We present the case of a now 42-year-old woman with a history of unilateral amblyopia, due to an optic nerve coloboma (Fig. 1a–c), and mental retardation since infancy, who developed a severe gait disorder over the last decade due to multiple ischemic cerebral lesions. Diagnostic evaluation established, by means of digital subtraction angiography, a diagnosis of Moyamoya arteriopathy affecting both the anterior and posterior cerebral circulation, as visualized on digital subtraction angiography (d) and magnetic resonance tomography (a, c; black arrows).

References
ly elevated (8 mg/l; n < 0.4). Serum cholesterol, LDL, HDL, triglyceride levels, proteins C and S and a transesophageal echocardiogram were normal. The CD4+ lymphocyte cell count was 3 cells/μl (normal = 600–1,500) and HIV RNA load was >228,000 copies/ml. Cerebrospinal fluid (CSF) analysis did not reveal any abnormalities. CSF cryptococcal antigen, treponemal and Toxoplasma antibodies were absent.

One month later, he was readmitted with disorientation and confusion. HIV RNA load was >100,000 copies/ml, suggesting poor compliance with HAART. On examination, he was disoriented and had left central facial paresis. Upon MRI examination, a new infarction in the right caudate and internal capsule was noted (fig. 1b). A magnetic resonance angiogram (MRA) showed bilateral stenosis of the anterior, middle and posterior cerebral arteries, both proximally and in distal smaller branches (fig. 1c, f). A repeated MRA scan, 4 months later, showed significant progression, with high-grade stenosis of the anterior, middle and posterior cerebral arteries and occlusion of the right vertebral artery (fig. 1d, g). On questioning the family, it was noted that about 3 months after the second stroke the patient moved in with his mother, who monitored his medication, and only then did he become totally compliant with HAART. HIV RNA load then remained low for the next 6 months (138–380 copies/ml). About 2 months after second stroke, the patient had been started on prednisone (60 mg/day). Cyclophosphamide (50 mg/day) was also added for a few weeks with a diagnosis of presumed cerebral vasculitis. One month later, the patient developed complications of hyperglycemia, lethargy and fever. Cyclophosphamide was discontinued and prednisone was reduced to 30 mg/day.

The patient has been doing well for the past 6 months on low-dose prednisone and regular HAART, with no new complaints or neurological abnormalities, and is fully alert, oriented and ambulatory. The CD4+ lymphocyte cell count is 13 cell/μl and HIV RNA load is 319 copies/ml. A final MRI/MRA study, 9 months after the onset of symptoms, did not show any new infarcts and showed improved vascular flow in the right vertebral, left anterior cerebral, posterior cerebral and distal right middle cerebral artery branches (fig. 1e, h).

**Discussion**

In autopsy series of AIDS patients, researchers have found a 4–29% prevalence of cerebral infarction [2]. Most of these infarcts are associated with cardioembolic causes, coagulopathies or non-HIV central nervous system infections such as cytomegalovirus, tuberculosis, Cryptococcus, varicella zoster, hepatitis B or C [3]. When these causes are excluded, strokes in an HIV-infected individual have been linked to a less well-defined entity, HIV vasculopathy [6]. In children with AIDS, vasculopathy has been reported to present with multiple cerebrovascular aneurysms [4, 6]. Adults develop large vessel (primarily aortic) aneurysmal disease [6]. Pathologically, these cases show subintimal fibrosis, damage to internal elastic lamina and adventitial inflammatory infiltrate [6]. The etiopathogenesis of such changes, whether directly related to HIV infection or immune-mediated vasculitic changes, is unclear. In some studies, HIV glycoprotein 41 has been demonstrated in mononuclear cells of the intima of intracranial vessels [7], while others have not found HIV in affected vessels [8].

Our patient was unique because we could document, on sequential MRI studies, the rapid progression of severe cerebrovascular stenosis and its subsequent improvement, and correlate this with his therapy, HIV RNA load and clinical status. Over 3 months, the MRA documented his very rapid progression of high-grade cerebral vascular stenosis (without associated aneurysmal dilatation), while he had a very high HIV viral load. Since his infarcts occurred when he was noncompliant with HAART (with uncontrolled viral proliferation and a very high HIV viral RNA load [≥100,000 to >228,000 copies/ml]), we speculate that cerebral arteriopathy was related to HIV infection of the cerebral vessels. On follow-up, his HIV RNA load remained low (<400 copies/ml), and he remained neurologically normal without new cerebral lesions. After 6 months of adequate HAART, a MRA study confirmed improved vascular flow in multiple cerebral arteries, suggesting that the progression of arteriopathy was arrested after adequate anti-retroviral therapy. We considered the alternative diagnosis of immune-mediated vasculitis unlikely because recurrent infarcts occurred in the setting of severe immunosuppression (CD4+ count, 3 cells/μl), negative antibody tests and the absence of headaches or abnormal CSF findings. Furthermore, MRA studies showed that the vascular stenoses improved significantly, even while steroids were being markedly decreased. Also, rapid clinical improvement on HAART, the absence of typical brain MRI findings and negative laboratory tests made other opportunistic non-HIV infections of the central nervous system unlikely.

A larger number of AIDS patients with cryptogenic strokes and autopsy studies are needed to understand better the pathogenesis of HIV vasculopathy. Our patient suggests that untreated or poorly treated AIDS with a high viral load may be associated with rapidly progressing cerebrovascular stenosis and infarcts. Prompt initiation of HAART, with close monitoring of the decreased HIV RNA viral load, may be of benefit in ameliorating the arteriopathy associated with HIV.
References


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