Hemiplegia as a presentation of HIV infection in children: A report of 3 cases

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ABSTRACT

Strokes are a rare neurological manifestation of HIV in children with multifactorial etiologies. We present three HIV-infected children who presented to us with stroke out of which two had cerebral infarcts and who responded to antiretroviral therapy (ART). Third patient had tuberculous meningitis who was lost to follow-up before ART could be initiated.

Keywords: Cerebrovascular accident, children, hemiplegia, HIV, stroke

Introduction

Neurologic dysfunction is a common manifestation of HIV infection in both adults and children and most of them present with delayed development, seizures, and focal neurological deficits. Clinically, significant nervous system involvement most often occurs in conjunction with profound immunosuppression and in the presence of other AIDS-defining illnesses, however, neurological problems may be the first manifestation of HIV in 10%–20%. Central nervous system (CNS) infarcts are however rare. Cerebrovascular complications have been reported in 4%–29% of adult patients with AIDS. HIV-1-related strokes although usually asymptomatic may present with hemiparesis, hemiplegia, hemianesthesia, encephalopathy, headache, language disturbance, abnormal vision, and rarely transient chorea. The underlying cause of cerebrovascular disease varies widely. Direct involvement of the arterial wall by HIV, cardiogenic emboli, thrombocytopenia, and infectious vasculitis are among the most commonly reported causes. Isolated reports of cerebrovascular disease in children with HIV have described aneurysms, infarctions, and hemorrhage. We present 3 HIV-infected children who presented with hemiparesis. Two children had cerebral infaricts whereas in one child neuroimaging revealed ventricular dilatation with white matter hyperintensities due to tuberculous meningitis.

Case Report

Case 1

A 10-year-old newly diagnosed HIV-infected boy was referred to us for further management. He was not on antiretroviral therapy (ART). He had right-sided upper limb weakness. On examination, his weight was 21 kg and height was 115 cm. He had right upper limb spasticity with brisk deep tendon reflexes. Computed tomography brain showed irregular hypodense areas in the left frontoparietal subcortical white matter with the involvement of cerebral cortex with hypodensities in the left basal ganglia suggestive of infarcts. CD4 count was 99 cells/μl (11%). He was started on ART consisting of zidovudine, lamivudine (3TC), and efavirenz. In 6 months, his right upper limb weakness had improved, and in 1½ years, his CD4 count was 423 (22%). He is on ART and on regular follow-up.

Case 2

A 6½-year-old boy presented with low-grade fever for 2 months. He had been started on antituberculous therapy (ATT) for previous 1½ months in view of chest X-ray showing right hilar nodules. He was then referred to us for follow-up. On examination, he had right upper limb weakness. Computed tomography brain showed irregular hypodense areas in the left frontoparietal subcortical white matter with the involvement of cerebral cortex with hypodensities in the left basal ganglia suggestive of infarcts. CD4 count was 99 cells/μl (11%). He was started on ART consisting of zidovudine, lamivudine (3TC), and efavirenz. In 6 months, his right upper limb weakness had improved, and in 1½ years, his CD4 count was 423 (22%). He is on ART and on regular follow-up.
paracardiac haziness. He had progressive weakness of the right upper limb for 1 month followed by decreased movement of the right lower limb and inability to speak. There was no convulsion or altered sensorium. On examination, his weight was 15 kg, height was 100 cm. He had splenomegaly with circumduction gait and spasticity of all 4 limbs with brisk reflexes and hemiparesis on the right side of the body. Cranial nerves were normal. MRI brain showed marked dilatation of both the lateral, 3rd and 4th ventricles. There was marked widening of bilateral cortical cerebral sulci, Sylvian cisterns, and perimesencephalic cisterns with bilateral frontoparietal paraventricular deep white matter T2 hyperintensities. Cerebrospinal fluid (CSF) examination was normal. Tuberculosis (TB) culture or PCR were not done. HIV-Elisa was positive. He was advised regarding ART but was subsequently lost to follow-up.

Case 3
A 3-year 4-month-old male child presented with left-sided hemiparesis and right-sided facial weakness for 15 days. He had recurrent bilateral otorrhea for 5 months. There was no fever, altered sensorium or other illnesses in the past. He was a full term normal delivery with birth weight of 1.75 kg and required Neonatal Intensive Care Unit stay for 25 days for neonatal hyperbilirubinemia. His milestones and immunization were appropriate for age. On examination, weight was 10 kg and height was 81 cm. He had large hepatomegaly and mild splenomegaly. On CNS examination, he had left-sided hemiparesis with hypertonia and brisk deep tendon reflexes on the left side. There were no meningeal signs. MRI brain showed right basal ganglia, internal capsule, corona radiata, perisylvian fronto-temporoparietal cortical, and subcortical acute and subacute infarcts. CSF was normal. His antiphospholipid antibody IgM and IgG were positive (17.4 and 19.2 mg/dl, respectively). USG Abdomen showed hepatosplenomegaly. Parents subsequently gave a history of both being HIV infected. The child was also tested for HIV and was found to be HIV infected. His CD4 count was 1645 (28%) cells/cumm. He was started on ART consisting of stavudine (d4T), lamivudine (3TC), and nevirapine, following which he had complete recovery of his hemiparesis. He is currently 5 years old, weighs 14 kg and is on regular follow-up and CD4 is 2335 (58.86%) cells/cumm with CD4: CD8 = 1.44.

Discussion
HIV infection can result in stroke due to opportunistic infections, cardioembolism, vasculopathy, and coagulopathy or it could be incidental. The various causes of cerebrovascular manifestations of HIV in children are arteritis with the formation of fusiform aneurysms and arterial sclerosis with vascular occlusion. In our first and third case, there was the presence of infarcts suggestive of cerebrovascular manifestation due to HIV itself. The pathogenesis of infarction is multifactorial. In adults, cardioembolism and vasculitis are common causes of infarction. Vasculitic changes in intracerebral vessels associated with ischemic strokes can be due to opportunistic infections or lymphomatoid granulomatosis and malignant lymphoma. In some cases, HIV-1 itself appears to be the cause of vasculitis. As part of the immunosuppression caused by the virus, a granulomatous inflammation involving small arteries and veins of the brain surface and leptomeninges termed primary angiitis of the CNS occurs. Autopsy findings of these patients reveal the presence of an asymptomatic vasculopathy characterized by small vessel wall thickening, perivascular space dilatation, rarefaction, and pigment deposition with vessel wall mineralization, and occasional perivascular inflammatory cell infiltrates without evidence of vasculitis. In our first patient, we could not identify the cause of the infarct, and it may have been due to HIV-1-induced arteritis. In fact in the third patient, due to the presence of infarcts in various stages of development, he was tested for various prothrombotic disorders and was detected to have an antiphospholipid syndrome which is not uncommon in untreated HIV-infected children due to polyclonal hypergammaglobulinemia. Autopsy series confirm that infarcts are usually small, located in the basal ganglia or the thalamus and the deep white matter, more rarely in the brainstem or the cerebellum, and frequently multiple. Similar findings were seen in our patients.

Various opportunistic infections associated with stroke in HIV are TB, syphilis, varicella zoster, candida albicans, and cytomegalovirus infection including bacterial endocarditis. Similarly, in our second patient, he was already on treatment for TB and imaging showed ventricular dilatation and hyperintensities in the white matter that could be due to TB itself or due to HIV virus itself. Although CSF was normal, it is done after 1½ months of ATT, thus, it is difficult to comment whether the hemiparesis was due to HIV or due to TB. Immune reconstitution promoted by HAART may exceptionally induce cerebral vasculitis. ART directly accelerates atherosclerosis. None of our patients were on HAART at the time of CNS manifestation.

Children and adults with HIV often suffer similar neurologic and psychiatric manifestations. However, since children's nervous system is still developing, special attention must be paid to the early detection of neurologic problems in pediatric patients. Appropriate and timely treatment of HIV-associated neurologic problems in children often leads to favorable outcomes. Both our patients with cerebral infarcts have responded to ART whereas the one with associated TB was lost to follow-up before ART could be started.

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Conflicts of interest
There are no conflicts of interest.

References
1. Patsalides AD, Wood LV, Atac GK, Sandifer E, Butman JA, Patronas NJ. Cerebrovascular disease in HIV-infected
pediatric patients: Neuroimaging findings. AJR Am J Roentgenol 2002;179:999-1003.

2. Udgirkar VS, Tullu MS, Bavdekar SB, Shahrao VB, Kamat JR, Hira PR. Neurological manifestations of HIV infection. Indian Pediatr 2003;40:230-4.

3. Lowenthal ED, Cruz N, Yin D. Neurologic and psychiatric manifestations of pediatric HIV infection. HIV Curriculum for the Health Professional. URL Available from: http://www.bipai.org/Curriculums/HIV-curriculums/14-Neurologic-and-Psychiatric-Manifestations-of-Pediatric-HIV.pdf. [Last accessed on 2016 Jun 10].

4. Moulignier A. Cerebrovascular Disease in HIV-Infected Patients. Cardiovascular Diseases in AIDS. URL Available form: http://www.eknygos.lsmuni.lt/springer/70/73-84. pdf. [Last accessed on 2016 Jun 10].

5. Nunes ML, Pinho AP, Sfoggia A. Cerebral aneurysmal dilatation in an infant with perinatally acquired HIV infection and HSV encephalitis. Arq Neuropsiquiatr 2001;59:116-8.

6. Benjamin LA, Bryer A, Emsley HC, Khoo S, Solomon T, Connor MD. HIV infection and stroke: Current perspectives and future directions. Lancet Neurol 2012;11:878-90.

7. Greist A. An update in prothrombotic states and stroke prothrombotic states in HIV disease and stroke complications. Sem Cerebrovasc Dis Stroke 2002;2:159-69.

8. Nagase H, Agematsu K, Kitano K, Takamoto M, Okubo Y, Komiyama A, et al. Mechanism of hypergammaglobulinemia by HIV infection: Circulating memory B-cell reduction with plasmacytosis. Clin Immunol 2001;100:250-9.