Case Report

Juvenile Spondyloarthritis and Severe Cardiac Involvement in a Female Patient

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ABSTRACT. Heart involvement is a recognized complication in 10-20% of all adults with spondyloarthritis. Until now only 8 cases of cardiac involvement in juvenile spondyloarthritis (JS) have been reported, all male patients. We describe the first female patient with JS, in whom progressive cardiac involvement developed, and summarize the pediatric JS cases with cardiac involvement. (J Rheumatol 2003;30:1087–9)

Key Indexing Terms:
AORTIC INSUFFICIENCY MITRAL INSUFFICIENCY ARTHRITIS
JUVENILE SPONDYLOARTHRITIS

Heart involvement is a recognized complication of spondyloarthritis in adults occurring in 10-20% of the patients. Juvenile spondyloarthritis (JS) is the second most common form of juvenile chronic arthropathies with an estimated prevalence of 11 to 86 per 100,000 children. Until now only 8 cases, all males, with juvenile spondyloarthropathies with cardiac involvement have been reported in the English medical literature. We report the first case of a female patient with JS, in whom a severe cardiac involvement was seen. All reported cases of JS with cardiac involvement in the English medical literature are reviewed.

CASE REPORT

One year before admission an 8-year-old Caucasian girl developed pain in the left groin. The hip ultrasound showed an effusion in the left hip. In the further course the arthritis in the left hip persisted and a decreased range of internal rotation developed. The patient suffered from several episodes of episcleritis associated with anterior uveitis.

The family history revealed that her father, who is HLA-B27 positive, had been diagnosed with a Morbus Reiter, associated with a chlamydial infection that had presented with arthritis in both knees and ankles, conjunctivitis, and urethritis.

Our patient was negative for antinuclear antibodies and HLA-B27, but positive for HLA-B07 and B57. JS was diagnosed based on the European Spondylarthropathy Group preliminary criteria for classification of spondyloarthropathy[1] (asymmetric synovitis, predominantly in the lower extremity and a positive family history) and according to the ILAR classification criteria for juvenile idiopathic enthesitis related arthritis[2] (arthritis and a family history of HLA-B27 associated disease and anterior uveitis, which is usually associated with pain, redness, and photophobia).

Two weeks before admission a grade 3 holosystolic heart murmur was first heard; the murmur was loudest at the heart apex. Echocardiography showed a mitral valve and aortic valve insufficiency. She was admitted to our hospital.

We saw a normally developed 9-year-old girl, heart rhythm normal, grade 3 holosystolic heart murmur audible in the apex, and a grade 2 diastolic decrescendo murmur in the left 2nd and 3rd intercostal space. The musculoskeletal examination showed a limited internal rotation of the left hip, which was painful at the end of the range; the other joints were normal. No other clinical abnormality was seen.

The following laboratory tests were all normal: hematologic values, C-reactive protein, serum electrolytes, transaminases and serum creatinine, iron and iron-binding capacity, antistreptolysine titer, anti-DNAseB-titer, complement factors, and sterile blood cultures.

Echocardiography (ECG) on admission showed a grade 3 mitral valve insufficiency with a prolapse of the anterior leaflet, dilated mitral anulus and dilated left atrium (34.8 mm), grade 3 aortic valve insufficiency with diastolic retrograde flow in the abdominal aorta (Figures 1,2), and no vegetation on the valves. The end-diastolic dimension of the left ventricle was enlarged (54.4 mm) due to volume overload caused by aortic regurgitation. The ECG was normal.

Our diagnosis was cardiac involvement consistent with juvenile spondylarthropathy. We began a therapy with furosemide (2 mg/kg/day) and enalapril (0.3 mg/kg/day) for management of heart failure. Despite this therapy her cardiac condition progressed, including increased aortic and mitral insufficiency. Therefore we started immunosuppressive treatment with 30 mg/kg of methylprednisolone as a pulse therapy with 10 mg/m^2 of methotrexate (MTX) orally once a week as a second line intended to reduce her cardiac inflammation and to avoid a future valve replacement. After 8 months, because cardiac function deteriorated, MTX was increased to 15 mg/m^2 weekly and the administration was changed from oral to subcutaneous. In the next 2 months her cardiac function worsened and she developed aortic insufficiency III and mitral insufficiency III-IV. The progressive valve insufficiency was the indication for the valve replacement of the aortic and mitral valve with a mechanical valve (Carbomedics®, Austin, TX, USA). The histology of the removed valves showed myxoid degeneration with some fibrinoid necrosis and focal signs of inflammation with the infiltration of lymphocytes and granulocytes. According to the histology and the macroscopic description, no subaortic structures were involved. To date her disease has shown only joint involvement of her hip.

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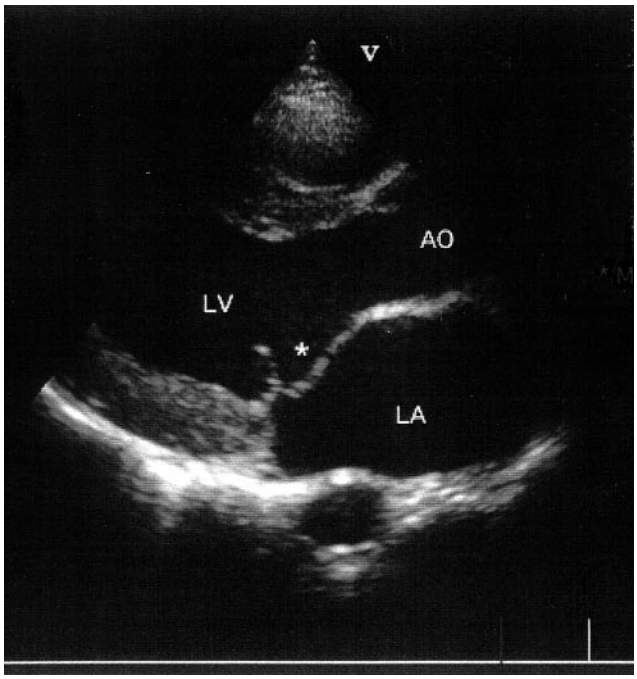

Figure 1. Echocardiographic parasternal long axis view showing prolapse of the anterior leaflet of the mitral valve (*).

DISCUSSION

We describe the first case of a female patient with JS and cardiac involvement. The diagnosis was based on the recurrent episcleritis with acute anterior uveitis with red eyes, joint involvement only affecting the lower extremity, and a positive family history of Reiter's syndrome in the father, who is HLA-B27 positive. All other reported cases were male[3-8] (Table 1). All cases reported to date were HLA-B27 positive. Interestingly, one patient had Reiter's syndrome[9] at disease onset and developed a chronic disease course that resembled juvenile spondyloarthropathy. Another patient[8] did not fulfill the criteria for enthesitis related arthritis[2]. His positive family history of psoriasis and the arthritis onset before the age of 8 years suggest psoriatic arthritis.

The mean elapsed time between disease onset and cardiac involvement was 1.8 years. In 5 of 9 patients an aortic and mitral involvement was seen. Our patient has a severe cardiac involvement with progressive mitral and aortic insufficiency requiring not only anticongestive treatment but methylprednisolone pulse therapy and immunosuppressive treatment with MTX. We initiated an aggressive treatment because published case reports indicate that progressive cardiac involvement can be severely destructive. In 3 pediatric patients, including ours, a valve replacement was necessary[4] and in another pediatric patient a Bentall operation[3] was carried out due to a worsening cardiac function.

Table 1. Summary of the reported cases of juvenile spondyloarthropathy with cardiac involvement.

Author	Diagnosis	Age at Onset of Rheumatic Disease (yrs)	Age at Onset of Cardiac Involvement (yrs)	HLA B 27 Positive	Sex	Cardiac Involvement	Remarks
Kim, *et al*[3]	Spondyloarthritis	11	15	+	M	Saccular dilatation of the ascending aorta	Bentall operation (operation for acute aortic dissection)
Stewart, *et al*[10]	Spondyloarthritis	16	16	+	M	Aortic and mitral regurgitation	Emergency mitral and aortic valve replacement
Reid, *et al*[8]	Spondyloarthritis (Psoriatic Arthritis)	9	10	+	M	Aortic root dilated, thickening of the aortic mitral leaflet, aortic regurgitation	Mild aortic insufficiency at one year followup
Pelkonen,*et al*[4]	Spondyloarthritis	12.5	15	+	M	Aortic and mitral regurgitation, prolapse of the left coronary cusp toward the left ventricle	Valve replacement at 16 mo after onset of cardiac involvement
Gore, *et al*[6]	Spondyloarthritis	9	11	+	M	Aortic regurgitation, mitral regurgitation	
Simpson, *et al*[5]	Spondyloarthritis	13.5	14	+	M	Aortic root at the level of sinuses of valve dilated, thickening of the right coronary cusp and prolapse of the left leaflet	After 8 mo unchanged cardiac findings. Clinically asymptomatic
Hubscher, *et al*[9]	Reiter's Syndrome (Spondyloarthritis)	6	9	+	M	Aortic regurgitation, dilatation of the ascending aorta	
Kean, *et al*[7]	Spondyloarthritis	15	16	+	M	Mild aortic regurgitation	Good long term outcome at 10 yrs followup period
Foeldvari, *et al* (present report)	Spondyloarthritis	8	9	–	F	Progressive mitral and aortic valve insufficiency	Requiring pulse methylprednisolone and methotrexate and later valve replacement

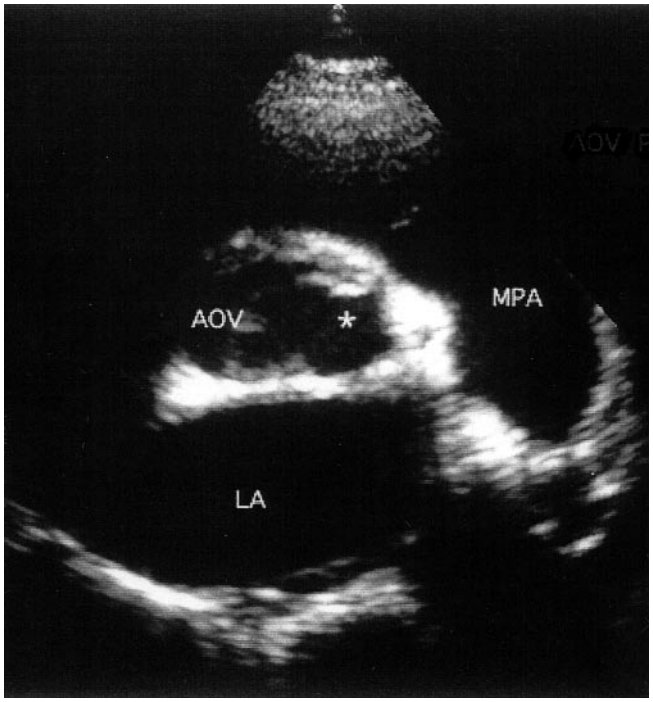

Figure 2. Modified echocardiographic parasternal short axis view showing prolapse of the left coronary of the aortic valve (*).

In the 3 pediatric patients with valve replacement the histology showed in each a slightly different picture. In the first patient[3] there was an obliterative endarteritis of the vasa vasorum of the aorta, rimmed by infiltration of lymphocytes and plasma cells; in the second patient[10], there was a fibrous thickening of the aortic valve and the anterior mitral valve and the infiltration of the papillary muscle with plasma cells and lymphocytes; and in the third patient[4] there were myxomatous and strongly fibrotic changes of the aortic valve. In an autopsy series of adult patients with cardiac involvement and spondyloarthropathy[11] the changes resembled inflammatory reactions found in joints, and consisted of cellular proliferation and a scar formation involving the aorta and valve cusps with resultant valve insufficiency. Scar tissue extended into the subaortic area and infiltrated the membranous and muscular septum, producing mitral insufficiency and affecting the conduction system with resultant disturbance and heart block. Involvement of the subaortic area is quite specific for the spondyloarthropathies[11]. In our patient the histology of the removed valves showed a focal mixed cellular infiltrate of lymphocytes and granulocytes, and myxoid degeneration in the mitral valve fibrinoid necrosis was also described. No subaortic changes were observed in our case, but neither in the other pediatric cases. The histology in our case resembled the components of the histology of the other pediatric cases.

The prevalence of JS with cardiac involvement (Table 1) is significantly lower than in adults and it occurs in the reported cases mostly in the first 2 years of the disease course. In adults with spondyloarthritis, in whom 10-20% develop a cardiac involvement during the disease course, cardiac involvement occurs later, on average about 15 years after spondyloarthritis onset. In the autopsy series[11], 2 of the 8 patients had a pediatric onset, but the cardiac involvement was first seen in adulthood.

Our case report should contribute to awareness of cardiac involvement associated with juvenile spondyloarthropathy. It can occur shortly after disease onset in pediatric patients and even in female patients, without being associated with HLA-B-27-positivity.

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