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HIV-Associated CNS Vasculopathy in the Modern Era

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Dear Editor,

Advances in the treatment of illnesses related to the human immunodeficiency virus (HIV) have resulted in prolonged survival mainly due to the application of highly active antiretroviral therapy (HAART). Some of the longer-surviving patients suffer ischemic stroke that may be attributed to age-related atheromatous etiology; however, the present study indicates that underlying treatable infection should not be overlooked.

The three cases described herein were seen by a neurohospitalist in an academic center over the past 2 years. They represent a wide spectrum of strokes in those harboring HIV infection, ranging from a *de novo* presentation of acquired immunodeficiency syndrome (AIDS) to an unusual recurrent viral induced vasculopathy.

Case 1: a 52-year-old man with chronic hypertension presented with dysarthria and left-arm clumsiness following several days of headaches. His admission blood pressure was 135/85 mm Hg, and diffusion-weighted MRI images revealed a small ischemic stroke involving the right internal capsule and left cerebellum. Further history-taking revealed an acne-like lesion on the nose that had first appeared several weeks previously. The findings of CT angiography of the head and neck and transesophageal echocardiography were unremarkable. A CSF examination revealed an opening pressure of 22 cm CSF, 36 white blood cells (WBCs)/mm^3, positivity for cryptococcal antigen, and a negative venereal disease research laboratory (VDRL) test. Serum HIV and fluorescent treponemal antibody absorption (FTA-ABS) tests were positive. Biopsy of the nodular lesion on the nose revealed it to be a cryptococcoma. The patient was diagnosed with AIDS complicated by systemic cryptococcal infection including meningitis and possible neurosyphilis. The headache resolved following the intravenous administration of penicillin and amphotericin.

Case 2: a 50-year-old hypertensive smoker with an HIV-positive status who had been on HAART for the past 8 years presented with right hemiparesis without aphasia. He had been treated for syphilis some 30 years previously and denied any history of AIDS-defining illnesses. He mentioned that the stroke had cured his chronic daily headache that had been present for the past 2 years. MRI confirmed an acute left internal capsular infarct. CSF was acellular but with a positive cryptococcal antigen titer of 1:64 despite a negative serum titer. A serum FTA-ABS test was positive but CSF was nonreactive in a VDRL test. He was treated with intravenous amphotericin and penicillin, the latter due to the possibility of neurosyphilis.

Case 3: a 28-year-old man with AIDS receiving intermittent HAART suffered left hemiparesis from a right cerebral peduncular stroke (Fig. 1A) several weeks following a vesicular eruption on the right cheek and lip. At that time the CSF exhibited lymphocytic dominant pleocytosis (24 WBCs/mm^3) with a positive PCR for HSV-2 but negative for the varicella-zoster virus (VZV). Four months later he experienced sudden vertigo and diplopia accompanied by upbeating nystagmus and left-arm ataxia. Brain MRI revealed a left superior cerebellar peduncular infarct (Fig. 1B). A CSF examination revealed 14 WBC/mm^3 with again PCR positivity for HSV-2. Continuation of the intrathecal infection was confirmed by an ele-

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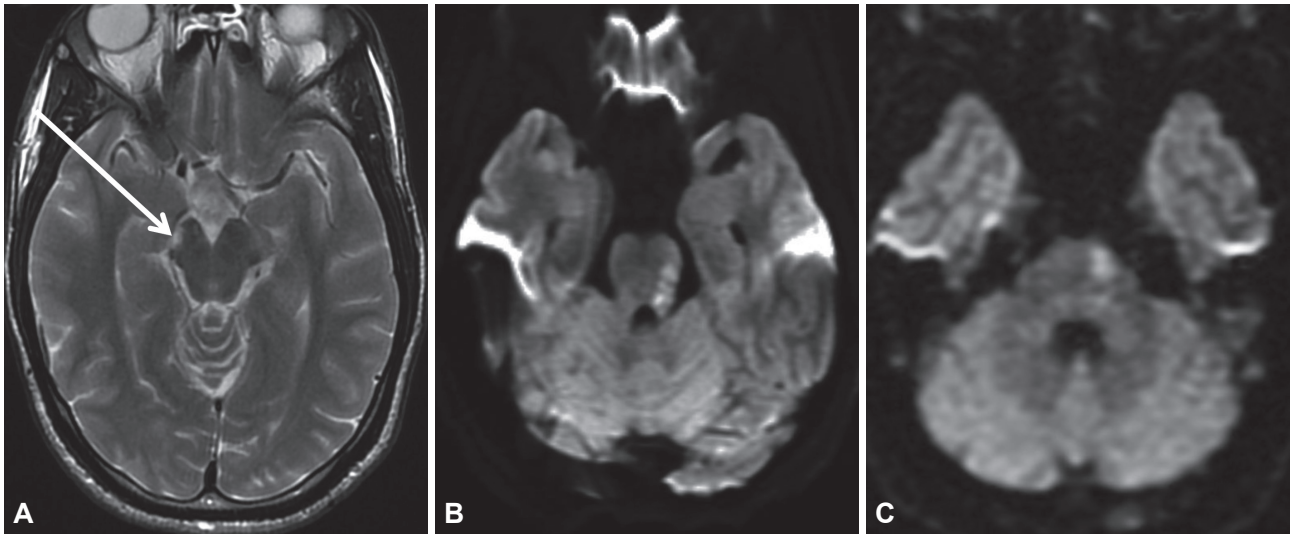

Fig. 1. Axial brain MRI performed at different times in case 3. FLAIR sequence revealing a subacute right peduncular infarction (A, white arrow). DWI sequences showing acute ischemic infarctions involving predominantly the left superior cerebellar peduncle (B) and the left ventral pontine tegmentum (C).

vated HSV-2 CSF/serum IgG index (23.82/6.67). The findings of tests for toxoplasma, VZV, and Epstein-Barr virus, and the VDRL test, cryptococcal antigen titer, and PCR were all unremarkable in serum and/or CSF. He was treated with intravenous acyclovir followed by daily oral valacyclovir. Several months later he suffered a small left pontine infarction (Fig. 1C) in the setting of poor compliance. Significant improvement again followed with the restarting of HAART and oral valacyclovir medications.

The first two cases represented older adults with chronic hypertension presenting with typical lacunar stroke syndromes. Lacunes with a multivessel distribution on MRI following several days of unexplained headache led to a lumbar puncture in case 1, with an eventual diagnosis of AIDS complicated by systemic cryptococcal infection and possible neurosyphilis. Case 2 was a patient with known HIV and a remote history of syphilis but without previous AIDS-defining illnesses on HAART who had been suffering from unexplained chronic headache. The CSF examination led to a diagnosis of cryptococcal meningitis. Both cases highlight the significance of unexplained headaches in HIV-positive patients with small-vessel ischemic strokes.

Zepper et al.[1] reported a case of an immune-competent man with HSV-2-associated meningitis and vasculitis who suffered both ischemic and hemorrhagic strokes. Although recurrent benign aseptic meningitis due to HSV-2 is common,[2] secondary ischemic infarctions are rare. Our case 3 suggests that HAART and antiviral therapy are effective in the background of unusual HSV-2 brainstem meningitis and vasculitis.

These three cases highlight the diagnostic importance of headaches in those with lacunar infarcts (cases 1 and 2) even without a previous history of HIV (case 1). Case 3 demonstrates that recurrent brainstem strokes may result from a treatable viral etiology.

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