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ORIGINAL ARTICLE

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Juvenile ankylosing spondylitis—is it the same disease as adult ankylosing spondylitis?

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Abstract *Objectives*: Juvenile and adult forms of ankylosing spondylitis (AS) have been shown to have different clinical presentation and outcome in Caucasians. We did this retrospective analysis to see if similar differences exist in the Indian population. *Patients and methods*: Case records of 210 Indian patients diagnosed with AS according to modified New York criteria were reviewed. Data were collected regarding age of onset, clinical features, drug treatment, and outcome at last follow-up. Patients with onset before 17 years of age were classified as having juvenile AS (JAS) and the rest with adult AS (AAS). *Results*: There were 150 patients with AAS and 60 with JAS. The latter had higher male preponderance, more frequent onset with peripheral arthritis, and greater involvement of hip and knee joints. Valvular dysfunction was seen only in patients with JAS. *Conclusion*: In this group of subjects, juvenile AS had onset more often with oligoarthritis and enthesitis than with spinal disease. Hip and knee joint involvement was more common in JAS than AAS.

Keywords Enthesitis-related arthritis · Juvenile idiopathic arthritis · Juvenile spondyloarthropathy

Introduction

Spondyloarthropathies are a group of diseases affecting the sacroiliiac joints and spine. Ankylosing spondylitis (AS) is a prototypical form of spondyloarthropathy. It can occur at any age but has peak incidence in the third decade of life. Juvenile AS (JAS), that is with disease onset before 17 years of age, has a different phenotype and prognosis than adult AS (AAS). The criteria for the diagnosis of AS are, however, the same for children as for adults. Most of the children take years or decades to develop radiological evidence of sacroiliitis, a mandatory criterion for diagnosis.

Compared to adults, who present predominantly with axial skeletal involvement, children present with peripheral oligoarthritis and enthesitis and only later develop the characteristic spinal and sacroiliac involvement [1]. This difference in presentation has been noticed in many ethnic groups [2, 3]. Since no data are available from the Indian subcontinent, we decided to conduct this retrospective analysis.

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Patients and methods

Retrospective analysis of case records of patients with AS was done (New York clinical criteria [4]). They were grouped according to age: those with onset of symptoms before the age of 17 years were classified as having JAS, and patients older than 17 at onset were classified as having AAS. A total of 150 patients with AAS and 60 with JAS were included in this analysis.

Data on age at disease onset, clinical features, uveitis, duration of disease at presentation, treatment received, and length of follow-up were recorded. Long-term complications such as cardiac conduction disturbances, aortic regurgitation, apical pulmonary fibrosis, amyloidosis, atlantoaxial dislocation, and cauda equina syndrome were also recorded. Further, the requirement for joint replacement was also recorded. Among patients with disease onset with peripheral arthritis, the time required to involve the axial skeleton was noted. Intergroup comparison was done using the chi-squared test.

Results

There were 150 patients (138 male and 12 female) in the adult disease onset group, with mean age at onset being 25.9 ± 8.6 years. The juvenile onset group consisted of 60 patients (58 male and two female) with mean age at onset of 12.3 ± 2.5 years. Median duration of disease at presentation was 8.9 years in JAS and 7.5 years in AAS.

Of 60 patients in the JAS group, only nine (15%) had disease onset with spinal and/or sacroiliac involvement,

whereas 69 (46%) of the 150 adult patients had axial involvement as the first disease symptom. Of the juvenile group, 85% had disease onset with oligoarthritis of lower limbs only, while 54% of adults had similar presentation. All the patients had grade 3-4 sacroiliitis along with lumbar and dorsal spine involvement at the time of first presentation to us. The incidence of cervical spine involvement was 26.6% (16/60) in the JAS group vs 51.3% (77/150) in AAS ($P < 0.001$). The mean duration required for involvement of axial skeleton in patients who presented initially with peripheral arthritis alone was 7 years in the JAS group and 1 year in the AAS group.

The prevalence of hip and knee joint involvement at presentation was significantly higher: 50.6% and 61.6% in the JAS group and 28% and 36%, respectively, in AAS (Tab. 1). The incidence of enthesitis was comparable in both groups: 40% (24 patients) in JAS and 37.3% (56 patients) in AAS. Positive family history was present in 11 JAS patients (18.3%) and 44 (29.3%) in the adult group. The incidence of anterior uveitis was also comparable: 25% (15 patients) in JAS and 21.3% (32 patients) in AAS.

Mean duration of follow-up was 24 months in JAS and 30 months in AAS. Most of the patients were managed with nonsteroidal anti-inflammatory drugs (NSAID) and physiotherapy only. Eleven patients in the JAS group and 24 in AAS were given disease-modifying drugs: salazopyrine (in the majority) and methotrexate.

Two JAS patients and one in the adult group underwent hip joint replacement. There were two patients in the JAS group with aortic regurgitation, whereas one AAS patient had secondary amyloidosis. No patient had apical pulmonary fibrosis, atlantoaxial dislocation, or cauda equina syndrome.

Discussion

Our data show that JAS has onset more often with oligoarthritis and enthesitis than with spinal disease. Hip and knee joint involvement is more common in JAS than AAS. Extra-articular manifestations are similar in the two groups. The majority of children with JAS had onset with peripheral arthritis, and only after a mean duration of 7 years did they develop spinal symptoms. Thus, diagnosis based on adult criteria such as the New York criteria takes a long time. It has been proposed that the presence of enthesopathy, midtarsal joint disease, and sparing of hand joints in children with juvenile arthritis strongly suggests a progression to JAS [5]. Further, sacroiliitis is more often present on follow-up in children with late onset, early hip disease, and the presence of human leukocyte antigen (HLA)-B27 [6]. Most such children are diagnosed as having juvenile rheumatoid arthritis or seronegative enthesopathy arthritis syndrome. The recent International League Against Rheumatism criteria [7] have a category of enthesitis-related arthritis which helps in classifying children with early JAS.

There is a need for development and standardization of diagnostic criteria for JAS. In addition, the criteria developed for adults are not applicable in JAS, as data for some of the physical measurements are not available for children, limitation of spine and chest movement occurs late in the course of disease, and radiological sacroiliitis takes years to develop.

Further, it is not entirely clear that JAS and AAS are the same disease, although they are closely linked [8]. It is very unlikely that age of onset determines the phenotype of a disease; e.g., in systemic lupus erythematosus, the disease is more severe in children but the phenotype is the same. At first glance, JAS resembles chronic reactive arthritis in which there is peripheral arthritis and enthesitis, and a proportion of patients progress to AS. Only a minority of children who have onset with inflammatory back pain may be true cases of JAS. This issue needs to be resolved by prospective study of children with enthesitis-related arthritis.

The male preponderance was also more marked in JAS (29:1) than in adults (11.5:1). Other studies [1, 9] reported a ratio of seven boys to one girl. This preponderance could be related to referral bias, as patients with severe disease are referred to tertiary care hospitalsl, and in females the disease is usually mild and thus may be asymptomatic.

More patients with AAS had positive family histories than in JAS. This could be partly related to the fact that this disease manifests late and that siblings of children with JAS may not have had expression of the disease. The familial clustering is more in sibs who share HLA-B27 [10].

Cervical spine disease is less common in JAS. Late involvement of spine in JAS and also, as the spinal disease usually ascends, cervical spine involvement take a long time to manifest. Cardiac involvement was seen in a minority of patients. In AAS, 5% of patients develop cardiac disease after 15 years of AS, whereas in JAS only a few cases with severe aortic regurgitation have been reported. Subclinical abnormalities on echocardiography such as regurgitation on color Doppler may be seen in 15% of children with JAS at 4.3 years of disease

Table 1 Joint involvement in juvenile-onset ankylosing spondylitis (JAS) and adult-onset ankylosing spondylitis (AAS) at presentation

	JAS ($n = 60$)	AAS ($n = 150$)
Cervical spine	16 (26.6%)	77 (51.3%)*
Hip joint	31 (50.6%)	42 (28%)**
Shoulder	10 (16.6%)	18 (12%)
Knee	37 (61.6%)	54 (36%)**
Ankle	23 (38.3%)	33 (22%)***
Others	13 (21.6%)	25 (16.6%)
Enthesitis	24 (40%)	56 (37.3%)

*$P < 0.001$ by chi-squared test
**$P < 0.005$
***$P < 0.05$

duration [11]. We had two children with clinical aortic regurgitation among 60 patients with JAS. Our incidence of uveitis (25%) is quite similar to those reported by Ansell (27% among 71 children) and Hafner (14% among 77 children) [1]. In AAS, a figure of around 20% is reported in most studies.

Most children are managed with NSAID. Sulphasalazine has been used with limited success in AS [12]. Outcome data on children with JAS are very limited [13]. In a 15-year follow-up study, 50% of patients had significant functional disability (Steinbroker class III and IV) [2]. In comparative studies, outcome has been worse in JAS than in AS, with increased requirement of hip joint replacement. Persistence of peripheral arthritis and hip joint disease is more often a problem in JAS [2, 3].

Thus we can conclude that JAS has more peripheral arthritis and uveitis, whereas AAS has a greater prevalence of spinal disease.

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