals may significantly alter the long term course of the disease. The chance of further transmission of HIV through the implementation of safe sex practices can have benefits to the wider community. Postexposure prophylaxis for sexual partners can be offered as well as follow up contact tracing.

Acute or primary HIV infection

When HIV enters an uninfected person it usually takes 10–14 days before any symptoms show, but symptoms can start as early as three days after infection or as late as 10 weeks after infection.[1,2] While not all patients have any symptoms or signs, approximately 50–90% do so.[3,4] The virus replicates rapidly in lymphoid tissue having travelled down the lymphatic channels to regional lymph nodes from the site of inoculation. Human immunodeficiency virus shows a tropism toward the cells of the lymphoid, central nervous system (CNS) and gastrointestinal systems (Table 1). The flu-like symptoms of primary HIV infection are caused by the release of cytokines during the body's own immune response.

The most important aspect of the diagnosis of possible primary HIV infection is a history of recent HIV transmission risk behaviour. Raising the topic of risk behaviours can be the most difficult part of the consultation even for experienced general practitioners. However, it must be done or else an important diagnosis may be missed and opportunities lost for individual and public health interventions. Stereotyping or assuming a lack of risk behaviours because of ethnic origin, age, physical appearance, marital status or occupation, is the biggest potential trap.

How to make a risk assessment?

The patient may make it easy for you and raise their own concerns about risky behaviour before you do. If the patient doesn't help you out by volunteering their own concerns then you will need to ask. Remember that the patient may see no connection between their flu-like symptoms and the possibility of HIV infection. I usually ask a similar question to that listed in Table 2. Most people respond in the negative for any risk behaviours and I continue with the usual consultation.

If the patient describes any risk behaviours or concerns then do a risk behaviour assessment. Questioning for the risk assessment needs to be sensitive to a patient's cultural and social background. The GP needs to be nonjudgmental and not over intrusive, while obtaining enough information to assess the risk of HIV transmission. Use simple nonjargon language and ask the patient to explain particular sexual practices of which you have not heard. At the end of the history, the GP needs to know how likely primary HIV infection is to assist decision making on further tests.

Differentiating primary HIV infection from other conditions

The symptoms of primary HIV infection (PHI) are very common in everyday general practice. These symptoms are also caused by the flu, viruses, gastro, etc. So how does one start to differentiate the patient with PHI infection when you're running 30 minutes late and have four patients waiting? There's no easy answer but the features that stand out for me are:

- a generally unwell person
- fever lasting longer than three days
- flu-like symptoms out of flu season
- recent history of high HIV transmission risk behaviour.

In a recent USA study[5] of 258 patients with clinical suspicion of PHI infection, 40 of whom actually had HIV, the more sensitive symptom predictors (sensitivity >70%) for the diagnosis of PHI were fever (80%) and tiredness (78%). The more specific symptoms (specificity >80%) included recent weight loss of more than 2.5 kg (86%), oral ulcers (85%), and rash (82%). Common PHI symptoms such as headache, diarrhoea and night sweats were also common in people without HIV, and therefore tended to be nonspecific (<60% specificity).

Table 1. Key symptoms and signs of acute HIV

General
Flu-like illness, ie:
Fever - three or more days (90% of cases)
Lethargy and malaise
Mylagia and arthralagia
Lymphadenopathy (40-70% of cases)
CNS
Headache especially retro-orbital and worse on lateral eye movements
Signs of meningism with stiff neck on passive flexion
Photophobia
Skin
Rash particularly a maculopapular rash on the thorax and arms
Dequamation reactions of the hands and feet
Gastrointestinal
Diarrhoea
Mouth ulcers
Sore throat (sometimes candidal)

As one can see from the USA study, you have to get a lot of false alarms just to pick up 40 acute infections out of 258 patients that you were worried about enough to do extra tests.

Pathology tests

Tests for HIV antibodies may be negative for up to three weeks after the start of the PHI illness despite recent improvements in EIA test performance.[5]

As HIV appears in the blood in the early days of the illness, it can be detected by tests that detect virus particles. These are:

- proviral DNA
- polymerase chain reaction,
- branched chain DNA HIV viral load assays, and
- viral proteins such as protein 24 (p24 antigen).

Newer tests are in development that measure both antigen and antibody at the same time but are not widely available in Australia.

However, some of these tests can show false positive results. In the USA study[5] there were false positive rates of 5% for the Chiron/Bayer B-DNA and 3% for the Roche Amplicor RT-PCR assays.[5] The false positives on the B-DNA assay ranged up

Table 2. Asking about risk behaviour

'I'm sorry to have to ask you this question, but nowadays when people come to see me with a flu-like illness (or these types of symptoms) I need to ask them a sensitive question. Have you done anything in the past few weeks that could possibly put you at risk of acquiring HIV infection?'

to 2058 copies/mL while the false positives for the RT-PCR ranged up to 103 copies/mL. If the sample was retested using the same assay the previously false positives were negative, and only one person with confirmed PHI was in this range. The p24 antigen test is less sensitive (77%), but was more specific (99.5%). After three weeks it usually becomes undetectable again.[6]

Seek the advice of specialist pathology laboratories if possible before ordering and interpreting tests. State and territory infectious disease reference laboratories are usually an excellent source of advice on appropriate tests and their interpretation.

Find out when test results will be available and inform the patient when they will need to make an appointment for follow up. Good clinical practice (and state law in many states) requires all patients to return for their HIV test results as this type of sensitive information should be given in person.

Management of the diagnosis of PHI

Patients with PHI infection can usually be managed in the community by their own GP with the support of either an HIV experienced GP and/or a hospital based specialist.

Most of the physical symptoms such as fever, headache and nausea can be treated with simple analgesics and antiemetics. Hospital admission may be required occasionally for rehydration or management of rare associated diseases but on the whole the patient can stay at home.

The psychological impact of a new HIV diagnosis on the individual and their partner, friends and family cannot be underestimated. The GP can provide individual support, empathetic listening and referral to counselling and peer support groups. Early and frequent follow up with a caring attitude has been demonstrated to reduce long term psychological sequelae of HIV diagnosis.[8]

Table 3. Pathology tests for diagnosis of primary HIV infection[7]

HIV antigen tests	
P24 antigen	P24 antigen may become positive within a few days of symptoms and be absent after two weeks
Qualitative PCR HIV DNA	HIV DNA may become positive within a few days of symptoms and remain positive Recommended if immediate diagnosis is required Qualitative proviral DNA tests better in setting of seroconversion than qualitative
Quantitative HIV RNA viral load RT PCR or b-DNA	HIV RNA viral load may become positive within a few days However, the quantitative viral load assay is generally not by recommended to diagnose acute HIV infection due to false positives
HIV antibody tests	
HIV antibodies (EIA or ELISA)	EIA may take up to three weeks to become positive after onset of clinical signs and symptoms
HIV antibodies (Western Blot)	Western Blot may take up to three weeks to become positive after onset of clinical signs and symptoms

Note: Other tests may be indicated and should be performed in conjunction with specialist centres and laboratories

Very early treatment with antiretrovirals

Treatment of HIV infection during the early phase of PHI infection with combination antiretroviral medications has been advocated in recent years. The potential benefits are:

- minimisation of immune system damage
- lowering of the viral replication 'set point', and
- reduction in viral seeding of CNS.

The possible harms could be:

- disturbance of immune response to HIV
- short and long term effects of antiretrovirals.

The lack of data on clinical outcomes from prospective long term randomised controlled trials of antiretrovirals in PHI infection makes them still controversial. If the potential benefits of antiretrovirals are to be realised, time is of the essence. A phone call to a colleague more experienced in HIV medicine, either an HIV experienced GP or a hospital clinician can assist with seeking the current best clinical practice.

Long term management of HIV

This article does not aim to cover the long term management of the HIV infected patient which is well covered in the Australasian Society for HIV Medicine (ASHM) monograph, HIV/hepatitis C

and primary care, obtainable at: www.ashm.org.au.

Postexposure prophylaxis and the GP

Postexposure prophylaxis (PEP) of occupational and nonoccupational exposures to HIV has been used in Australia over the past few years. A four week course of 2–3 antiretroviral drugs taken within 72 hours or less of exposure to HIV infection may reduce the risk of the exposed uninfected person becoming infected.[9]

Antiretroviral drugs cause common side effects such as nausea and diarrhoea as well as rare, severe side effects. In a recent study, 67% of patients taking PEP for occupational and nonoccupational exposures had side effects and 25% discontinued their PEP before completing four weeks.[10]

A study based at the National Centre in HIV Epidemiology and Clinical Research has shown that nonoccupational PEP programs instituted through a network of hospitals, GPs and sexual health centres in New South Wales, can be safe and apparently effective in reducing individual transmission risk after high risk behaviours without leading to a concomitant rise in later risk behaviour.[11] Other states have followed suit and instituted programs. In Victoria, PEP is only available in one metropolitan teaching hospital, the Alfred Hospital. Unfortunately access has not been widened to GPs or to any other hospitals yet, raising serious questions about equity of access.

Antiretroviral therapy for HIV infection is listed under Section 100 of the Pharmaceutical Benefits Scheme and can only be prescribed by GPs who have been through a recognised HIV prescriber's education program, as well as hospital based physicians. For details on courses in your area check out the Australasian Society of HIV medicine website: www.ashm.org.au.

PEP risk assessment

Postexposure prophylaxis risk assessment requires a similar approach to that required for PHI infection. The highest risk for transmission is unprotected receptive anal or vaginal sex with someone who is HIV infected or whose HIV status is unknown. In these cases, risk per transmission is 1 in 50 to 1 in 200 or lower depending on individual factors such as stage of the infected person's HIV status, ie. acute, chronic or late stage.[12]

The risk of insertive unprotected anal or vaginal sex is slightly less at 1 in 100 to 1 in 200. Receptive oral sex is of very low risk but not 'no risk'. Reliable evidence based data on HIV transmission risk for oral sex is difficult to find but figures quoted range from 1 in 1250 to 1 in 20 000 episodes.[13]

Following assessment, all individuals with high risk exposures should be immediately referred to an approved antiretroviral prescriber such as an HIV experienced GP, sexual health centre, or the emergency department of a major hospital for the discussion about the provision of PEP. The sooner the postexposure antiretroviral treatment is commenced, the greater the theoretical chance of success.

Patients taking PEP may get side effects and need psychological support by their GP through a difficult time. They will also need follow up blood tests for HIV and to check for PEP associated liver and bone marrow toxicities.

National guidelines on the use of PEP for nonoccupational HIV exposures have been produced and are available at: www.ancahrd.org/pubs/index.htm.

SUMMARY OF IMPORTANT POINTS

- GPs are usually the first point of contact for someone with primary HIV infection.
- HIV seroconversion reactions have similar presentations to flu and other common viral infections in general practice.
- Think: 'Could it be HIV?'
- Ask about risk behaviours.
- Listen with sensitivity and without making judgments.
- Consult with more HIV experienced colleagues early.
- Act without delay if the diagnosis is confirmed.
- Remember: 'Ask and you shall see'.

Conflict of interest: none declared.

Resource

For more details on GP HIV training programs in your area contact: www.ashm.org.au.

Author's note

Attention is drawn to the ASHM monograph HIV/viral

hepatitis: A guide for primary care. Chapter 4: Exposure and acute infection. Anderson J, ed; which was used extensively as a reference point for this article. Copies of the monograph can be obtained from the Australasian Society of HIV Medicine, Locked Mail Bag 5057, Darlinghurst, NSW 1300. Phone: 61 2 9368 2700 Email: ashm@ashm.org.au

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