Stroke Caused by Human Immunodeficiency Virus–Associated Intracranial Large-Vessel Aneurysmal Vasculopathy

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Background: Intracranial aneurysms related to human immunodeficiency virus (HIV) infection have been well described in pediatric patients but not in adults.

Objective: To describe a case of intracranial large-vessel aneurysmal vasculopathy causing stroke in a 27-year-old HIV-infected woman.

Design: Comparison of clinical and histological data with previously published cases.

Setting: A referral hospital stroke unit.

Patient: A 27-year-old HIV-infected woman presenting with stroke; neuroimaging demonstrated fusiform aneurysmal dilation of the left internal carotid and the left middle cerebral artery and its branches.

Results: Autopsy showed degeneration of the elastic lamina, myxoid degeneration, and medial atrophy, causing consequent ectasia of the involved intracranial vessels.

Conclusion: Aneurysmal dilation of the intracranial arteries occurs in HIV-infected adults, but the pathogenic role of HIV remains unknown.

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Human immunodeficiency virus (HIV) infection is associated with vascular disease and an increased incidence of stroke in adults. In addition, childhood HIV–associated intracranial aneurysmal vasculopathy has been described. This report describes an adult HIV-infected woman who had a cerebral infarct caused by aneurysmal dilatation of the arteries in the circle of Willis. To the best of our knowledge, this is the first description of HIV-associated intracranial aneurysmal vasculopathy in an adult with postmortem histopathology.

Case Report

A 27-year-old woman with World Health Organization stage IV HIV infection and a CD4 count of 14 cells/µL presented with a right hemiparesis. Computed tomography with intravenous contrast showed an infarct of the left basal ganglia and fusiform dilation of the left middle and anterior cerebral arteries, as well as the distal basilar artery. Angiography showed a protein level of 1.0 g/L; cerebrospinal fluid glucose level of 41 mg/dL (2.3 mmol/L); blood glucose level of 72 mg/dL (4.0 mmol/L); 7 lymphocytes per cubic millimeter; 3 polymorphs per cubic millimeter; negative cryptococcal latex antigen fixation; negative rapid plasma reagin; and negative culture for bacteria, fungi, and tuberculosis.

The patient died of bacterial pneumonia 25 days after her initial presentation. Cranial autopsy examination showed fusiform dilation of the left internal carotid, and of the left middle cerebral artery and branches. Thrombus was present in the left middle cerebral artery, including the anterior branch. Histological examination of the left internal carotid and middle cerebral arteries showed luminal thrombosis, concentric intimal fibrosis with hyalinization, atrophic media, and fragmentation and thinning of the elastic lamina. Neutrophils were present on the luminal surface related to the thrombus. Arteries on the nonsymptomatic right side had thickened internal elastic lamina with fragmentation and focal intimal proliferation with calcification. The media was pre-
served. Alcian blue staining of vessels on the right as well as severely affected vessels on the left showed deposition of mucopolysaccharides in the intima and media of the arteries with splaying of the myocytes (Figure 4). No microorganisms or cytopathic changes were observed and immunoperoxidase stains showed moderate numbers of CD68+ macrophages and some CD3+ lymphocytes. Human immunodeficiency virus p24 antigen staining of the vessel sections was negative. Sections of the left caudate infarct showed liquefactive necrosis and perivascular chronic inflammation.

**COMMENT**

Fusiform dilation of intracranial arteries has been described in HIV-positive children (32 cases)\(^2\)-\(^{16}\) and in only 2 studies of HIV-positive adults (5 cases)\(^ {18,19}\). Clinical manifestations varied from cerebral infarcts (14 children), transient ischemic attacks (2 adults), intracranial hemorrhages (5 children), subarachnoid hemorrhage (3 adults), seizures (3 children), and movement disorders (3 children). One study reports an incidence of fus-
form intracranial artery dilation of 1.9% in 426 HIV-positive children.4

The pathogenesis of intracranial aneurysms in HIV infection is postulated to be caused by immune activation in response to transendothelial migration of HIV strains with tropism for cerebral mononuclear cells,6 and an alteration of dynamic vascular responsiveness to pulsatile blood flow regulated by alterations in circulating cytokines and growth factors leading to vascular remodeling.20 Opportunistic infections associated with HIV that are known to involve vessels—such as varicella-zoster virus, herpes simplex virus, cytomegalovirus, Epstein-Barr virus, Treponema pallidum, Candida albicans, Cryptococcus neoformans, and Mycobacterium tuberculosis—may contribute to the production of these cytokines and growth factors.1

Repeated infections may contribute to an increase in elastases, leading to the fragmentation and thinning of the internal elastic lamina, an early histological finding in the development of fusiform aneurysms.6,13 Although it was absent in our patient, HIV glycoprotein 41 has been demonstrated in mononuclear cells within the intima of aneurysmal intracranial arteries in 1 case.13 Extracranial aneurysms in HIV-positive patients are due to vasculitis of the vasa vasorum, which are absent in the intracranial arteries, implying that the pathogenesis is different.21

The survival of patients with aneurysmal HIV-associated vasculopathy prior to the availability of highly active antiretroviral therapy was less than 1 year.5,7,12,13,16 Stabilization of intracranial aneurysms has been reported in 3 patients after 4 months of highly active antiretroviral therapy, and in 1 case of resolution after 15 months of highly active antiretroviral therapy.5 It remains to be seen whether highly active antiretroviral therapy will arrest progression or promote resolution of intracranial aneurysms in adults, thereby confirming the role of HIV in the pathogenesis of intracranial arterial aneurysm formation.

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