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Brief Report

Vasculopathy of the large arteries in children infected by the human immune deficiency virus

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Abstract We report on two children with advanced acquired immune deficiency syndrome presenting with vasculopathy involving the large vessels. Both patients had extensive involvement of the aorta and its branches. One patient presented with heart failure, and mild systemic hypertension secondary to renal arterial stenosis, while the other patient manifested with gangrene of both arms.

Keywords: Tuberculosis; cardiac failure; paediatric cardiac disease

While arteriopathy involving small and medium arteries is known to be a complication of infection of young children by the human immunodeficiency virus, cases involving the large vessels have mainly been reported in young adults. We recently encountered two children infected with the human immune deficiency virus who presented with extensive disease of the aorta and its branches. We describe our findings in this report.

Case reports

Patient 1

A 3-year 8-month-old African boy presented with a chronic cough, loss of weight, recurrent skin sores, and fever. Physical examination revealed a wasted child with signs of cardiomegaly, heart failure, and pulmonary hypertension. He had mild systemic hypertension, with a blood pressure of 135 over 70 millimetres of mercury. Other clinical findings were generalized lymphadenopathy, hepatomegaly, pallor, clubbing of the digits, bilateral non-tender parotidomegaly, and generalized infection of the skin by scabies. The lungs and central nervous system were normal. A mantoux skin test for tuberculosis was reactive, measuring 20 millimetres. The enzyme-linked immunosorbent assay was positive for the human immune deficiency virus, with a count of cluster differentiation 4 T-cells of 325×10^6. The normal range is 500 to 2010. Haemoglobin was measured at 7.8 grams per decilitre, the count of white cells was 12.8×10^9 per litre, platelets were counted at 553×10 per litre, serum globulin was measured at 60 grams per decilitre, serum albumin at 27 grams per decilitre, and blood cultures were negative. The chest radiograph showed cardiomegaly and bilateral reticulonodular infiltrates, consistent with lymphoid interstitial pneumonitis. Transthoracic echocardiography revealed biventricular dilation, with depressed left ventricular function, and an ejection fraction of 35%. We also noted a dilated brachiocephalic trunk, and an eccentric suprarenal aneurysmal dilation of the descending aorta together with an intraluminal thrombus. An ultrasonic examination showed a small right kidney, measured at 6.3 centimetres, compared to the left kidney, which measured 8.1 centimetres. Angiography of the ascending aorta confirmed the echocardiographic findings (Fig. 1). Dilation of the origin of the left coronary artery, and an extensive stenosis of the right renal artery, were also apparent.

The patient was treated for tuberculosis, hypertension, and heart failure with rifampicin, isoniazid, pyrazinamide, captopril, digoxin, and lasix. Oral

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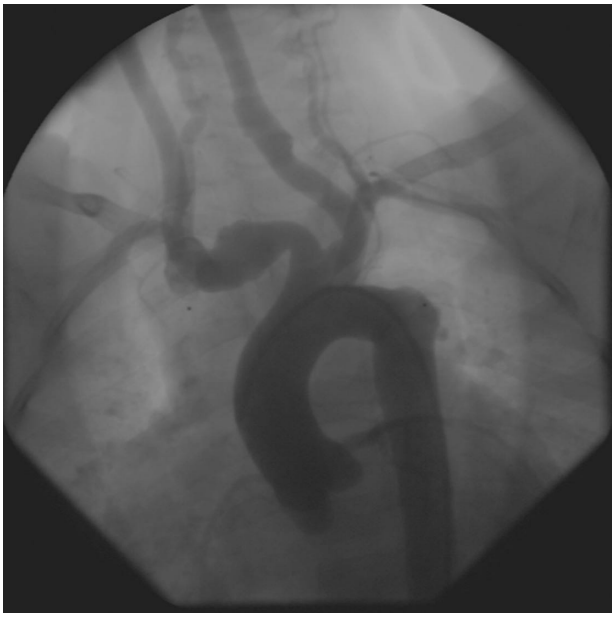

Figure 1.
Angiogram showing aneurysmal dilations of the aortic arch at the junction of the transverse and descending aorta, and the proximal part of the brachiocephalic trunk.

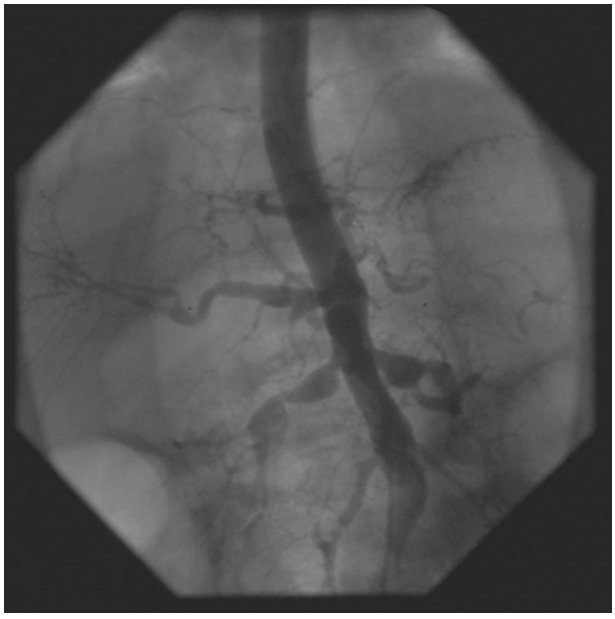

Figure 2.
Angiogram showing irregularity of the descending aorta below the coeliac plexus. Note also the dilated and irregular hepatic artery, as well as the aneurysmal dilations and stenosis of both renal arteries.

prednisone was prescribed for a presumed arteritis of the large arteries. At six weeks follow up, the patient had improved markedly. He was no longer in heart failure, and the blood pressure had settled to 100 over 60 millimetres of mercury, but growth remained stunted.

Patient 2

A 16-month-old African female child, known to be infected with the human immune deficiency virus according to Category C of the classification developed by the Centre for Disease Control, and presumed to be vertically transmitted, presented with acute gangrene of right hand and the third and fourth digits of the left hand. There was rapid progression of dry gangrene up both arms to the level of the elbows over the next ten days, at which time the toes of the left foot turned black. Both the brachial pulses were absent, but the femoral pulses were present, and slightly weaker on the left side. The patient was grossly undernourished, with significant generalized lymphadenopathy and hepatosplenomegaly. A diagnosis of pulmonary tuberculosis had been made six months prior to the present admission, for which she was receiving treatment intermittently due to poor compliance. Laboratory studies showed a haemoglobin of 7 grams per decilitre, white cell count of 26×10^9 per litre, platelet count of 246×10^9 per litre, and a count of cluster differentiation 4 cells of 451, below the normal values of 500 to 2010. Echocardiographic examination revealed mild left ventricular dysfunction, with an ejection fraction of 54%. There was no visible intracardiac thrombosis. The left coronary artery was dilated, and the descending aorta was irregular below the level of the diaphragm. An angiographic study revealed dilated coronary arteries, and an abrupt discontinuation of both subclavian vessels. Other abnormalities of the descending aorta and its branches can be seen in Figure 2. The subsequent fate of the patient is not known, as the family requested an immediate discharge, and there was no follow up.

Discussion

Although involvement of the aorta and its main branches is well recognized in adults infected with the human immune deficiency virus,[1–4] and vasculopathy of the small and medium vessels is described at autopsy in children,[5] as far as we know there has been no documentation of vasculopathy involving the large vessels in young children. To our knowledge, therefore, the two children we describe in this report are the youngest yet documented with vasculopathy of the large vessels subsequent to infection with the human immune deficiency virus.

It is young black patients between the ages of 21 and 60 years who appear to be most at risk.[2,3] Aneurysmal dilations, and or occlusion of the large vessels, are well described in such patients.[1–3] The aneurysms have a predilection for unusual sites, and

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show a tendency toward multiplicity.[1–3] Depression of the count of cluster differentiation 4 T-cells is universally present.

The precise pathogenesis of vascular disease subsequent to infection by the human immune deficiency virus remains unclear. Hypotheses include immunosuppression resulting in bacteraemia with secondary mycotic aneurysms, weakening of the arterial wall caused by direct action of the virus itself, and ischaemia of the vessel wall resulting from inflammatory occlusion of its feeding vessels.[1–3,6]

There are striking similarities to Takayasu's arteritis, the aetiology of which is also unknown. The common features include the young age of the patients, the presence of multiple aneurysms, involvement of the large vessels, and the absence of an obvious causative agent.[1,2,7]

The frequent association of tuberculosis and infection by the human immune deficiency virus is manifest in both our cases. Tuberculosis has also been implicated in the pathogenesis of Takayasu's arteritis.[7,8] It is possible that our two cases are examples of a fulminant form of Takayasu's disease exacerbated by the infection with the human immune deficiency virus. In the absence of histological evidence, nonetheless, the underlying pathological process in the two cases remains speculative.

The coronary arteries were involved in both our cases. This association has been documented previously in one postmortem report of a coronary arterial aneurysm occluded with thrombus in a young child with acquired immune deficiency syndrome.[5]

Surgery is the mainstay of management in adult patients with vasculopathy due to the human immune deficiency virus.[2,3,6] A depressed count of the cluster differentiation 4 T-cells is associated with a poor surgical outcome. Antiretroviral treatment given preoperatively in adults has produced a marked reduction in viral loads, and improvement in the numbers of cluster differentiation 4 T-cells, with better surgical outcomes.[3] This type of management may helpfully be extrapolated to children.

The presence of vasculopathy involving the large vessels, therefore, should be strongly suspected in children infected with the human immune deficiency virus. In such cases, echocardiography has proven to be a useful tool for screening.

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