Optic neuritis and HIV-1 infection

B J Sweeney, H Manji, R J C Gilson, M J G Harrison

Abstract
A patient is reported who developed acute optic neuritis in the context of severe immunodeficiency associated with HIV-1 infection. The clinical, laboratory, and radiological features are described and the possible associations with syphilis, multiple sclerosis, lymphoma, and HIV-1 infection are discussed.

(J Neurol Neurosurg Psychiatry 1993;56:705-707)

Although there have been case reports of optic neuritis occurring in patients with HIV-1 infection, they have usually been caused by syphilis or opportunistic organisms such as cryptococcus, histoplasma, herpes zoster, and cytomegalovirus.1-4 We report the case of a patient who developed clinical, laboratory, and radiological evidence of acute optic neuritis associated with HIV-1 infection, who had a partial recovery without intervention, and who subsequently developed a probable primary central nervous system lymphoma (PCNSL).

Case report
A 43 year old anti-HIV-1 seropositive bisexual man presented in April 1992 with a gradual loss of vision in the left eye. He first noticed a clouding of vision in the left upper quadrant which progressed to involve the central field of his left eye and eventually to total loss of light perception in that eye over a 15 day period. There were no symptoms in the right eye. Medical history included: treatment of latent syphilis in 1982 and retreatment in 1991; chronic hepatitis B virus infection diagnosed in 1987; and shingles affecting the left C4 dermatome in 1990. He was found to be anti-HIV-1 seropositive in 1990: retrospective testing of stored sera showed that he had been seropositive since at least 1987. He developed thrombocytopenia in 1990 and constitutional symptoms consistent with the AIDS related complex (ARC) in 1991. He had not had an AIDS defining diagnosis although his CD4 lymphocyte count had fallen to a level associated with severe immunosuppression (<0.2 x 10^9/L). Medications since April 1991 were zidovudine 250 mg four times daily and cotrimoxazole 960 mg daily. He did not smoke and drank alcohol moderately.

The general physical examination was normal but neurological examination showed no perception of light in the left eye with an afferent pupillary defect and a normal appearance of the retina and optic disc. The right eye had a normal visual field, acuity, pupillary response, and fundus. There was no meningism and the rest of the neurological examination was normal. The clinical impression was of an isolated lesion of the left optic nerve.

Investigations
Haemoglobin 11.8 g/l, white cell count 4.1 x 10^9/L with a total lymphocyte count of 1.4 x 10^9/L, CD4 lymphocyte count 0.09 x 10^9/L (normal 0.35–2.2 x 10^9/L), platelets 31 x 10^9/L; erythrocyte sedimentation rate 30 mm/hour; urea and electrolyte normal; liver function tests normal; hepatitis B virus surface and e–antigens detected; serum cryptococcal antigen negative.

CSF analysis. Protein 0.3 g/l, glucose 3.3 mmol/l (serum 5.6 mmol/l); oligoclonal bands negative; no cells; Gram, india ink, and Ziehl-Nielsen stains negative; cryptococcal antigen negative; culture and sensitivity for fungi and bacteria negative; viral culture for cytomegalovirus, herpes zoster, and herpes simplex negative; cytology negative.

Toxoplasma antibodies negative in serum and CSF. Syphilis serology: serum RPR negative; TPHA positive; FTA absorbed weakly positive (consistent with past or treated infection); CSF TPHA negative.

MRI scan (1.5 T) showed an abnormal signal from the optic chiasm and retrobulbar portion of the left optic nerve on T2 weighted spin echo sequence. An MRI scan using T1 weighted spin echo sequence and following dimeglumine gadopentate injection showed abnormal enhancement, particularly in the retrobulbar portion of the left optic nerve (fig). There were no lesions in the brain.

The final diagnosis was that of an acute optic neuritis. The patient began to recover vision spontaneously after 18 days with restoration of the visual field, a near vision of N12 and a normal pupillary response in the left eye 70 days after the development of symptoms. A T2 weighted spin echo sequence MRI scan during his final admission
Dimeglumine gadopentate enhancement of the retrolubar portion of the left optic nerve on T1 weighted spin echo sequence.

(see below) showed a normal signal from the optic chiasm and left optic nerve. At approximately 74 days after initial admission he developed a severe occipital headache and was admitted to hospital for investigation. Neurological and general physical examination revealed mild meningism but no other signs. MRI scan showed lesions of the inferior cerebellar hemispheres on T2 weighted spin echo sequence which were associated with mass effect. Repeat serum anti-toxoplasma antibodies and cryptococcal antigen were negative. He began anti-toxoplasmosis treatment. He did not respond to this therapy and died before a planned biopsy, just over 90 days following his first symptoms of visual loss. He did not have a postmortem examination.

Discussion
This anti-HIV-1 seropositive patient had a clinical and radiological remission of an optic neuritis without evidence of opportunistic central nervous system infection or infiltration at first presentation. The clinical and radiological picture of the subsequent illness was most compatible with PCNSL, although other disorders such as toxoplasmosis cannot definitely be ruled out.

The slow progression of the visual loss and almost complete recovery are also against a vascular cause. The normal protein, glucose, absence of pleocytosis, negative oligoclonal bands, and negative serology in the CSF are against the diagnosis of syphilis. The history of adequate treatment for latent syphilis in 1982 with retreatment in 1991 and the improvement without further antibiotic therapy further diminish the likelihood of syphilis as a cause.

Berger and Gray have reported on the occurrence of a multiple sclerosis-like illness at all stages of HIV-1 infection, although this may represent the chance association of two illnesses prevalent in the same age group. Acute optic neuritis is followed by clinical multiple sclerosis (MS) in up to 75% of patients who do not have HIV-1 infection. The lesions seen in the cerebellum on MRI scan 70 days after the onset of visual loss could represent MS plaques with associated mass effect. However the normal CSF analysis and absence of oligoclonal bands were against this diagnosis and fulminating MS is rare. Furthermore, although the clinical syndromes may be similar, the depletion of cell-mediated immunity in patients with HIV-1 infection suggests a different pathogenesis for this illness than the demyelination occurring in MS, in which helper CD4 cell activation is proposed as a crucial early event in lesion development.

There are a number of neurological and neuropathological syndromes which are caused directly by HIV-1, including HIV-1 encephalitis, diffuse leukoencephalopathy, vacuolar myelopathy, and peripheral neuropathy. This patient did not have clinical or imaging evidence of any of these conditions. There is no well recognised clinical syndrome of optic neuritis specifically caused by HIV-1, although a recent postmortem study by Tenhula et al found a 40% reduction in optic nerve axonal population in AIDS patients compared with controls on morphometric comparison. It may be that there is a direct or indirect neurotoxic effect of HIV-1 on optic nerve fibres similar to that seen elsewhere in the CNS and that HIV-1 infection itself contributed to the development of optic neuritis in this case.

Meningeal lymphoma is a cause of cranial nerve palsies and in this case the optic neuritis was followed by the development of a probable lymphoma in the cerebellum. These palsies tend to be progressive and to recover only with therapy for the lymphoma. However, there are case reports of spontaneously remitting optic neuritis occurring in association with lymphoma. In addition Galetta et al have recently reported the case of an anti-HIV-1 seronegative patient who developed a transient right third cranial nerve palsy 12 months before presenting with a polyradiculopathy caused by a B cell lymphoma. At first presentation their patient had intrinsic abnormalities of both third nerves seen on gadolinium enhanced MRI scan which resolved on follow up. Our patient had a similar outcome to his optic nerve lesion and also developed a probable PCNSL. If the optic neuritis and cerebellar lesions in this patient were causally linked it is unclear whether the cranial nerve involvement represented a paraneoplastic inflammatory neuritis or nerve invasion by lymphomatous B cells.

We conclude that patients with HIV-1 infection can develop a spontaneously remitting optic neuritis, in association with probable CNS lymphoma in this instance. The cause of this optic neuritis remains obscure.
Patients with or at risk of HIV-1 infection presenting with optic neuritis warrant careful initial evaluation and follow up.