Delayed diagnosis of HIV in patients with reactive lymphadenopathy

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INTRODUCTION

Lymphadenopathy is common in human immunodeficiency virus (HIV) infection, and may be the presenting feature. This article describes five patients who underwent biopsy for unexplained lymphadenopathy. Their biopsies showed reactive hyperplasia and four of the patients were discharged without a firm diagnosis; within 5 years, all were subsequently diagnosed HIV positive. In contrast, lymphadenopathy in the fifth case prompted a rapid diagnosis of HIV infection.

The annual number of new cases of HIV infection in the UK has remained constant at about 2600 since 1994 (Anon, 1998). These cases highlight the continuing need to consider HIV infection when faced with unexplained lymphadenopathy, particularly in patients who appear superficially to be at low risk.

DISCUSSION

Lymphadenopathy is extremely common in clinical practice. Finding non-specific, reactive hyperplasia in a diagnostic lymph node biopsy is also common and often disregarded, despite numerous possible causes, including HIV and Castleman's disease (Krishnan et al, 1993). The latter is characterized by lymphadenopathy and lymphoid masses involving multiple systems.

In early HIV infection, persistent generalized lymphadenopathy affects up to one-third of patients who may be otherwise asymptomatic (Weller et al, 1996). Histologically, the lymphoid follicles are most often hyperplastic (Baroni and Uccini, 1993). It has been suggested that florid follicular hyperplasia in a lymph node, while not specific to HIV, is characteristic enough to indicate the need for HIV testing (Butler and Osborne, 1988). The proportion of biopsied lymph nodes suggestive of primary HIV lymphadenopathy varies geographically according to HIV prevalence, but may be as high as 22% (Bem et al, 1996).

In four patients, the diagnosis of HIV infection was delayed by 1–5 years despite biopsy of their lymph nodes. Cases 1 and 2 occurred early during the HIV epidemic, when awareness was still low. In cases 3 and 4, the diagnosis was not considered, presumably because of perceived lack of risk. An open mind and careful history-taking would have elicited their risk factors. Factors associated with delayed diagnosis of HIV include being heterosexual, aged 15–24 years or over 50 years, and being non-white (Porter et al, 1993). In contrast, the fifth patient was diagnosed within hours of presentation because of an easily apparent lifestyle risk factor.

There are benefits in diagnosing HIV infection early. Highly active antiretroviral therapy and prophylaxis

CASE REPORT 1

In 1983 a 41-year-old West African seaman presented with pyrexia, anaemia and lymphadenopathy. A *Toxoplasma* dye test was strongly positive at 64 000 iu. Axillary lymph node biopsy showed 'no recognizable infection', with prominent angiofollicular hyperplasia suggestive of Castleman's disease. The patient received pyrimethamine, sulphadoxine and spiramycin. He was subsequently lost to follow-up. In 1988 his serum, stored from 1983, was retrospectively found to contain HIV antibodies.

CASE REPORT 2

In 1984, a 25-year-old homosexual man with 8 months of generalized lymphadenopathy underwent cervical node biopsy, histology of which showed follicular hyperplasia. He was discharged from surgical clinic with a diagnosis of 'glandular fever-type disease' and his lymphadenopathy resolved over the next 6 months. In 1985, a HIV antibody test was positive. Retrospective testing of serum stored before the onset of lymphadenopathy was negative for HIV. In 1987 he presented with oral candida and leukoplakia. He developed *Pneumocystis carinii* pneumonia, *Pseudomonas* sepsis and cytomegalovirus retinitis before dying in 1990.

CASE REPORT 3

In 1995, a 37-year-old married woman was referred to a surgical clinic with a neck lump. The biopsy was reported as a reactive lymph node, and she was discharged. She remained well until 1998, when she presented with confusion, ataxia and neutropenia. Bone marrow examination showed relative leukopenia, and she tested positive for HIV antibodies. Magnetic resonance imaging was compatible with HIV encephalopathy. Her CD4 count was 234×10^6/litre and her HIV viral load was 39 000 copies/ml. On closer questioning, she had no obvious risk factors for HIV apart from the fact that her husband had died young of 'cancer'. She has improved on antiretroviral therapy.

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against opportunistic infections are now standards of care (Carpenter et al, 1998; Kovacs and Masur, 2000; Moyle, 2000). Infected patients can be counseled to modify behaviour, and prevent further transmission. Finally, there are medicolegal implications if the diagnosis is missed or delayed (Hirsch, 1993).

CONCLUSIONS

Biopsy remains a vital investigation in patients with unexplained lymphadenopathy. It is essential in areas with high incidences of HIV-related tuberculosis to exclude tuberculous lymphadenitis from other HIV-related infections and tumours. The finding of reactive follicular hyperplasia has many causes, including HIV infection. Risk factors for HIV must therefore be actively sought in all patients. Delayed diagnosis of HIV infection may be disastrous for the patient, his/her contacts, and the doctor. **HM**

CASE REPORT 4

In 1995, a 56-year-old heterosexual married man had a submandibular gland resected for chronic sialadenitis. The presence of a follicular hyperplastic lymph node within the excised tissue was incidentally noted. In 1998 he had a positive HIV test after his wife presented with AIDS-related cerebral toxoplasmosis. His only clinical problem was mild seborrheic dermatitis, but his CD4 count was 41 x 10^6/litre and HIV viral load was 57 000 copies/ml. Detailed history revealed that he had worked in Africa for some years. Antiretroviral treatment was started.

CASE REPORT 5

In 1997, a 28-year-old homosexual hairdresser was referred to a medical clinic with generalized lymphadenopathy. He was diagnosed as being HIV positive on the same day. Lymph node histology showed follicular hyperplasia. His CD4 count was 661 x 10^6/litre and his HIV viral load was 25 000 copies/ml. He remains well on antiretroviral therapy.

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