lesson of the month (1)

Brian F Menezes MB BS, Core Medical Training ST2

Penelope Williams MB ChB, Core Medical Training ST1

Jason Ramtahal MRCP, Neurology Registrar

Mike Boggild FRCP, Consultant Neurologist

The Walton Centre for Neurology and Neurosurgery, Liverpool

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The significance of early HIV testing

Prolonged diagnostic dilemma and poor clinical outcome in the absence of early HIV testing.

Lesson

A 37-year-old British woman presented in March 2005 with ataxia. She admitted to no risk factors for an immunocompromised state (ie no positive history of foreign travel, unsafe sexual intercourse, blood transfusion or organ transplant, or intimate family members or sexual partners having HIV/AIDS). Neurological examination revealed no deficits other than a small central scotoma. Magnetic resonance imaging (MRI) showed small T2 hyperintensities in the posterior fossa (Fig 1a). Cerebrospinal fluid (CSF) analysis detected high protein (1.15 g/l) with matched oligoclonal bands. CSF microscopy/cytology, visual evoked potentials and autoantibody screen were normal.

By July 2005, she developed progression of ataxia. Repeat MRI showed no interval changes. Immunoglobulins and tumour markers were normal. Antigliadin IgA, Whipple's polymerase chain reaction (PCR) and mitochondrial disease DNA analysis were negative. Serum angiotensin-converting enzyme (ACE) level was >100 U/l but urinary calcium and gallium scan were normal, thus excluding neurosarcoidosis. An empirical course of intravenous methylprednisolone provided no clinical improvement.

Repeat MRI in September 2005 showed scattered T2 high signal lesions in the posterior fossa. Brain biopsy was deferred due to their position.

In April 2006, MRI was repeated again due to further deterioration. This revealed a new right hemispheric lesion in the sensorimotor cortex (Fig 1b). Biopsy revealed prominent macrophages and abnormal oligodendrocytes with enlarged nuclei. Cerebrospinal fluid PCR for John Cunningham virus (JCV) and electron microscopy confirmed progressive multifocal leukoencephalopathy (PML). HIV testing undertaken at this point was positive. It was only at this stage that it was revealed that the patient's sister had died of AIDS 10 years previously – though the patient was unaware of this diagnosis – and that the patient had cared for her during the terminal stages of her illness.

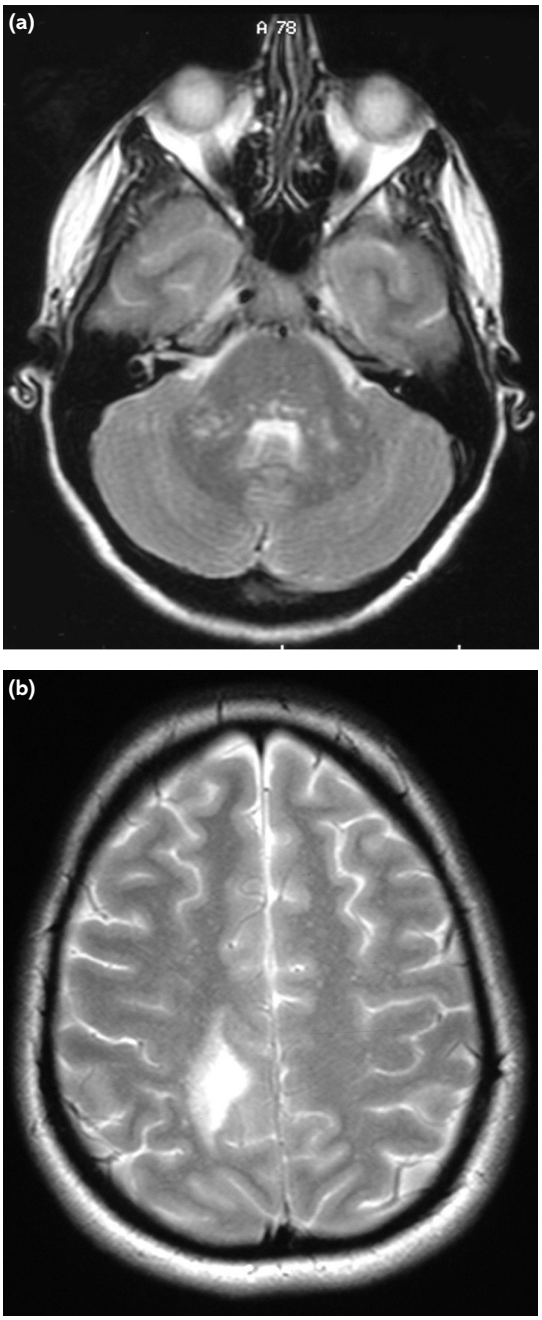

Fig 1. Progression of primary lesion on imaging: magnetic resonance image (MRI) at initial presentation **(a)** and MRI at 12 months of presentation **(b)**.

Despite antiretroviral treatment, she continued to deteriorate and died 17 months after her initial presentation.

Comment

Progressive multifocal leukoencephalopathy is a fatal demyelinating disease associated with infection of oligodendrocytes by JCV in impaired cell-mediated immunity. Until recently, it was a virtual medical curiosity. However, since the AIDS pandemic, the epidemiology of PML has changed dramatically. A 20-fold increase in PML was reported in Florida within a decade and nearly all cases identified were AIDS-related.[1] Of AIDS patients 4% develop PML and in half of these it is the AIDS-defining illness.[2]

The differential diagnosis of cerebral mass lesions in AIDS/HIV includes toxoplasmosis, central nervous system lymphoma, PML, tuberculous/fungal abscess, focal encephalitis, metastatic Kaposi's sarcoma, acute stroke and AIDS dementia complex. These were not initially considered in this case as the patient's HIV status remained unknown. This resulted in a tortuous investigatory course and delayed a definitive diagnosis. Early HIV testing, as has been advocated by Delpierre *et al*, may have resulted in a swifter resolution of this diagnostic dilemma.[3]

The British HIV Association has reported that late diagnosis accounts for 35% of HIV-related deaths. Moreover, Sullivan *et al* noted that many of those diagnosed late had been in contact with a healthcare professional in the preceding year with symptoms that were retrospectively likely to be related to HIV.[4]

The Centers for Disease Control and Prevention now recommend that diagnostic HIV testing and opt-out screening should be part of routine clinical care in all settings. More recently, the Department of Health has urged healthcare providers to offer HIV tests to patients if there is a possibility that they have had exposure to HIV and to recommend that they should accept testing. There is therefore a need for a very high index of suspicion for the diagnosis of HIV infection and the importance of early HIV testing to facilitate early diagnosis and treatment of HIV/AIDS and its associated illnesses.

References

1 Berger JR, Pall L, Lanska D, Whiteman M. Progressive multifocal leukoencephalopathy in patients with HIV infection. *J Neurovirol* 1998;4:59–68.

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3 Delpierre C, Cuzin L, Lert F. Routine testing to reduce late HIV diagnosis in France. *BMJ* 2007;334:1354–6.

4 Sullivan AK, Curtis H, Sabin CA, Johnson MA. Newly diagnosed HIV infections: review in UK and Ireland. *BMJ* 2005;330:1301–2.