We describe a child with human immunodeficiency virus infection who presented with a large subarachnoid hemorrhage. She had multiple vascular and fusiform aneurysms in the proximal cerebral arterial circulation and no evidence of bacterial or fungal infection. The arteriopathy coincided with a high human immunodeficiency virus RNA load. Human immunodeficiency virus may cause cerebral arteriopathy with potentially life-threatening complications.

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Introduction

Intracranial arterial aneurysms are rare in children [1,2]. Mycotic aneurysms are even less common and, with the exception of human immunodeficiency virus (HIV), are rarely observed in the absence of congenital heart disease. Intracranial hemorrhage is a well-documented complica-

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Five months before presentation, the patient’s CD4 count was 650 cells/μL, and her viral RNA load was greater than 750,000 copies/mL. Four months after beginning triple combination therapy, the CD4+ count increased to 1,092 cells/μL, and the viral RNA load was undetectable. A second magnetic resonance angiogram (not presented) done at this time revealed no new aneurysms and no change in the existing ones.

Discussion

Our patient had multiple aneurysms in the proximal cerebral arterial system in the setting of HIV encephalo-pathy. Her aneurysms were clinically silent until she had acute SAH, probably from the right posterior cerebral artery aneurysm. The proximal location and large size of this child’s aneurysms are atypical for mycotic aneurysms, which tend to be fusiform and located in distal arterial branches.

Cerebral arterial aneurysms have previously been demonstrated in patients with HIV infection. Mankier and Hunt [6] described berry aneurysms of the circle of Willis in six adults with acquired immunodeficiency syndrome. Husson et al. [7] prospectively identified multiple fusiform and saccular aneurysms of large intracranial vessels in two HIV-infected children by magnetic resonance imaging. In one case, contrast cerebral angiography did not reveal additional small- or medium-vessel aneurysms, and chest and abdomen magnetic resonance imaging revealed no extracranial large-vessel aneurysms. In the second case the aneurysms appeared (as observed on serial magnetic resonance angiograms) over an interval during which the serum p24 antigen load increased dramatically, without evidence of an inflammatory or congestive process. Both patients had no signs referable to their aneurysms.

HIV infection has been associated with arteriopathy of small, medium, and large cerebral arteries, both in isolation and in the presence of cerebral aneurysms and...
infarcts. Aneurysmal dilation of the circle of Willis was found at postmortem examination in one of six HIV-infected children with stroke [8,9]. The affected arteries exhibited marked intimal fibroplasia with medial thickening and elastic lamina destruction or reduplication. The intima of this patient’s cerebral arteries stained positive for the major von Willebrand glycoprotein of FVIII, gp41. Another patient in this series had a healed arteriopathy of large to medium-size mesencephalic and leptomeningeal arteries, with intimal hyperplasia and endothelial prominence. Infectious inflammation was absent. In another series of six children with acquired immunodeficiency syndrome, Joshi et al. [10] described fibrosis of the intima with fragmentation of elastic tissue and fibrosis and calcification of media with variable luminal narrowing in multiple organs. In five patients the brain was involved; the cerebral arteries were the only vessels that also exhibited inflammation, supporting a relationship between HIV encephalopathy and arteriopathy. Intimal fibrosis with thickening of the media was also observed in the aorta’s vasa vasorum of a child with HIV infection [11].

The mechanism by which HIV results in central nervous system arterial damage is unknown. Postulated mechanisms include direct HIV invasion of cerebrovascular endothelium, damage resulting from exposure to toxic cytokines produced systemic (blood) or local (central nervous system) meningeal infiltrates [12], or less likely from recent HIV-1 systemic infection [10]. In favor of a direct HIV-related pathogenesis for the arteriopathy is its association with high viral titers (as in our patient) and viral antigens [7] and the positive HIV antigens present in affected vessels [8]. Recently, staining of an aneurysmal brain vein was positive for antigen in an HIV-infected child who died of SAP [13]. This finding, coupled with the frequent coexistence of HIV with VZV found in one series of children with HIV arteriopathy (four of 13 patients), has linked VZV to HIV arteriopathy [14]. However, a greater number of VZV staining studies of unaffected vessels are needed to interpret the causal relationship of this association.

The known tropism of certain HIV strain for brain mononuclear cells [15], coupled with the transendothelial migration postulated to occur during HIV neuroinvasion and its accompanying immune activation [16], may explain the formation of aneurysms in cerebral arteries in the absence of systemic arterial aneurysms [7,10] and account for the frequent co-occurrence of HIV encephalopathy and HIV vasculopathy.

One of the patients reported by Husson et al. [7] developed multiple intracerebral aneurysms during a period of increase in his serum p24 antigen concentration. This patient’s viral load was very high (greater than 600,000 copies/mL; Fig. 2) 5 months before the hemorrhage occurred and was still high (greater than 100,000) 1 month before the event. Her arteriopathy was probably progressing during this period, given the subsequent spontaneous aneurysm rupture. The viral load was reduced to undetectable levels a few weeks after initiating antiretroviral therapy. This suggests that early antiretroviral therapy can alter the development and natural history of HIV-related aneurysms. In our patient, no change in aneurysm size was observed by magnetic resonance imaging during 4 months later, suggesting a possible arrest in the progression of arteriopathy after beginning antiretroviral therapy.

The pathologic, imaging, and clinical studies discussed above suggest that HIV infection may be associated, with damage to the wall of the large cerebral arteries, leading to arteriosclerosis. Fibrosis of these aneurysms can rupture and lead to devastating SAP. Cranial computed tomography performed only 3 weeks before the hemorrhage in the current patient did not reveal any aneurysms, illustrating the limitations of computed tomography in assessing their presence. Magnetic resonance imaging also may be useful in identifying the incidence of HIV-related arteriopathy and in monitoring the course of arteriopathy in individual patients—perhaps indicating the time when antiretroviral or antiretroviral strategies are indicated. It may also help monitor the effectiveness of antiretroviral therapy. We suggest that magnetic resonance imaging or magnetic resonance angiography (or both) may be indicated in HIV-infected children with sustained high viral loads, especially those refractory to treatment or with evidence of encephalopathy. Early identification of HIV arteriopathy may or may not lead to a benefit of antiretroviral therapy and may represent intracranial hemorrhage.

References


