ECHOCARDIOGRAPHIC ASPECTS IN HIV INFECTED/AIDS CHILDREN AND ADOLESCENTS

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Abstract. Cardiac lesions are described in HIV infected patients, including children. The most characteristic anatomic aspect on echocardiography in HIV cardiomyopathy is dilated left ventricle. Cardiomyopathy correlates with low survival rate. We performed a retrospective study on 59 HIV infected children and adolescents to identify the echocardiographic changes associated with AIDS. Main cardiac lesions found were dilated cardiomyopathy and left ventricle hypertrophy. Cardiac involvement was more frequent in immunosuppressed patients.

Keywords: HIV, immunosuppression, cardiomyopathy, children, echocardiography

Introduction

Cardiac involvement in HIV infection was mentioned from the beginning of HIV epidemic when histology studies showed that the prevalence of myocardial abnormalities in HIV-positive patients ranged from 25% to 75% [1,2].

Data from the pre HAART era showed that 2% of all HIV infected patients will die because of cardiac complications [3]. Early studies conclude that HIV infected newborns have a higher risk to die if they have cardiac lesions at birth compared to those without cardiac involvement. 78% of the HIV infected newborns with severe left ventricle dysfunction and 29% with moderate left ventricle dysfunction died during first year of life compared to 8% death in HIV infected newborns with normal cardiac function and 0% newborn not HIV infected but with HIV infected mothers.[4].

Correlation of cardiomyopathy with immunosuppression and AIDS defining associated diseases is well documented in literature [5]. The most frequent association of cardiomyopathy was with HIV encephalopathy [6] Several studies showed that patients with encephalopathy have a higher risk to die of heart failure than HIV infected patients without encephalopathy.

Introduction of Highly Active Antiretroviral Therapy (HAART) transformed HIV infection into a manageable disease and increased patients’ survival, but brought a new challenge: metabolic complication and cardiovascular risk as a long term adverse events of antiretroviral drugs. [7].

In this context it is clear that there are a large number of etiologic agents that can cause cardiac lesions in HIV infection. Etiologic agents, proven or possible cause of cardiac disease, associated with HIV infection range from HIV itself to opportunistic agents and from malignancies to antivirals, antibiotics and antifungal agents (table I)[4,8-16]

Even though the myocytes are not the primary target of HIV, they can be infected in early stages of the disease, starting the cardiac lesions associated with HIV infection. Another aspect that should be considered is that opportunistic infections and
neoplasms associated with AIDS and the drugs used to treat them can induce cardiac abnormalities as well.

The etiopathogenesis of atherosclerosis in treated HIV infected patients is complex and is not fully understood yet. It is clearly proven that most of the antiretroviral combinations used determine metabolic changes that pose a high cardiovascular risk on long term [13].

Echocardiography is the most sensitive and specific method in the evaluation of cardiomyopathy, although the gold standard for diagnosis is endomyocardial biopsy [17].

Taking these aspects into consideration we conducted an observational retrospective study regarding cardiac echographic aspects in 59 HIV infected children and adolescents admitted to the National Institute of Infectious Diseases, Bucharest between 01.01.2000 and 31.12.2004. Mean age in studied patients was: 12.31 years. Sex distribution in studied patients was: male/female= 35/24. We used CDC revised classification for HIV staging and we found 4 patients in B1 stage, 12 in stage B2, 10 in stage B3, 14 in stage C2 and 19 in stage C3. There was no patient in stages A or C1.

Echocardiography We performed Doppler echocardiography at the Institute for Mother and Child Care “Alfred Rusescu” evaluating anatomic and functional indexes:
- anatomic: volumes and diameters for left and right ventricles
- functional: ejection fraction of left ventricle

We compared the cardiac indexes’ values with the normal values for actual body surface and not for age since HIV infected children had body indexes (weight and height) below normal values. [18].

For cardiomyopathy diagnosis we used the clas-
Male/female ratio was 1.4 in patients with abnormal echocardiography and 1.5 in the other group. There is no statistical significance in differences between sex distribution among the studied groups, p=0.9 (OR=0.92, CI95%: 0.27-3.09).

Given the fact that those two groups have similar distribution regarding age and sex, we used the group of children with normal echocardiography as comparison group in our statistical analysis.

The stage of HIV infection in both groups at the time of echocardiography is illustrated in figure 2.

The compared characteristics of the studied patients are summarized in table II.

The mean age in patients with cardiomyopathy was 12.8 years and, in those with normal echocardiography, it was 11.6 years. Figure 1 shows the age distribution in the two studied groups and the mean trend. The differences in age distribution between the studied groups had no statistical significance.

Sex distribution was similar in both groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with Cardiomyopathy (N=34)</th>
<th>Patients with Normal echocardiography (N=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean 12.8 Standard deviation 2.13</td>
<td>Mean 11.8 Standard deviation 2.7</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>Min 4 Max 19</td>
<td>Min 1 Max 14</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.6 1.6</td>
<td>0.5 1.5</td>
</tr>
<tr>
<td>Body surface (m²)</td>
<td>1.04 1.6</td>
<td>1.03 0.25</td>
</tr>
<tr>
<td>CD4 (cell/mm³)</td>
<td>274 272</td>
<td>302 267</td>
</tr>
<tr>
<td></td>
<td>Min 7 Max 899</td>
<td>Min 10 Max 890</td>
</tr>
</tbody>
</table>

Table II. Characteristics of Studied Patients with and without Cardiomyopathy (Echocardiographic Diagnosis)
As figure 2 shows, most of the patients with cardiomyopathy have advanced HIV infection, respectively C stage, whereas most of the patients with normal echocardiography are in B stage. However, the differences between different stages in studied groups have no statistical significance.

The most frequent infection found in our study was recurrent pneumonia and candidiasis. The rate was similar among children with cardiomyopathy and with normal echocardiographic measurements. HIV encephalopathy was more frequent in patients with cardiomyopathy, statistically significant versus patients with normal echocardiography (p=0.04) (table III).

### Anatomic indexes

Out of 34 patients with abnormal echocardiography, 14 patients had enlarged LV volume (figure 3), 8 had hypertrophic LV, and 2 had enlarged volume associated with hypertrophy of LV. Enlarged right ventricle volume was found in 5 children. In 5 cases, both ventricles were enlarged.

The image in figure 3 shows enlarged left ventricle volume in one studied patient at the end of systole and at the end of diastole. These two parameters define the dilated cardiomyopathy associated with HIV infection.

In patients with left ventricle hypertrophy we found no cases with arterial hypertension, or with anatomic or functional valvular lesions.

### Functional indexes

14 children had low left ventricle (LV) ejection fraction, meaning 41% of the patients with cardiomyopathy had the ejection fraction below the normal limit of 49% [20]

The HIV infection stage in patients with dilated left ventricle was: C3 - 9 cases, B3 - 5 cases, in patients with normal echocardiography there were 4 cases with B3 stage and 5 cases with C3 stage (table IV).

Immunosuppression level was measured by CD4 count in our study. In patients with impaired car-

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**Table III.** Opportunistic Diseases associated to HIV/AIDS in studied patients

<table>
<thead>
<tr>
<th>Opportunistic Diseases</th>
<th>Cardiomyopathy</th>
<th>Normal</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>11</td>
<td>6</td>
<td>0.6</td>
</tr>
<tr>
<td>HIV encephalopathy</td>
<td>10</td>
<td>2</td>
<td>0.04</td>
</tr>
<tr>
<td>Recurrent pneumonia</td>
<td>19</td>
<td>9</td>
<td>0.9</td>
</tr>
<tr>
<td>Digestive Candidiasis</td>
<td>20</td>
<td>16</td>
<td>0.5</td>
</tr>
<tr>
<td>Wasting syndrome</td>
<td>3</td>
<td>2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Table IV.** HIV infection stage in the studied patients with dilated left ventricle

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with Dilated Left Ventricle (N=20)</th>
<th>Patients with normal echocardiography (N=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>13</td>
<td>11.8</td>
</tr>
<tr>
<td>Mean Body surface (m²)</td>
<td>1.06</td>
<td>1.03</td>
</tr>
<tr>
<td>Mean CD4 (cell/mm³)</td>
<td>220</td>
<td>302</td>
</tr>
<tr>
<td>HIV stage (number of patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>B2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>B3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>C1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>C3</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>
Echocardiographic aspects in HIV infected/AIDS children and adolescents

The mean CD4 levels in our patients was 274 cells/mm³ in the group with cardiomyopathy and 302 cells/mm³, higher than the values that literature showed to be associated with cardiomyopathy 145 cells/mm³ and respectively 210 cells/mm³ in a cohort study on 416 infected adult patients in Rwanda [5]. This can explain why we did not find a strong correlation between low CD4 levels and cardiomyopathy in our study. The high CD4 levels found in our patients can be the result of HAART or a different duration of HIV infection between the patients we studied and those reported in literature. There is little literature data regarding cardiomyopathy in children.

In our study the most frequent cardiac lesion was dilated left ventricle 21/57 (36.8%), followed by hypertrophy of the left ventricle 8/57 (14%) and dilated right ventricle 5/57 (8.7%). This data is similar with other authors’ reports, showing that dilated cardiomyopathy is the main cardiac abnormality in HIV infected patients. [6]

Association between cardiomyopathy and HIV encephalopathy in our study was similar to literature data [6], suggesting that cardiac involvement in the HIV infection appears in late stages and it is mainly caused by intense viral replication and immunodepression. Similar rates of recurrent pneumonia among the two studied groups underscore the fact that heart manifestation are not a sign of cor pulmonale, but more likely are a direct consequence of HIV infection.

Limitations

We performed a retrospective observational study which allowed us to identify some of the echocardiographic aspects in HIV infected children and adolescents. The main limitation in our study was the low number of patients which impacted on our statistical analysis. We did not assess the impact of antiretroviral treatment on studied patients.

Conclusions

Literature data on cardiomyopathy associated with HIV in children are scarce, that is why we consider that this echocardiographic assessment on 57 patients brought useful information in this area. In our study the most frequent finding was the dilated left ventricle as single lesion or associated with hypertrophic left ventricle or dilated right ventricle. As we suspected, most of the patients with cardiomyopathy were in late stages of HIV infection.
infection and had low CD4 levels.

We consider that periodic echocardiography in HIV infected children is indicated, especially in those with immunosuppression with opportunistic infections that can mask discrete cardiac symptoms.

References


