Original Article

Cardiac involvement in Sudanese children with connective tissue disease

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Background
Connective tissue diseases (CTD) are associated with a variable range of cardiac abnormalities.

Methods
We identified all patients with CTD and cardiac involvement seen at Jafar Ibn Ouf Children's Hospital and the Sudan Heart Centre by one cardiologist between Jan 2005 and January 2010. Clinical and echocardiographic evaluations were done and arranged consultation with rheumatologist.

Results
Nine patients were identified, three males and six females. Five patients (62%) were initially seen by the cardiologist and CTD was suspected by clinical examination in four patients and in one patient diagnosed by routine screening during workup for pulmonary hypertension. Symptoms were present for one month to 3 years before presentation to the cardiologist. In three patients (30%) the cardiac symptoms preceded the rheumatological symptoms. In one patient, aortic valve replacement for presumed rheumatic aortic regurgitation preceded arthritis by 12 months.

Conclusion
Patients with CTD may present first to the cardiologist with findings that mimic common cardiac lesions. All patients with CTD should have routine evaluation by the cardiologist so as to implement optimal early interventions.

Key words: Cardiac; connective tissue disease.

Introduction
Connective tissue disease can be associated with a range of cardiac abnormalities. Juvenile Idiopathic Arthritis (JIA) had been associated
with aortic regurgitation (AR) and mitral regurgitation (MR) which can be severe enough to necessitate valve replacement\(^1,2\). Systemic Lupus Erythmatosus (SLE) is associated with pericarditis, valve regurgitation and pulmonary hypertension\(^3\). To study the true frequency of cardiac abnormalities in patients with CTD we need to screen a large number of patients as many of the manifestations can be asymptomatic until they reach advanced stages. Paediatric cardiology as well as adult and paediatric rheumatology as sub specialties are new in the Sudan however collaboration is highly needed between them in order to detect these patients at early stages. In this case series we describe the clinical and echocardiographic features of cardiac abnormalities in nine paediatric patients with CTD.

**Patients and Methods**

Patients were seen at Jaafar Ibn Ouf Children’s Hospital and Sudan Heart Centre in the period between Jan 2005 and Jan 2010. Clinical examination, electrocardiograms and a detailed echocardiography/doppler study were done for each patient. Patients were referred for evaluation and were followed-up prospectively. Diagnosis of CTD was based on clinical and laboratory findings. JIA was diagnosed according to International League of Associations for Rheumatology (ILAR) criteria and SLE and mixed CTD were diagnosed according to the American College of Rheumatology criteria\(^4\).

**Results**

Nine patients were diagnosed to have CTD and cardiac abnormalities, their clinical and echocardiographic findings are shown in Table 1.

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age</th>
<th>Sex</th>
<th>Type of CTD</th>
<th>Clinical Features and Investigations</th>
<th>Echo features</th>
<th>Management &amp; Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15 yrs</td>
<td>F</td>
<td>SLE</td>
<td>Severe right heart failure, atrial fibrillation, mild arthritis. Normal renal function. ANA positive, Rh factor negative.</td>
<td>Severe pulmonary hypertension. Tricuspid regurgitation gradient 80mmHg</td>
<td>Methotrexate, steroids, warfarin, furosemide, sildenafil. Symptoms controlled, pulmonary pressure still high.</td>
</tr>
<tr>
<td>3</td>
<td>9 yrs</td>
<td>F</td>
<td>SLE</td>
<td>Right heart failure, Nephritis. ECG: right axis deviation, right ventricle hypertrophy. ANA positive, Rh factor negative.</td>
<td>Moderate pulmonary hypertension. Tricuspid regurgitation gradient 60 mmHg.</td>
<td>Furosemide, sildenafil. Symptoms improved. Pulmonary pressure still high</td>
</tr>
<tr>
<td>4</td>
<td>7 yrs</td>
<td>F</td>
<td>JIA (Pauciarticular)</td>
<td>Knee arthritis for 6 months (Fig. 1), apical pansystolic murmur, Rh factor negative</td>
<td>Moderate mitral regurgitation</td>
<td>MethotrexateFurosemide, captopril. Symptoms improved.</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>Gender</td>
<td>Diagnosis</td>
<td>Cardiac Symptoms</td>
<td>Treatment</td>
<td></td>
</tr>
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<tr>
<td>5</td>
<td>9 yrs</td>
<td>F</td>
<td>JIA (Polyarticular)</td>
<td>Moderate mitral stenosis (<a href="#">Fig. 2</a>), moderate aortic regurgitation.</td>
<td>Furosemide, spironolactone. Methotrexate</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>12 months</td>
<td>F</td>
<td>JIA (Systemic onset)</td>
<td>Prolonged fever (6 months), polyarthritis, skin rash. Initially managed as Kawasaki Disease. Rh factor negative.</td>
<td>Pericardial effusion, coronary artery dilatation (transient)</td>
<td>Steroids, Lost to follow up</td>
</tr>
<tr>
<td>7</td>
<td>12 months</td>
<td>M</td>
<td>JIA (Systemic onset)</td>
<td>Pericarditis (with pericardial rub), polyarthritis, fever.</td>
<td>Pericardial effusion</td>
<td>Pericarditis resolved on nonsteroidal anti-inflammatory, Lost to follow up</td>
</tr>
<tr>
<td>8</td>
<td>1 month</td>
<td>M</td>
<td>Neonatal lupus</td>
<td>Skin rash (<a href="#">Fig. 3</a>), complete heart block, heart rate 50/min. Normal blood counts. Mother is asymptomatic. Both mother and baby were positive for anti Ro and anti La antibodies. Previous baby died at 6/12 of age with cardiomyopathy</td>
<td>Borderline low ejection fraction 55%. No valve regurgitation or effusion</td>
<td>Permanent epicardial pacemaker.</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>F</td>
<td>Mixed CTD</td>
<td>Fever, fatigue, wasting. Proximal myopathy, arthritis.</td>
<td>Dilated left ventricle with low ejection fraction 47%. Noncompacted myocardium</td>
<td>High dose steroids</td>
</tr>
</tbody>
</table>

There were 3 males and 6 females. Five patients (62%) were initially seen by the cardiologist and the CTD was suspected by clinical examination in four patients and in one patient (patient no. 1) diagnosed by routine screening during workup for pulmonary hypertension. Symptoms were present for one month to 3 years before presentation to the cardiologist. In three patients (patients no. 1, 2 and 8) the cardiac symptoms preceded by rheumatological symptoms. In patient no. 2, aortic valve replacement for presumed rheumatic aortic regurgitation preceded arthritis by 12 months.
Fig. 1: (Patient no. 4)
Picture showing swollen right knee joint in a patient with pauciarticular JIA and moderate mitral regurgitation.

Fig. 2: (Patient no. 5)
Echocardiographic parasternal long axis in diastole showing thickened and fused mitral valve leaflets (arrow).

Fig. 3: (Patient no. 8)
A baby with neonatal lupus: erythematous rounded skin lesions with central scaling involving the back.

**Discussion**

Cardiac involvement is reported in up to 47% of patients with SLE and up to 5% of those with JIA. The most common cardiac abnormalities in SLE by Yeh et al in 157 cases were cardiomegaly, pericarditis and conduction abnormalities\(^3,^5\). In JIA the most common cardiac manifestations are pericarditis, myocarditis and valvulitis while myocarditis and cardiomyopathy are well known manifestations of mixed CTD\(^5,^6,^7\).

Cardiac evaluation is indicated in all patients with CTD by clinical examination and echocardiography as the latter is an excellent non invasive tool and can detect cardiac abnormalities before they become clinically evident\(^8\).

Striking features in our patients were the variable time of diagnosis of cardiac problem which was detected by routine screening during workup of pulmonary hypertension in one patient and one year after aortic valve replacement for presumed rheumatic heart disease in another. Over 60% of our patients were initially diagnosed as CTD by the cardiologist. This indicates the need for a high index of suspicion for CTD in patients with similar cardiac problems. Aortic regurgitation that needs valve replacement is rare in adult patients with SLE\(^9\). In our patient no. 2, the valve replacement was done 12 months before the diagnosis of SLE, to our knowledge there were no similar cases reported in the literature.

Mitral stenosis with aortic regurgitation is rare in JIA as was reported by Panwar et al\(^10\). As rheumatic heart disease (RHD) is common in this area it has to be carefully ruled out in such patients. Features that help the clinician to differentiate these entities are the pattern of joint involvement which is typically migratory, transient, involves large joints and associated with severe pain in rheumatic fever as compared with mild pain, chronic course, residual joint deformity with small and large joint involvement in JIA. On the other hand
arthritis is present in 90% of patients with SLE with less swelling but more pain of large joints as opposed to the arthritis of JIA. On echocardiography the classical changes of the mitral valve in RHD are thickened prolapsing anterior leaflet with tethered posterior leaflet. In SLE, there can be a specific type of endocarditis (Libman Sacks endocarditis) which is characterized by irregular vegetation 2-4 mm in diameter on mitral or aortic valves, however, this is a rare manifestation and the echocardiographic changes are commonly non specific leaflet thickening.

Systemic onset JIA can be associated with coronary artery dilatation, mimicking Kawasaki disease as in patient no. 6(11). This can lead to diagnostic difficulty at the time of initial presentation, however, the chronic/relapsing course of JIA helps to differentiate these two entities.

Neonatal lupus is a unique clinical entity that is often the only/initial manifestation of maternal SLE, therefore, routine SLE screening is indicated for mothers of patients with congenital heart block. Early diagnosis can help to prevent fetal heart block by treatment of mothers with steroids(12).

Treatment of patients with cardiac problems and CTD is challenging and needs close collaboration between the paediatrician, paediatric cardiologist and paediatric rheumatologist. We noticed that patients were often treated for long periods by nonsteroidal anti-inflammatory drugs and present with joint deformities and established valvular lesions. Control of inflammation by steroids, and nonsteroidal anti-inflammatory drugs can help to ameliorate the clinical course but generally does not change the long term prognosis. However, early introduction of disease modifying anti-rheumatic drugs (DMARD) has proved to improve the long term prognosis of arthritis in CTD. Uncontrolled trials have demonstrated slowing of radiographic progression suggesting a true "disease MODIFYING " action(13). Treatment of pulmonary hypertension is particularly difficult but recent drugs like bosentan and sildenafil helped to improve the symptoms of many patients(14).

We used Sildenafil (phosphodiesterase 5 inhibitor) in 11 patients with pulmonary hypertension primary or secondary to different causes and observed that there was good clinical and echocardiographic improvement with an excellent safety profile(15).

In conclusion, we highlighted some of the cardiac problems in children with CTD. Patients may present first to the cardiologist and a high index of suspicion for CTD should be present. All patients with CTD should have routine evaluation by the cardiologist so as to implement optimal early interventions.

References

Original Article  
CTD Sulafa KM Ali


