Juvenile chronic arthritis in Black and Indian South African children

I. E. HAFFEJEE, J. RAGA, H. M. COOVADIA

Summary

Although juvenile chronic arthritis (JCA) has been studied extensively in Whites in Western countries, very few data exist on JCA in children in developing countries and particularly in Africa. Accordingly, a retrospective study of 60 Black and Indian children with JCA was undertaken. The main findings were predominance of JCA of polyarticular onset with a relatively low occurrence of JCA of pauci-articular onset, a high prevalence of positive rheumatoid factor tests and a very low number of patients positive for antinuclear factor, and an equal overall sex ratio (however, there was a preponderance of males in the subgroup with JCA involving only 2 - 4 joints). Moreover, the vast majority of patients initially had a low haemoglobin concentration, a normal white cell count, an elevated erythrocyte sedimentation rate and a positive antistreptolysin O titre. The main differences between Black and Indian South African children with JCA and White children with the disease in Europe and North America appear to be the high prevalences of polyarticular onset and seropositivity, the equal sex ratio and the absence of a specific subgroup with pauci-articular onset and a positive antinuclear factor test.

Juvenile chronic arthritis (JCA) has been studied extensively in developed countries and is widely accepted as being a heterogeneous disorder embracing a number of different disease profiles. The various syndromes which comprise the generic term JCA were defined at the 1977 meeting of the European League against Rheumatism (EULAR) and the World Health Organization (WHO). The establishment of these criteria makes diagnosis more accurate and provides a firm basis for comparison of disease presentations among children from different countries. During the past 2 decades JCA has been described in a few reports from tropical and central Africa, but no consistent pattern of the disease is discernible. The clinical, radiological and laboratory findings in patients with JCA in Nigeria resemble those in European children. However, studies from Uganda and Zambia suggest that polyarthritis in juveniles may have certain unusual features. We therefore report the results of a retrospective analysis of JCA, defined according to the EULAR/WHO criteria, in Black and Indian children in Durban between 1975 and 1982.

Patients and methods

The records of all Black and Indian children aged between 1 and 16 years who fulfilled the EULAR/WHO criteria for the diagnosis of JCA and who had been admitted to the King Edward VIII and R. K. Khan Hospitals in Durban during 1975-1982 were studied. Clinical, haematological, immunological, radiological and synovial biopsy findings and relevant facts from the histories were obtained from the inpatient records of these patients.

Diagnostic criteria

Criteria for inclusion in the series were: (i) onset of JCA before the age of 16 years; (ii) minimum duration of 3 months; (iii) a recognized mode of onset, viz. systemic, polyarticular (involving 5 or more joints) or pauci-articular (involving 4 or less joints); and (iv) exclusion of other causes of chronic arthritis.

Results

Clinical features

Sixty patients were studied, of whom 42 were Black and 18 Indian.

Age at onset. This ranged from 1 to 16 years, most of the children having been affected at between 4 and 12 years of age (Fig. 1), with a peak at between 4 and 7 years for Indian children. In 7 out of the 9 patients (77.7%) with systemic onset this occurred before 7 years of age (Fig. 2). Polyarticular-onset JCA showed a peak at 4 - 7 years (Fig. 3), whereas this peak occurred later (between 8 and 12 years) in the group with pauci-articular onset (Fig. 4).

Sex. The overall sex ratio was 1,0 (Table I). For the three main modes of onset there was again no appreciable difference between the sexes. However, when the pauci-articular group was further subdivided into a mono-articular subgroup and a subgroup with involvement of 2 - 4 joints, there was a striking male preponderance in the latter. More patients with a positive rheumatoid factor test were female (male : female ratio 0,47).

Modes of onset. Table II shows the percentages of patients with different modes of onset. Fifteen per cent had a systemic onset of disease, 48,3% a polyarticular and 36,7% a pauci-articular onset. Table II also compares the percentages in each

<table>
<thead>
<tr>
<th>Mode of Onset</th>
<th>No.</th>
<th>Ratio</th>
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<tr>
<td>Overall</td>
<td>30 : 30</td>
<td>1,0</td>
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<tr>
<td>Systemic</td>
<td>4 : 5</td>
<td>0,80</td>
</tr>
<tr>
<td>Polyarticular</td>
<td>14 : 15</td>
<td>0,93</td>
</tr>
<tr>
<td>Pauci-articular</td>
<td>12 : 10</td>
<td>1,2</td>
</tr>
<tr>
<td>Mono-articular</td>
<td>3 : 5</td>
<td>0,6</td>
</tr>
<tr>
<td>2 - 4 joints</td>
<td>9 : 5</td>
<td>1,8</td>
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TABLE I. SEX RATIOS FOR DIFFERENT MODES OF ONSET OF JCA

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Fig. 1. Age of onset of JCA in Black and Indian children.

Fig. 2. Age of onset of systemic JCA in Black and Indian children.

Fig. 3. Age of onset of polyarticular JCA in Black and Indian children.

Fig. 4. Age of onset of pauci-articular JCA in Black and Indian children.
category with the findings of Calabro et al. in the USA and Ansell in the UK. There is a preponderance of polyarticular-onset JCA in the current study in contrast to the British series in which the pauci-articular group predominated. There was no difference as regarded mode of onset between the two racial groups studied (Table III).

All 9 patients with systemic onset presented with fever, while 7 also had lymphadenopathy, 3 an enlarged spleen and 3 hepatomegaly; only 1 had a rash compatible with JCA.

**Site of joint involvement** (Fig. 5). The knees were most commonly involved, followed by the ankles, wrists and elbows, in that order. The arthritis was predominantly symmetrical, except in the pauci-articular group. The relative frequency of hip involvement is of interest. This occurred in 23.3% of the patients and accounted for a large proportion of deformity and loss of joint function. The temporomandibular joints (3.3%) were only rarely involved.

**Monoarthritis.** Of the 22 patients with pauci-articular onset, only one joint was involved in 8 (36%) - the knee in 6 and the hip in 2. Five of these patients were Black and 3 Indian.

**Severity of arthritis.** The severity of joint involvement was assessed in all patients at the initial and at subsequent examinations. Children with gross limitation of movement, deformities, contractures and/or erosive changes, ankylosis or fusion of bones on radiography were classed as having 'severe' JCA. There were 19 such patients (31.6%), most of whom required orthopaedic surgery. The mean age of onset in 18 of these patients was 8.1 years (range 1.5 - 13 years); 1 patient presented with fixed flexion deformities of the knees of uncertain duration (precise age of onset being unknown) at the age of 15 years. Nine patients with severe JCA were male and 10 were female, giving a male : female ratio of 0.9. Two had JCA of systemic onset, 12 had poly- and 5 pauci-articular onset. One or both hip joints were involved in 12 of these patients. Permanent limitation of neck movement caused by cervical fusion and atlanto-axial subluxation was present in 1 male Indian child. Rheumatoid factor was present in 9 of the 19 patients with severe JCA; these 9 patients all had the 'adult' type of disease now known as 'juvenile rheumatoid arthritis'.

**Eye involvement.** This was found in 5 patients (8.3%) either at the first presentation or on follow-up. Three patients had mild acute anterior uveitis or iridocyclitis, 1 had severe chronic iridocyclitis with subsequent development of a membrane over the lens as well as a cataract, and 1 presented with blindness due to a panophthalmitis in one eye and severe iridocyclitis in the other. In 3 of the 5 patients the onset of JCA was polyarticular, while it was pauci-articular in the remaining 2. Antinuclear antibodies (ANA) were sought in 4 of these patients but detected in none.

**Subcutaneous nodules.** Only 3 patients, 2 with poly- and 1 with pauci-articular onset, had nodules. All were Indian children; 2 were seropositive and 1 was seronegative.

**Cardiac involvement.** This was detected in 3 patients. Two had myocarditis as evidenced by clinical and radiological cardiomegaly, the absence of significant murmurs, and ST-T changes on the electrocardiogram; 1 of these had systemic-onset JCA, the other polyarticular onset with cardiac involvement later in the course of the disease. One patient had pericarditis — this was a Black child who had polyarticular-onset JCA with persistent disease activity; the child later developed pericarditis and subsequently died from infective endocarditis.

**Serological findings**

**Rheumatoid factor** was present in 22 patients (36.6%). Table IV shows the relationship between rheumatoid factor positivity and mode of onset of JCA; the majority of seropositive patients (17 out of 22) had either a polyarticular or a systemic

<table>
<thead>
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<th>Mode of onset</th>
<th>No.</th>
<th>%</th>
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<tr>
<td>Systemic</td>
<td>9</td>
<td>44.4</td>
</tr>
<tr>
<td>Polyarticular</td>
<td>29</td>
<td>44.8</td>
</tr>
<tr>
<td>Pauci-articular</td>
<td>22</td>
<td>22.7</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>36.6</td>
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onset of JCA. Nine patients in whom rheumatoid factor was present had the 'adult' type of JCA, juvenile rheumatoid arthritis. The frequency of positivity was similar in Black and Indian children (Table V).

ANA's were present in only 3 of 44 children (6,8%), 2 with polyarticular and 1 with pauci-articular onset. In none of these was uveitis present, either on initial or subsequent examination. The antistreptolysin O titre was measured in 32 patients. The cut-off point for a raised titre in our laboratories is 166 IU. A titre higher than this was found in 21 patients (66%), the vast majority of whom had titres of 200 IU or above (mean 463,5 IU; range 200 - 1,600 IU).

Haematological findings

Haemoglobin concentration. The haemoglobin concentration (mean ± SD) for the 57 patients in whom it was estimated on admission was 10,66 ± 1,79 g/dl.

White cell count. This was performed in 55 cases. In the 32 children aged between 1 and 10 years the mean (± SD) white cell count was 10,43 ± 4,75 x 10³ (upper limit of normal 15 x 10³), while the 23 children over 10 years of age had a mean white cell count of 8,83 ± 2,65 x 10³ (upper limit of normal 12 x 10³).

Erythrocyte sedimentation rate. Forty-eight patients underwent this test on admission. The mean rate for these was 70,8 ± 36,2 mm/h, the normal range being between 3 and 14 mm/h.

Chest radiographs. These were taken in 34 children, 8 (23,5%) of whom had changes in the lungs characterized mainly by bronchopneumonia (6 patients) and lamellar effusions (2 patients). The remaining 76,5% of the patients had normal chest radiographs.

Radiography of joints. Of the 42 patients who underwent radiography of the involved joints, 15 (36%) showed no changes. In the remaining 27 patients soft-tissue swelling was seen in 14, osteoporosis in 10, erosions in 6, bony ankylosis involving mainly vertebrae or carpal bones in 6, joint space narrowing in 6, and periosteal elevation in 4; 3 patients had subluxation of the hip (2 of these also had arthritic changes in the acetabulum) and 1 had subluxation of the atlanto-axial joint. (Many patients had more than one abnormality.) Synovial biopsies were performed on 17 patients; all specimens showed the features of a nonspecific arthritis consistent with rheumatoid arthritis.

Treatment

The choice of drugs by the consultants in charge of individual cases varied. The vast majority of patients (59%) were given aspirin alone, while 8% received a combination of aspirin and other non-steroidal anti-inflammatory drugs such as indomethacin, ibuprofen or tolmetin; 6% required the addition of either penicillamine or gold to their regimen, while a further 6% required corticosteroid therapy. As regards the remaining 21%, either no drugs were given (especially for those presenting with orthopaedic problems at a late inactive stage) or no information could be obtained from the clinical records.

Physiotherapy was used routinely, and many patients also received hydrotherapy. Orthopaedic surgical procedures such as traction, osteotomy, arthrodesis or open reduction were carried out where indicated.

Discussion

This comparatively large, retrospective study of the clinical, immunological and haematological features of JCA in Black and Indian children shows that this condition is not uncommon. The principal findings were as follows: an equal overall sex ratio, polyarticular onset of JCA in 48,3% of patients, pauci-articular onset in 36,7% and systemic onset in 15%, a positive rheumatoid factor in as many as 36,6%, and severe disease — defined by deformities, ankylosis, loss of joint function and erosive bone changes — in one-third of the patients.

Comparing these findings with those in Western countries, we found the proportions of patients in the various clinical subgroups to be similar to those described by Calabro in the USA. However, there was a distinct difference here between our series and that of Ansell in the UK, where only 13,6% had polyarticular onset and as many as 64,6% pauci-articular onset. It is difficult to explain this finding; one possibility is that since both hospitals in which our studies were carried out are referral centres, milder cases of pauci-articular disease may conceivably have been treated elsewhere. Studies elsewhere in Africa have shown a preponderance of polyarthritides in Uganda and of systemic-onset disease in Nigeria.

In the pauci-articular group, both Blacks (15 patients - 35,7%) and Indians (7 patients - 38,9%) were affected. Of these, 8 had a mono-arthritis (5 Blacks and 3 Indians). Reports from elsewhere in Africa show a much lower incidence of pauci-articular JCA, while mono-articular involvement has been described in only one previous report. The incidence of mono-artritic JCA in Whites varies from 12% to 31%.

Roughly one-third of our patients had severe disease with deformities and poor articualr function often with loss of mobility and/or erosive changes on radiography; of these about half (9 out of 19) could be labelled as having 'adult'-type rheumatoid arthritis with a positive rheumatoid factor test. Most of these required orthopaedic surgical management. Many of our patients presented for the first time very late in the course of their disease, often with established deformities; this is the most likely reason for the relatively high proportion of patients with severe disease. We cannot, however, discount genetic susceptibility since HLA studies were not routinely performed.

Most Western studies indicate that the joints most commonly involved in JCA are the knees, followed by the wrists and ankles. Our findings are comparable to those of Ansell, but in contrast to the British series we also found a relatively high frequency of elbow and hip involvement, the latter especially leading to severe disability. The Nigerian study by Greenwood referred to previously showed a somewhat similar picture to that in our series, except that he found the ankles to be the joints most commonly involved; in both his study and ours involvement of the temporomandibular joints and the cervical spine was rare. A study carried out recently in Zambia showed similar findings, except for a very high prevalence of neck involvement; however, since only 8 patients were studied there the findings are not strictly comparable to ours.

Other clinical manifestations of the disease were all rare. Iridocyclitis was found in 5 patients (8,3%), subcutaneous nodules in 3 (5%) and cardiac involvement in 3 (5%). With the exception of the finding of subcutaneous nodules in 12% of patients from Uganda, these findings are similar to those elsewhere in Africa, although it is conceded that the percentage of patients with eye involvement could conceivably increase with the passage of time, since this is a retrospective study. Only 1
patient with systemic-onset disease had the typical rash of Still's disease; this is in marked contrast to the situation in the Western world, where it is present in over 90% of children with systemic-onset JCA. 10

Nine patients had the typical 'adult' type of rheumatoid factor-positive rheumatoid arthritis with progressive deformities and joint destruction. These accounted for 15% of the total series, which conforms with the findings of Ansell. 3 However, in 7 of these (77.7%) the onset was at between 2 and 8 years of age, contrary to the British experience where in over 70% the onset was at or after the age of 10 years. Furthermore, only 1 patient in our series with the 'adult' type of disease had subcutaneous nodules.

The classic teaching that only about 12% of children with JCA are positive for IgM rheumatoid factor 1,8,9 does not appear to be true for the patients we studied. While 15% of our patients had rheumatoid factor-positive 'adult'-type disease, our total positivity rate of 36.6% is much higher than the 12% found in Britain 4 and Uganda 2 and the even lower rate in Nigeria. 6 One explanation for a positive rheumatoid factor test in patients without the 'adult'-type disease is that this is a nonspecific response to a variety of chronic inflammatory processes. It can, for example, be present in cases of parasitic infestations, 11 tuberculosis, 12 chronic liver disease, 13 malaria 14 and infective endocarditis, 15 and also in apparently normal individuals. 14,15 Chalmers et al. 11 found rheumatoid factor in 21 - 25% of adult Black inpatients without any joint disease at the King Edward VIII Hospital in Durban. Apart from parasitic infestations, none of the above illnesses was present in our rheumatoid factor-positive patients. In a prospective study Hanson et al. 16 noted that in almost 80% of rheumatoid factor-positive patients the onset of disease was at between 12 and 16 years. Our findings do not support this (Fig. 6); apart from a slight peak at 4 - 7 years of age there is an even distribution of seropositivity throughout childhood.

The other serological marker for JCA, ANA, is said to be found in 25 - 45% of patients, 14,16 particularly in girls under 5 years of age with pauci-articular-onset JCA, and these children are especially at risk of developing chronic iridocyclitis. 4,9 We found a positive result for ANA in only 3 patients (6.8%) out of the 44 in whom this test was done; 2 of these patients (both Black) had poly- and 1 (an Indian child) pauci-articular onset JCA, and there was no association with iridocyclitis. In fact, in all 4 patients out of the 5 with iridocyclitis in whom the ANA test was performed, it was negative. Pauci-articular JCA with positive ANA, described as a specific subgroup by Ansell, 3 has to the best of our knowledge not been reported in Black children. Our findings confirm this.

Therefore, on the basis of results in this series, which to our knowledge is the largest one reported from the African continent so far, it appears that JCA in Black and Indian children in South Africa differs from the disease in children in Western countries.

Fig. 6. Age distribution of seronegative and seropositive patients with JCA.

REFERENCES

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