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CASE REPORTS

DILATED CARDIOMYOPATHY IN HIV INFECTED ADOLESCENT ON HAART- CASE REPORT

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Abstract. Even though cardiac disease is not frequent in HIV infected children, it is associated with poor prognosis. Dilated cardiomyopathy is the most frequent heart disease associated with HIV infection. In HIV children the most frequent cardiac lesion is dysfunction and/or enlarged dimensions of the left ventricle. The pathogenesis is complex, the most important factor is HIV itself. Human immunodeficiency virus can affect the heart directly or by secondary chronic inflammation and immune activation.
We present a case of an HIV-infected teenager diagnosed with dilated cardiomyopathy and the evolution of heart disease during antiretroviral therapy.
Keywords: HIV dilated cardiomyopathy, antiretroviral therapy, echocardiography

Introduction

Cardiac involvement in HIV infected children is a rare condition, but it is associated with poor prognosis [1,2].

Dilated cardiomyopathy is the most frequent heart disease associated with HIV infection. It can be observed in all stages of HIV infection, but it is more frequently associated with late stages of AIDS [3].

The pathogenic mechanisms of HIV cardiomyopathy are complex. There are many factors involved: HIV itself, immune response and inflammation induced by chronic infection, opportunistic viruses: cytomegalovirus, Epstein Barr virus. The immune response and inflammation of cardiac muscle is mediated by cytokines released by activated lymphocytes. Chronic inflammation of the heart muscle leads to necrosis and finally to myocardial fibrosis [4].

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Left ventricle dysfunction progression leads to cardiomyopathy and heart failure [5]. In children, HIV cardiomyopathy is due to enlargement of the left or both ventricles and is associated with depressed contractility of heart muscle. The most frequent cardiac finding in HIV infected children is left ventricle dysfunction [6].

Usually, clinical findings are unremarkable and the diagnosis is based on imagistic aspects.

The most reliable diagnostic tool is the echocardiography, that shows low systolic and diastolic functions of the left ventricle in affected children and/or hypertrophic or dilated cardiac muscle.

Case presentation

We will present the case of a boy born on October 15, 1987 diagnosed with HIV infection and HBV chronic infection in 1994. The relevant medical history shows: HIV negative parents, blood transfusion in 1989 for severe hemorrhage after tonsillectomy. He started antiretroviral treatment in 1996 with zidovudine (AZT) and dideoxycytosine (ddC). At that moment the HIV status was B2 [7].

Between March and October 1998 he received

treatment with 3 million units per dose, 3 days per week, Interferon alpha-2a (Roferon) for the HBV infection.

As it can be observed from chart 1, he underwent several changes in antiretroviral combinations, but he did not achieve undetectable levels of HIV RNA before December 2004. He started with a combination of two reverse transcriptase inhibitors: zidovudine (AZT) and lamivudine (3TC); after approximately 18 months a protease inhibitor, nelfinavir (NFV) was added. In June 1999, the viral load was 46 800 copies/ml (4.67log$_{10}$) and the combination was changed to another protease inhibitor with introducing of a new class, a non-nucleoside reversetranscriptase inhibitor, efavirenz (EFV). Lamivudine was maintained for HBV coinfection. The first year during this combination of drugs the viral load decreased with one log and the CD4 count raised, but stayed under 200 cells/mm^3. As you can see in figure 1, the undetectability of HIV RNA and the immunologic recovery was not obtained.

In May 2004 the patient had virologic and immunologic failure. An HIV genotypic resistance test was performed and the therapy was changed again. In the last combination a new antiretroviral class was added - fusion inhibitor, *enfuvirtide*. In six months the viral load became undetectable and the CD4 count raised, but stayed within the limits of severe immunosuppression [7].

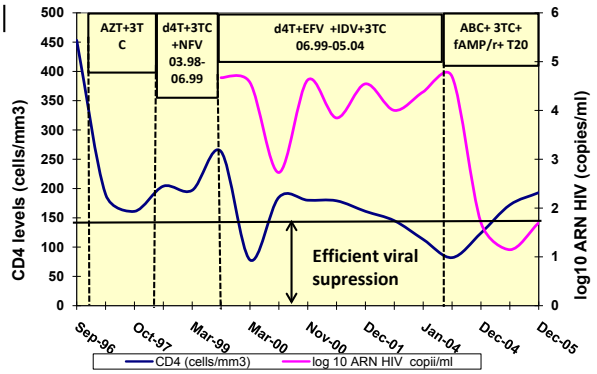

Figure 1. HIV infection history in a boy with dilated cardiomyopathy

During the follow up period he was evaluated for heart disease twice. The first time he was referred to a pediatric cardiologist in June 2002 at the age of 15 for a routine checkup. He had no symptoms or clinical signs suggesting cardiac disease. At this moment he was treated with Indinavir, Efavirenz, Stavudine and Lamivudine for HIV infection and the CD4 count was 213 cells/mm^3.

HIV RNa was 7820 copies/ml and HBV DNA was undetectable. He had no signs of an acute infection. Physical examination was normal except for a mild hepatomegaly. The height of 168 cm and the weight of 68 were normal for his age and gender [8]. Body surface aria was 1.6 m^2.

The electrocardiographic recording was normal, but the echocardiography revealed enlarged ventricles (figure 2), with end-diastolic diameters higher than normal ranges for age, gender, weight and height (table I). Normal ranges for echocardiographic parameters are calculated according to the body surface area [9].

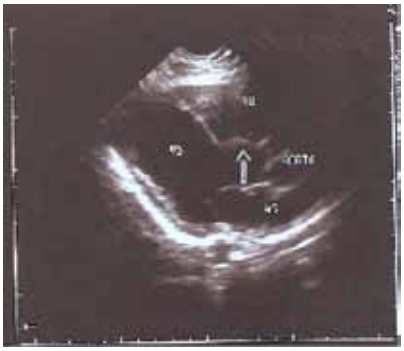

Figure 2. Ecocardiographic aspect at the first evaluation (June 2004)

The echocardiographic parameters recorded were: aortic root diameter (AOD) 29 mm, left atria diameter (LA) 28 mm, right ventricle end diastolic diameter (RVEDD) 28 mm, interventricular septum thickness (IVS) 8.3 mm, left ventricle posterior wall (LVPW) 9 mm, left ventricle end diastolic diameter (LVEDD) 54 mm, left ventricle end systolic diameter (LVESD) 47 mm, Left ventricle end diastolic volume (LVEDV) 148 ml, left ventricle end systolic volume (LVESV) 77 ml, stroke volume (SV) 71 ml, ejection fraction 48%, shortening fraction of the left ventricle (SF) 13%. Doppler examination revealed aneurismal aspect of the interventricular septum and decreased contractility of the left ventricle. In figure 2 we can notice the enlarged left ventricle, the aneurismal aspect of the interventricular septum with abnormal movement (arrow).

The abnormal echocardiographic parameters found in our patient were (table I): right ventricle diameter and left ventricle diameters and volumes. Wall thicknesses were normal. This is conclusive for the diagnosis of dilated cardiomyopathy.

In September 2005, at the age of 18, he was investigated for the second time by a cardiologist.

At this moment he had a viral load under 14.5 copies/ml, the CD4 count was 172 cells/mm^3, he displayed no signs of acute infections and a normal physical examination. He had normal levels of serum lipids as well.

The echocardiographic parameters were much better than 3 years earlier (figure 3 and table II)

Ejection fraction was 50%, shortening fraction was 23%, normal diameters and volumes for all heart chambers.

Echocardiac parameters	Normal ranges (max-min) for BSA=1.6 m^2	Observed values (2002)	Conclusions
RVEDD (mm)	20.3736 - 9.2562	28	Increased
LA (mm)	36.6557- 25.2155	28	Normal
IVS (mm)	10.61952 - 4.03454	8.3	Normal
LVPW (mm)	10.14236 - 6.46316	9	Normal
LVEDD (mm)	53.0256 - 42.5864	54	Increased
LVESD (mm)	34.9489 - 25.9711	47	Increased
LVEDV (ml)	121.6813 - 78.4349	148	Increased
LVESV (ml)	33.462 - 19.0964	77	Increased

Table I. Echocardiographic parameters recorded for the patient in June 2002 against normal ranges for same body surface aria

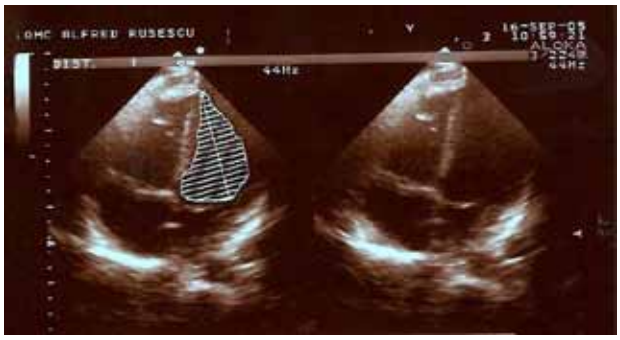

Figure 3. Echocardiographic aspect of the patient's heart in September 2005

In figure 3, the volume and diameter of the left ventricle at the end of diastole is marked. The diameter is markedly increased, but the volume is normal. The interventricular septum still had mild abnormal movements and it was hypertrophic. This shows the evolution of cardiomyopathy in this patient who developed ventricle hypertrophy and maintained the normal functions of the heart.

Discussion

HIV cardiomyopathy can have different clinical manifestations. In some cases, left ventricle dysfunction is present, but there are cases with normal ventricular contractility and impaired anatomic parameters. If the functional parameters are normal the patients have no clinical signs that can point out the cardiac lesions [5]. That is why in many cases HIV cardiomyopathy is silent. Sometimes a severe respiratory or systemic infection can reveal the heart lesions by increased cardiac functional stress, similar with the clinical features of senior patients.

In our case cardiomyopathy was diagnosed by a routine evaluation. There are a lot of possible causative agents and mechanisms of heart disease in HIV infected children. Besides HIV, dilated cardiomyopathy can be caused by other viruses like cytomegalovirus, Epstein Barr virus, coxsackie B3 virus and adenoviruses. [10]. In the same time, antiretroviral therapy, nucleoside reverse transcriptase inhibitors and protease inhibitors can produce cardiac lesions [13]. As it is well known, the most important adverse reaction for the first class of antiretrovirals mentioned is mitochondrial toxicity and it is considered a potential risk for cardiac muscle mitochondria. On the other hand protease inhibitors are associated with metabolic disturbances, like high levels of cholesterol and triglycerides. Dyslipidemia poses a high cardiovascular risk for treated HIV infected patients. After improving life expectancy

Echocardiac parameters	Normal ranges (max-min) for BSA=1.92 m^2	Observed values (2005)	Conclusions
RVEDD (mm)	21.54262 - 10.42522	33	Increased
LA (mm)	39.2656 - 35.332	33	Decreased
IVS (mm)	11.61175 - 5.026769	15	Increased
LVPW (mm)	11.29939 - 7.620187	11	Normal
LVEDD (mm)	58.9086 - 48.4694	81	Increased
LVESD (mm)	38.75805 - 29.78025	72	Increased
LVEDV (ml)	146.19675 - 102.94035	97	Normal
LVESV (ml)	38.183 - 23.3932	47	Increased

Table II. Echocardiographic parameters recorded for the patient in September 2005 against normal ranges for same body surface aria

with HAART, some studies showed an increased rate of myocardial infarction as a consequence of long lasting dyslipidemias [11].

The patient history and clinical situation showed in the first part of the article suggests that in this case the causative agent is HIV itself. He had no concurrent infections and after a longer period of HAART he had better cardiac parameters.

In our patient the echocardiographic abnormalities were associated with viral and immunological failure. The improvement was observed after a period of suppressed viral load, even in the absence of immunologic recovery.

This case suggests that HIV, through chronic inflammation and immunologic abnormalities, plays a bigger role in heart disease than antiretroviral drugs, especially on short term. On long term the high cardiovascular risk will increase the morbidity and mortality in HIV population. Some preventive measures that can be used are healthy diet and exercise. The newer antiretrovirals seems to have better metabolic profiles [12] and can be used in patients with high cardiovascular risk.

Conclusions

Cardiac disease in HIV infected children is a problem of untreated and treated patients as well.

In untreated patients or in those with inefficient viral suppression, the most frequent cardiac finding is dilated cardiomyopathy, which is a silent disease and it is associated with poor prognosis. Clinical manifestations of cardiac failure are present in late stages of HIV infection, but also in the late stages of cardiomyopathy. A severe respiratory or systemic infection can lead to cardiac functional decompensation in a patient with HIV cardiomyopathy, similar with senior patients.

In treated patients metabolic disturbances can increase the cardiovascular risk, causing myocardial infarction even in young patients.

We can conclude that HIV infection is associated with accelerated ageing in all patients' heart and vessels, treated and untreated, in children and in old persons as well. As medical care providers we have to be aware of this clinical particular aspect in HIV infected patients.

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