Extensive cerebrovascular disease and stroke with prolonged prodromal symptoms as first presentation of perinatally-acquired HIV infection in a young adult.

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ABSTRACT

A 26-year old black African woman presented with acute onset of hemiparesis and visual symptoms. This had been preceded several months previously by symptoms which were apparently psychiatric in nature. She had no apparent risk for cerebrovascular disease. Neurological evaluation revealed a striking burden of cerebrovascular disease for her age, including the rare stroke syndrome of basilar artery occlusion. HIV infection was identified during clinical assessment. This was judged to be perinatally-acquired, as there was no history of sexual debut or blood transfusion, her mother was taking antiretroviral therapy and she had planar warts and underlying bronchiectasis. Presentation of stroke should prompt HIV testing in young people. Perinatally-acquired infection can present in adulthood.

INTRODUCTION

Cerebrovascular disease and stroke have an unexpectedly high incidence in HIV-1 positive children and young adults [1][2]. An association between stroke and HIV, especially in young adults with no conventional cardiovascular risk factors has been described [1][2][3]. A recent prospective study from Malawi showed a clear association between HIV infection and stroke [4].

Stroke typically presents with acute focal neurological deficits with cerebral dysfunction conforming to a territorial vascular pattern. This presentation should prompt imaging studies to rapidly confirm the diagnosis or identify common stroke mimics. We report a young woman with prolonged prodromal symptoms before presentation with stroke, resulting in diagnosis of perinatally-acquired HIV infection.

CASE REPORT

A 26-year old black African woman presented with a one-week history of headache followed by total loss of vision from which she recovered after two hours. Diplopia and a right-sided limb weakness subsequently developed, which persisted until presentation. She denied fever and systems review was unremarkable. The patient had no significant past illness. Her father died when she was a child and her mother was alive and taking antiretroviral therapy (ART). Her siblings had not tested for HIV. She denied sexual debut and had never had a blood transfusion.

Eight months prior to this presentation, an emergency laparotomy for a ruptured appendix was performed. At that time, it was first noted by the attending anaesthetist that she exhibited "emotional instability and was unduly anxious". Approximately three months later, the patient was hospitalized for two weeks after developing symptoms that were interpreted as psychiatric. She had become rather detached and disengaged and gave delayed responses when spoken to. The psychiatrist commenced Citalopram and sulpiride with reported clinical improvement.

Following discharge from hospital, an HIV test was positive; CD4 count was 88 cells/μL. Tenofovir, lamivudine and nevirapine were started with co-trimoxazole prophylaxis.

On examination, she had normal stature and was not wasted. She had widespread facial planar warts. There was no lymphadenopathy and respiratory, cardiovascular and gastrointestinal examination was unremarkable. She was orientated and fully conscious and had normal

speech. She had a right hemiparesis (MRC power =4/5 in both limbs); cranial nerve and eye examination was normal.

Investigations showed haemoglobin =11.1g/dL, MCV =93.9 fL: WBC, platelet count, urea and electrolytes, LDH, albumin, bilirubin and transaminases were normal. ESR was 75 mm/1hr and CD4 count was now 174 cells/µL. Total cholesterol (6.7 mmol/L) and LDL cholesterol (4.28 mmol/L) were elevated; HDL cholesterol and triglycerides were normal. Serum Cryptococcal antigen (CrAg), syphilis serology and anti-nuclear factor were negative. Urine chemistry and microscopy were normal. Sputum culture and TB PCR/GeneXpert were negative. Chest radiography showed mild bronchiectasis in the right lower lobe. Cranial CT scan showed focal hyperdensity of the basilar artery with sub-acute ischaemic changes in the left hemi-pons and external capsule (Figure 1). CT angiography demonstrated a mid-basilar artery occlusion (Figure 2). The patient refused a lumbar puncture. Had she consented, CSF would have been obtained for microscopy and culture for bacteria/mycobacteria, syphilis and Toxoplasma serology, CrAg, HIV viral load, and PCR for herpesviruses (HSV, CMV, VZV, EBV). Consequently, HIV compartment syndrome remained un-excluded as a co-existing diagnosis.

She was treated for stroke with low-dose aspirin, rosuvastatin, anticoagulation (initially with heparin and later warfarin) as well as physical therapy for rehabilitaton. Antiretroviral treatment was continued but the psychiatric medication was stopped. Her symptoms and signs improved significantly over the next four weeks and were maintained on subsequent reviews.

DISCUSSION

We describe a young adult with a family history of HIV infection, no history of sexual debut, underlying bronchiectasis, and planar warts, all strongly suggestive of perinatally-acquired HIV infection, who presented with neurovascular disease and apparent psychiatric manifestations [5][6].

Stroke is well described in younger people with advanced HIV infection, typically associated with opportunistic intracranial infections including fungal or tuberculous meningitis and toxoplasmosis [1]. Atypical presentations, as illustrated by this case, are common [7].

HIV infection induces autoantibody production, including anti-cardiolipin, antiphospholipid and anti-prothrombin antibodies that increase the risk of thrombosis and atherogenesis [8]. Secondly, coagulopathy and thrombophilia are more prevalent in HIV infection.

It is unclear whether HIV itself can cause cerebral vasculitis [4]. However, HIV infects perivascular monocytes, macrophages and astrocytes leading to release of neurotoxic viral proteins that cause vascular endothelial damage [9] [10]. An association between HIV infection and thinning of arterial media, a potential precursor to aneurysmal arteriopathy, has been described [11]. Radiologically-documented cases of HIV-1 arteriopathy have responded to ART, thereby implying a pathogenic role for HIV [12].

HIV is associated with abnormalities in carotid intimal thickness [13], carotid arterial wall stiffness [14], and abnormal vascular compliance and distensibility [15], findings that are associated with atherosclerosis. HIV may drive atherogenesis through activation of endothelial and immune cells, increasing numbers of circulating atherogenic immune cells and altering lipid

levels and function [16]. Coinfection with cytomegalovirus, human herpes-virus-8, or hepatitis C may further increase inflammation and atherogenesis [17].

Posterior circulation stroke accounts for 15 to 20% of all ischaemic stroke: basilar artery occlusion representing only 1 to 4% [18]. Presentation usually follows long-term exposure to cardiovascular risks including hypertension, and most frequently occurs beyond the 6th decade of life. Embolic causes are more common in younger patients, sources being the heart, more proximal (such as vertebral) arteries, and arterial dissection. In our patient, there was segmental occlusion of the basilar artery, stenosis of the right vertebral artery and ischaemic change and infarcts in the brainstem and anterior circulation.

Basilar artery occlusion syndromes may mimic other non-stroke conditions, with resultant delay in neurological evaluation [18]. The interval between prodromal symptoms and stroke onset can vary between days to months. Thus, it is important to have a high index of suspicion.

While most perinatally-infected children have rapid disease progression and present in infancy or early childhood, a third have slow progressing disease with a median survival of at least 16 years [19]. As this case demonstrates, presentation with perinatally-acquired HIV can occur in adulthood, highlighting the importance of testing all children of HIV-infected mothers regardless of age.

In conclusion, this case demonstrates that patients with perinatally-acquired HIV can present late and with neuro-psychiatric problems secondary to cerebrovascular disease. HIV infection should be added to the list of risk factors for stroke.

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FIGURE LEGENDS

Figure 1

Pre-contrast cranial CT scan (left) showing focal hyperdensity of the basilar artery (arrow) with subacute ischaemic changes of the left hemi-pons (arrow). In addition there is also patchy chronic-appearing deep white matter ischaemic changes. Post contrast CT scan (right) showed a basilar artery filling defect (arrow).

 Figure 2

Maximum intensity projection (left) and volume rendered (right) CT images from a CT intracranial angiogram. Imaging demonstrates a long segment of irregular stenosis of the right vertebral artery extending to the confluence of the right and left vertebral arteries (green arrows). Mid-basilar artery occlusion is also noted measuring 5.1mm in length, with occlusion of pontine perforators (red arrows).