Case Report

The report of cardiomyopathy and mid aortic syndrome in a HIV infected child

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Introduction

Cardiomyopathy is a serious complication of Human Immunodeficiency virus (HIV) infection. Direct effects of HIV, cardiac autoimmunity, opportunistic infections (OIs), nutritional deficiencies (selenium) and severe immunesuppression have been implemented for HIV related cardiomyopathy (HIVAC)[1] ; Elevated anti-alpha myosin antibodies in HIV infection cause cardiac autoimmunity, selenium deficiency leads to cardiomyopathy, myosite invasion and cytokine release cause myocarditis whereas zidovudine triggers reversible and dose dependent myocyte toxicity[1].

HIV also catalyzes a cascade of indirect pathways that induce myocardial inflammation and damage. Cardiomyocyte apoptosis and myocardial macrophage infiltration are more common in patients with HIVAC than in HIV infected patients without cardiomyopathy. HIV infection has also increasingly been related for vascular diseases, mainly medium and large vessel related vasculopathy leading to aneurysmal and/or occlusive disorders[2]. The virus itself or viral proteins may trigger inflammation that cause endothelial dysfunction, smooth muscle proliferation resulting in vascular injury and thrombosis[3].

Midaortic syndrome (MAS) is a radiologic term used to define the localized narrowing of the distal thoracic or abdominal aorta regardless of etiology[4]. Congenital and several acquired causes such as Takayasu's disease, giant cell arteritides, fibromuscular dysplasia can lead to MAS[4]. As far as we know there is no case of MAS related with HIV infection in the published literature. Herein we present a first case of MAS in a HIV-infected child.

Case report

An 11 year-old girl with the diagnosis of congenital HIV infection presented with palpitation and respiratory distress, lasting for about a week. She was detected to have HIV infection on 15 months of age and started on antiretroviral treatment (ART) (zidovudine + lamivudine + lopinavir/ritonavir). Hovewer, due to socioeconomic reasons she could not take her medications regularly and presented a year ago with high viral load and severe immuesuppression (HIV RNA: 878.500 copies/mL, CD4: 0.46%). She was again started on zidovudine + lamivudine + lopinavir/ritonavir and was kept on follow-up schedule. There was no medical history of cardiac disease.

On admission, she was pale. Physical examination revealed tachicardia and tachypnea. Laboratory examination was summarized in Table-I. Echocardiography detected mitral and aortic insufficiency and decreased left cardiac output (ejection fraction, EF: %47). She was started on furosemide, enalapril and carvedilol.

Table-I. Laboratory parameters

Parameter	Data
Absolute lymphocyte count (cells/μL)	1100
Absolute CD4+ count (cells/μL)	5.1
HIV viral load (copies/mL)	309
hs-Troponin T (pg/mL, N<14)	59.5
pro-BNP (pg/mL, N<125)	7565
CMV PCR (copies/mL)	UD
HbsAg	negative
Anti-HCV	negative
Toxoplasma gondii IgM, IgG	negative
Cryptococcus neoformans antigen	negative
EBV PCR (copies/mL)	38.730
Serum selenium, ug/L, (N:46-143)	34

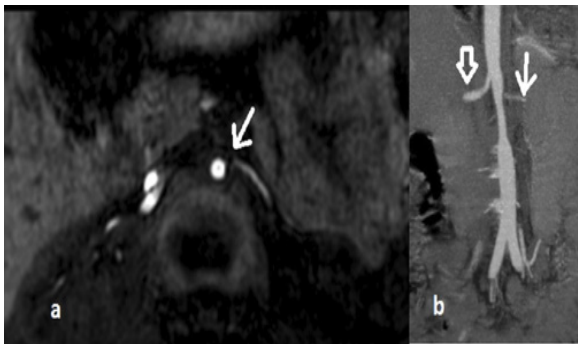

Figure 1: a. Axial section of the magnetic resonance angiography reveals severe renal ostial stenosis (arrow) and decreased renal artery flow. b. Coronal reformatted image of computed tomography angiography reveals mural thickening of the renal and infrarenal level of aorta and left renal artery stenosis (open arrow), decreased flow compared to right renal artery (closed arrow). 264x119mm (96 x 96 DPI)

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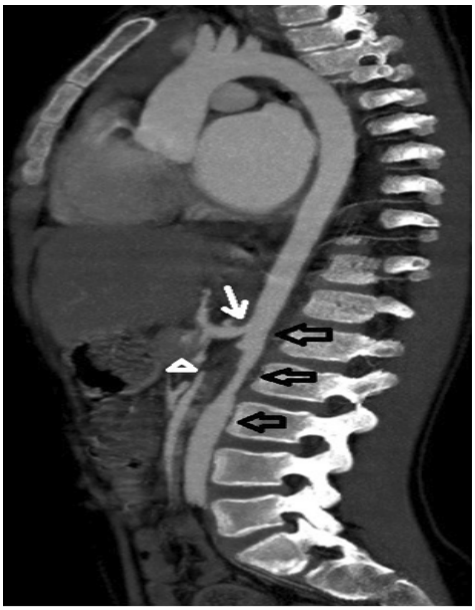

Figure 2. Sagittal reformatted image of the thoracoabdominal aorta presenting normal calibre and mural thickness of the arcus aorta and branches, while mild ostial celiac atery stenosis (white arrow) andpoststenotic dilatation, superior mesenteric artery occlusion (arrow head) and distal collateral flow, stenosis due to mural thickness within the infrarenal portion of the abdominal aorta were depicted.

85x167mm (96 x 96 DPI)

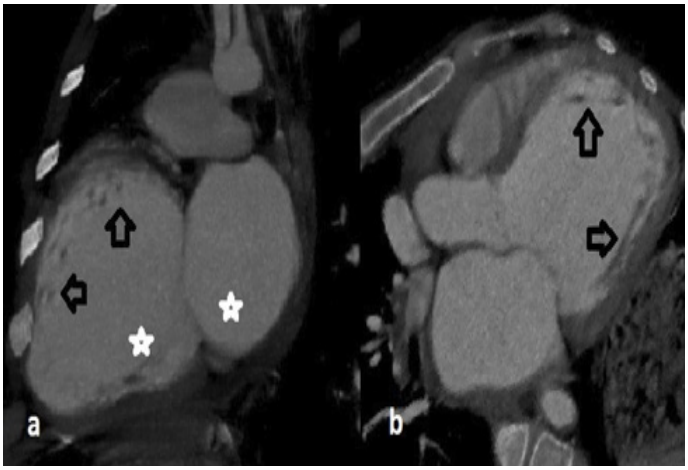

Figure 3. Two-chamber (a) and three-chamber (b) views of the cardiac computed tomography reveal the predominantly left atrial and left ventricular dilatation (asterix) along with apical and mid-ventricular increased trabeculation (arrows).

176x81mm (96 x 96 DPI)

Zidovudine was ceased because of cardiotoxicity risk. Ebstein-Barr Virus viral load was high (38.730 copies/mL, normal <150) and she was started on acyclovir which had to be stopped in the following days because of elevated creatinine levels. Syphilis, CMV, toxoplasma, varicella and tuberculosis screening was normal. Magnetic resonance (MR) angiography revealed decreased caliber in the left renal artery, occlusion within the proximal segment of the superior mesenteric artery, moderate stenosis in the celiac truncus orifis and diffuse intimal thickening along with luminal narrowing from the celiac artery level to just before the bifurcation compatible with MAS (Figure-1). Thoracic aorta and arcus aorta branches were normal in terms of calibre and mural thickness (Fig-2). We performed intra and extracranial MR angiography, any intimal hyperplasia, stenosis or aneurysm was not found. In addition, carotid artery and lower extremity doppler sonography (USG) examinations were normal. Cardiac MRI revealed incresed trabeculation secondary to dilated cardiomiyopathy (Fig-3).

A multidisciplinary council including pediatric cardiologist, cardiovascular surgeon and an invasive radiologist agreed on conservative approach. Her treatment was rearranged as spironolactone, furosemide and carvedilol. A detailed workup for possible prothrombotic condition was normal. Her serum selenium level was low, so she was given replacement therapy.

Three months later, her HIV viral load was undetectable, and CD4+ count raised to 280 cells/µl. Echocardiography revealed EF between 35-40%. Hovewer, control abdominal CT angiography revealed left renal atrophy, 2 cm decrease in the craniocaudal lenght of the left kidney, due to moderate renal artery stenosis. Multidisciplinary team reunited, and they agreed on that she was neither suitable for surgery nor invasive radiologic revascularization; but she could be a candidate for a possible cardiac transplant in the future. She is still being followed-up in our clinic with stable condition and controlled HIV infection.

Discussion

Increased incidence of cardiomyopathy, vascular disturbances and associated decreased survival rates have been reported in HIV infection. Several factors like OIs, nutrient deficiencies, severe immune suppression and high viral load contribute to HIVAC. In pathology, HIV-1 associated protein, gp-120 and transactivator of transcription protein signaling pathways cause mitochondrial dysfunction and cardiomyocyte apoptosis[7]. Our patient had been exposed to severe immune suppression, high HIV load for a long period of time and had increased EBV load which may also had contributed to her deteroiated clinical picture including heart failure. Other usual suspects' scan including CMV, Toxoplasma, cryptococcus, varicella and tuberculosis were negative. Syphilis, which has also increased incidence in HIV patients can cause vasculopathy. However repeated serologic tests for syphilis were negative in the present case.

Selenium is one of the essential micronutrients, required for the synthesis of glutathione peroxidase, an enzyme protecting myocardium from free oxygen radicals. The supplement of selenium either in the prophylaxis, or in the deficient states is recommended for the patients with HIVAC[8]. Our patient also demonstrated decreased serum selenium levels and was given replacement, as recommended. Zidovudine can cause mitochondrial damage and focal myocardial necrosis[9]. Our patient, although irregularly, had used zidovudine as a part of ART. HIV and MAS coexistence is not very surprising when we consider cause-effect relationship between HIV and vasculopathy. Accelerated atherosclerosis in HIV infection, together with many other co-factors have been blamed for vascular disorders[10]. Our patient did not have glucose intolerance, hypercoagulability states or any other atherosclerotic involvement. What we do not understand here was the localized involvement of these vasculitic event, since other vascular components of her body other than left renal artery were completely normal. The left renal arterial stenosis and decreased renal function seem to be related with acquired MAS since her initial abdominal doppler sonography was normal.

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In recent years, the other blaming notion on HIV associated vasculopathy is immune reconstitution inflammatory syndrome (IRIS)[11]. Although the exact mechanism has not been clarified yet, present data shows that it occurs during immune system recovery after the initiation of ART as in our patient.

In conclusion uncontrolled HIV infection, selenium deficiency, EBV co-infection and IRIS may have all contributed to HIVAC in the present case

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Conflicts of Interest

The authors have no conflicts of interest relevant to this article to disclose.

Contributors Statement

Dr Kara, Dr Torun, Dr Bayramoglu and conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr Aliyev, Ozdemircioglu, Kaba and Haccacoglu, Prof Acunas and Prof Nisli designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Prof Somer conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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