HIV dementia: a diagnosis to keep in mind

Introduction

Human immunodeficiency virus (HIV) dementia is a devastating complication of HIV disease and on average leads to death within 6 months if untreated (Navia et al, 1986). It is important to consider HIV when a patient presents with cognitive impairment first because dementia may be the first and only presentation of acquired immunodeficiency syndrome (AIDS) and also because HIV dementia is potentially reversible (McMurtray et al, 2006). It has long been accepted practice to test for syphilis in patients with neurocognitive impairment, and yet HIV is much more common than neurosyphilis. This case highlights the importance of considering HIV as a cause of dementia.

Discussion

This case serves to remind clinicians of the detrimental effects of missed opportunities to diagnose and treat HIV.

HIV dementia is the severe form of a spectrum of disease classified as HIV-associated neurocognitive disorder (Antinori et al, 2007), which affects 35–50% of patients with HIV (Cysique and Brew, 2011). Its features consist of a triad of behavioural, cognitive and motor disturbance (Navia et al, 1986). It is largely a sub-cortical dementia and a thorough neurological exam might reveal tremor, ataxia, loss of coordination of fine motor skills and frontal lobe release signs. Left untreated, signs of severe dementia may develop including mutism, incontinence and paraplegia (Navia et al, 1986). Cognitive testing should address fine and gross motor speed, concentration, processing, memory, learning, speech and language. Patients with HIV dementia may show slowness of thought and movement and a marked relative deficit in prospective memory, as was seen in this patient (Navia et al, 1986; Portegies et al, 1993).

A large range of differential diagnoses exist for HIV dementia including metabolic causes. However, this patient was markedly immunosuppressed and so investigations focussed on ruling out other infectious aetiologies such as progressive multifocal leucoencephalopathy, viral encephalitis, toxoplasmosis and neurosyphilis. As is usually the case, CSF analysis was normal for this patient but a mononuclear pleocytosis or a mildly raised protein level may be present. HIV is often detectable in the CSF without neurocognitive impairment and HIV RNA levels have not been shown to correlate with neurocognitive function and this patient did not, therefore, have a CSF HIV viral load.

Magnetic resonance imaging is necessary to help rule out the above pathologies and in addition may reveal cortical atrophy, dilated ventricles and white matter intensities as was seen in this case (Portegies et al, 1993).

Consideration should be given to commencing patients on antiretroviral therapy regimens which have been shown to better penetrate the CNS, as was the case in this patient. However, whether improved CNS penetration of antiretroviral therapy

Dr Christine M Kelly *is Academic Clinical Fellow, Institute of Infection and Global Health, University of Liverpool, Liverpool,* **Dr Alastair RO Miller** *is Consultant in Infectious Diseases, Department of Infectious Diseases and Tropical Medicine, Royal Liverpool University Hospital, Liverpool,* **Dr Baba Aji** *is Neurology Registrar, Walton Neuro-Centre NHS Foundation Trust, Liverpool, and* **Professor Tom Solomon** *is Director, Institute of Infection and Global Health, University of Liverpool, Liverpool L69 7BE and Chair, Division of Neurological Science, Walton Neuro-Centre NHS Foundation Trust, Liverpool*

Correspondence to: Professor T Solomon (tsolomon@liv.ac.uk)

Case Report

A 50-year-old Caucasian male of UK origin worked for a cruise line company and had travelled extensively. Symptoms began 3 months before presentation with vertigo, dizziness and some memory problems (he would forget telephone numbers and the password for his computer at work). He had also lost interest in hobbies and social activities. He was investigated in the USA with computed tomography and magnetic resonance imaging of the brain, lumbar puncture and electroencephalogram. Following this, he was given the diagnosis of normal pressure hydrocephalus. HIV testing was not considered.

He developed increasing difficulty with gait and suffered with frequent falls. He began to require a wheelchair for long distances. He lost his job and returned to the UK 7 months after initial symptom onset.

The only information of note in the medical history was that he had piercings and tattoos done over 5 years previously and admitted to having had unprotected sex with a male partner 10 years earlier.

General examination revealed seborrhoeic dermatitis. Neurologically, frontal release signs were present (palmar grasp reflex, pout reflex and snout reflex) and he had a broad ataxic gait but no myoclonus.

Results from his time in the USA were not available. On re-presentation to the UK he had routine blood tests as well as ammonia levels, angiotensin-converting enzyme levels, vitamin B_{12}, folate, erythrocyte sedimentation rate and blood cultures which were all normal. An electroencephalogram showed no abnormality and a magnetic resonance imaging scan revealed leukoencephalopathy, secondary cerebral atrophy and dilated ventricles (*Figure 1*), which was reported as non-obstructive hydrocephalus. A HIV test was then performed which was positive for HIV-1. The subsequent CD4 count was 9 cells/μl.

CSF results were normal: white cell count 3 cells/μl, red cell count 0 cells/μl, protein 0.38 g/litre, glucose 0.40 mmol/litre (blood glucose 7.3 mmol/litre). The Gram stain was negative and nothing was grown on culture. Additional CSF tests were performed for herpes simplex virus 1+2, adenovirus, enterovirus, varicella zoster, cryptococcus, toxoplasma, syphilis, Epstein–Barr virus, cytomegalovirus, BK/JC virus and tuberculosis. They were all negative. Formal neuropsychological testing confirmed marked impairment of prospective memory and motor speed.

An antiretroviral therapy regimen comprising nevirapine, lamivudine and zidovudine was commenced. The patient was discharged to a nursing home and having made an initial improvement, developed symptoms of florid psychosis and was relocated to a secure psychiatric unit. He now refuses all oral medications and is having antipsychotic treatment parentally.

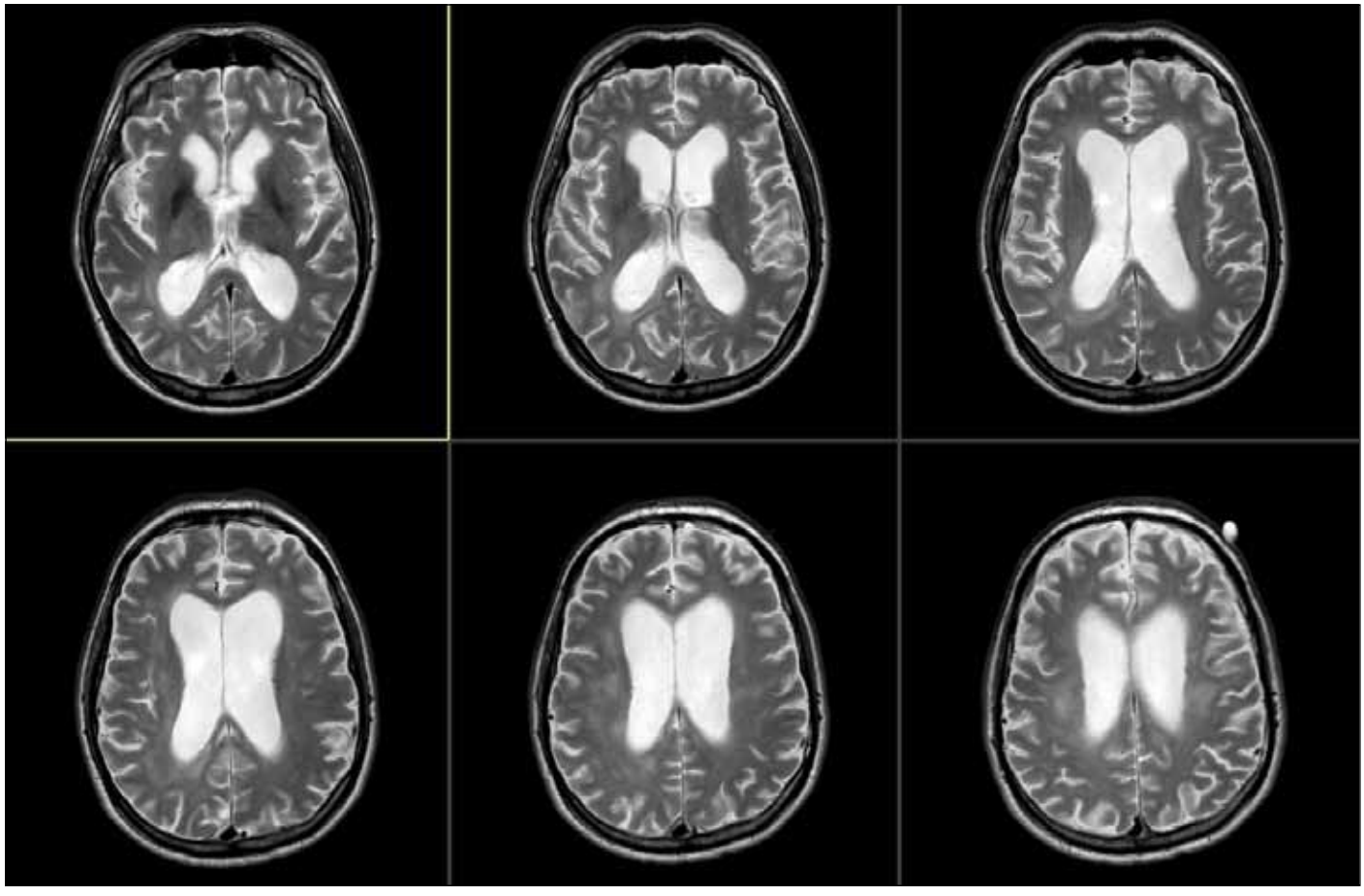

Figure 1. Magnetic resonance imaging brain scan showing dilated ventricles and atrophy typical of HIV dementia.

improves neuropsychological function in these patients remains unclear and is the subject of continued research (Cysique and Brew, 2009; Marra et al, 2009; Robertson et al, 2011).

British HIV Association (2008) guidelines clearly set out dementia as one of the qualifying conditions for the consideration of HIV testing. The National Institute of Clinical Excellence guidelines on dementia advise that HIV testing should be considered where risk factors exist (Fairbairn et al, 2006). A careful history from the patient or relatives should purposefully seek to elicit relevant risk factors, but if there is any uncertainty it is best just to offer the test. If the patient is unable to consent, the decision should be made by the clinical team according to the patient's best interests (British HIV Association, 2008). Under no circumstances should consent for HIV testing be sought from any family member.

Early diagnosis of HIV gives patients the best chance of a favourable outcome and opportunities to make the diagnosis should be maximized. BJHM

Antinori A, Arendt G, Becker JT et al (2007) Updated research nosology for HIV associated neurocognitive disorders. *Neurology* **69:** 1789–99

Cysique LA, Brew BJ (2009) Neuropsychological functioning and antiretroviral treatment in HIV/AIDS: a review. *Neuropsychol Rev* **19:** 169–85

Cysique LA, Brew BJ (2011) Prevalence of non-confounded HIV-associated neurocognitive impairment in the context of plasma HIV RNA suppression. *J Neurovirol* **17:** 176–83

Fairbairn A, Gould N, Kandall T et al (2006) *Dementia: A NICE-SCIE Guideline on supporting people with dementia and their carers in health and social care.* National Clinical Practice Guideline Number 42. The British Psychological Society and Gaskell, London

Marra CM, Zhao Y, Clifford D et al (2009) Impact of combination antiretroviral therapy on cerebrospinal fluid HIV RNA and neurocognitive performance. *AIDS* **23(11):** 1359–66

McMurtray A, Clarke DG, Christine D, Mendez MF (2006) Early-onset dementia: frequency and causes compared to late-onset dementia. *Dement Geriatr Cogn Disord* **21:** 59–64

Navia BA, Jordan BD, Price RW (1986) The AIDS dementia complex: I. Clinical features. *Ann Neurol* **19:** 517–24

Palfreeman A, Fisher M, Ong E et al (2008) UK National Guidelines for HIV Testing 2008. In British HIV Association, British Association of Sexual Health and HIV & British Infection Society (eds). British HIV Association, London

Portegies P, Enting RH, De Gans J, Algra PR, Derix MM, Lange JM, Goudsmit J (1993) Presentation and course of AIDS dementia complex: 10 years of follow-up in Amsterdam, The Netherlands. *AIDS* **7:** 669–75

Robertson K, Kumwenda J, Supparatpinyo K et al (2011) A multinational study of neurological performance in antiretroviral therapy-naïve HIV-1-infected persons in diverse resource-constrained settings. *J Neurovirol* **17**(5): 438–47

LEARNING POINTS

- HIV may present with cognitive impairment in the absence of other HIV-related illness.
- A careful history should be taken to elicit risk factors for HIV when assessing patients with cognitive impairment, especially patients with atypical presentations at a younger age.
- HIV dementia is usually a subcortical dementia and signs should be sought accordingly during the examination of a patient presenting with new cognitive impairment.
- HIV dementia is a potentially treatable cause of dementia and an early diagnosis gives a better chance of recovery.