MONARTICULAR JUVENILE RHEUMATOID ARTHRITIS

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Seven out of 22 children with monarticular juvenile rheumatoid arthritis (MJRA) developed involvement of other joints between six months and three and a half years from the onset. In the other 15 patients the disease has remained monarticular for between one and 16 years (mean six years). Chronic iridocyclitis was seen in three of the five boys, two with antinuclear antibodies. Children with MJRA and antinuclear antibodies should have periodic ophthalmic assessment. Synovial biopsy was of value primarily in excluding other causes of arthritis, but there was only limited correlation between the histological findings and the subsequent course of the disease.

The clinical diagnosis of juvenile rheumatoid arthritis (JRA) in the absence of a valid serological test is not easy and the difficulty is increased in a child whose disease occurs in a single joint. Among the large number of children presenting with chronic joint effusions it has been possible, using the criteria of Bywaters and Ansell (1965), to distinguish a small group suffering from monarticular juvenile rheumatoid arthritis (MJRA). Their criteria for diagnosis were pain and swelling in the joint, with or without limitation of movement, lasting for at least three months without involvement of another joint. Twenty-two such patients presented at the Royal Hospital for Sick Children, Glasgow, between 1963 and 1978. This report describes the features and the course of their disease, the period of study ranging from one to 16 years.

In our series of children with MJRA who satisfied the criteria of Bywaters and Ansell (1965) there were five boys and 17 girls, whose age at the onset of disease varied from one year to 12 years, 14 being under five years of age. Initial investigation included radiography, a Mantoux test, tests for antinuclear antibodies and rheumatoid factor, measurement of the erythrocyte sedimentation rate and a full blood count. Radiographs of the affected joints were graded according to the criteria of Goel, Rawson and Shanks (1974). Involved synovium was excised from each patient; the specimens were reviewed, without knowledge of clinical or radiographic findings, and graded according to the histological criteria established by Pitkeathly, Griffiths and Catto (1964) from a study of synovium from patients with known generalised rheumatoid arthritis, from control patients undergoing meniscectomy and from 45 patients in the age range 11 to 70 years presenting with monarthritis. These criteria were: Grade IV, "definite rheumatoid arthritis", when a strikingly frondose synovium with much villous hyper trophy was seen, the villi being packed with plasma cells and lymphocytes, the latter being distributed focally and showing germinal centres; Grade III, "suspicous of rheumatoid arthritis", where there was a severe or moderate infiltrate of plasma cells; Grade II, "some abnormal features", when a chronic diffuse or focal inflammatory infiltrate was found which was chiefly or wholly lymphocytic; and Grade I, "normal or insignificant features", when there was some proliferation of synovial cells, a little congestion or oedema, or at most a light sprinkling of lymphocytes in the superficial synovium.

The follow-up was from one to 16 years (average six years) and the functional state of the patients was graded as: helpless, when life was spent in chair or bed; moderate limitation of function, when occasional splintage was needed; slight limitation of function, when the child had a nearly normal school life but was excused games; and no limitations. The course of the disease was described as intermittent when periods of remission were interspersed with a few weeks or months of recurrent activity. Steroids were not used in the treatment of these children.

An attempt has also been made to ascertain the value of serological tests in this disease. Our practice with this series of children was based on the assumption that the Rheumaton test was adequate for screening the samples. If this test was negative, no further serological tests for rheumatoid factor were carried out. If the Rheumaton tests were positive, the R₃ dilution technique was used. Patients with a positive R₃ titre were assumed to correspond very closely to those with a positive reaction from the Rose-Waaler test of earlier
Involvement found at follow-up | Number of children | Mean duration of follow-up | Complications | Functional status |
--- | --- | --- | --- | --- |
Disease remained monarticular | 15 | 5.5 years | Chronic iridocyclitis (1) | No limitation (10) Slight limitation (4) Moderate limitation (1) |
Pauciarticular disease (involvement of two to three joints only) | 6 | 6.5 years | Chronic iridocyclitis (2) | No limitation (3) Slight limitation (1) Moderate limitation (2) |
Polarticular disease (involvement of four or more joints) | 1 | 3 years | Nil | Slight limitation (1) |
Total | 22 | | (3) | (22) |

Number in parenthesis denotes the number of cases.

Table II. Correlation of histological appearance of synovial membrane with other findings

| Histological appearance of synovium | Involvement found at follow-up | Mean duration of follow-up | Complications | Functional status |
--- | --- | --- | --- | --- |
Abnormal features (7) | Monarticular 4 Pauciarticular 2 Polarticular 1 | 8.5 years | Nil | No limitation (6) Slight limitation (1) |
Suspicious of rheumatoid arthritis (13) | 10 3 Nil | 4.5 years | Chronic iridocyclitis (3) | No limitation (7) Slight limitation (3) Moderate limitation (3) |
Diagnostic of rheumatoid arthritis (1) | Nil 1 Nil | 3 years | Nil | Slight limitation (1) |
Other: Biopsy inadequate (1) | 1 Nil Nil | 2 years | Nil | Slight limitation (1) |
Total (22) | 15 6 1 | (3) | (22) |

None of the patients showed normal or insignificant features on synovial biopsy.
Number in parenthesis denotes the number of cases.

In addition, antinuclear antibodies were estimated. Immunoglobulins (IgG, IgA and IgM) and complement C3 (β2, Cβ,A) globulins were also measured.

CLINICAL FEATURES AND PROGRESS

The presenting clinical picture was of a warm swollen joint, with non-tender thickening of capsular and synovial tissues, thought to contain an effusion. The Mantoux reaction was negative. Rheumatoid nodules were not seen and there was no specific incident of injury. The knee was the joint involved in 15 children, the ankle, hip and wrist in two children each and the metatarsophalangeal joint was the presenting area in one child aged 12 years. The course of the disease was intermittent in all patients. Table I shows the progress in these 22 children.

In only one child did the disease become a true polyarthritis, starting in the left ankle and involving the right knee and ankle and both feet after one and a half years. The progression from one joint to less than four other joints, seen in six children, comprised: bilateral involvement of the wrist in two children whose disease had started in the left knee one year earlier; from right knee to left ankle in one girl after six months; from left hip to left knee in a boy after two years; from right wrist to left knee and cervical spine in another boy in two years; and from right knee to left in a six-year-old after three and a half years. Progression to other joints was not seen in any child whose arthritis had remained in one joint for three and a half years. We could find no relationship between progression of the disease and the sex or the age of the child or the clinical severity of the original monarthritis. The relationship between the outcome and the histological grading of the original samples of the synovium was not close (Table II): the three children with moderate limitation of function—the worst result in this series—had a Grade III “suspicious of rheumatoid arthritis” tissue reaction; and the single example of Grade IV, "definitely rheumatoid arthritis", was in a child with only slight limitation of function.
Table III Correlation between a positive test for antinuclear antibodies (ANA) and a positive test for rheumatoid factor and other findings

<table>
<thead>
<tr>
<th>Results of serological tests</th>
<th>Number of children</th>
<th>Involvement found at follow-up</th>
<th>Complications</th>
<th>Functional status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive for antinuclear antibodies</td>
<td>5*</td>
<td>Monarticular 2 Pauciarticular 3 Polarticular Nil</td>
<td>Chronic iridocyclitis (2)</td>
<td>No limitation (1) Slight limitation (2) Moderate limitation (2)</td>
</tr>
<tr>
<td>Positive for rheumatoid factor:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Rheumaton but negative R₃ titre</td>
<td>4</td>
<td>Monarticular 3 Pauciarticular 1* Polarticular Nil</td>
<td>Chronic iridocyclitis (1)</td>
<td>No limitation (2) Slight limitation (1) Moderate limitation (1)</td>
</tr>
<tr>
<td>Positive Rheumaton and positive R₃ titre in 1/128</td>
<td>1</td>
<td>Monarticular 1 Polarticular — — —</td>
<td>—</td>
<td>Slight limitation (1)</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>6 4</td>
<td>(3)</td>
<td>(10)</td>
</tr>
</tbody>
</table>

*denotes single child with positive ANA and rheumatoid factor

Table IV. Correlation of radiological grading with other findings

<table>
<thead>
<tr>
<th>Radiological grading at the onset of disease</th>
<th>Number of children</th>
<th>Involvement found at follow-up</th>
<th>Complications</th>
<th>Functional status</th>
</tr>
</thead>
<tbody>
<tr>
<td>No abnormality on the radiographs (Grade 0)</td>
<td>5</td>
<td>Monarticular 5 Pauciarticular — Polarticular —</td>
<td>Nil</td>
<td>No limitation (3) Slight limitation (2)</td>
</tr>
<tr>
<td>Swelling of soft tissue, pauciarticular osteoporosis and periosteal new bone formation (Grade I)</td>
<td>15</td>
<td>Monarticular 10 Pauciarticular 4 Polarticular 1</td>
<td>Chronic iridocyclitis (2)</td>
<td>No limitation (10) Slight limitation (3) Moderate limitation (2)</td>
</tr>
<tr>
<td>Grade I plus narrowing of joint space and overgrowth of epiphysis (Grade II)</td>
<td>2</td>
<td>— Pauciarticular 2 Polarticular —</td>
<td>Chronic iridocyclitis (1)</td>
<td>Slight limitation (1) Moderate limitation (1)</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>15 6 1</td>
<td>(3)</td>
<td>(22)</td>
</tr>
</tbody>
</table>

Number in parenthesis denotes the number of cases

In the six children followed for more than 12 years intermittent monarthritis has continued. At present, 19 children have the disease in remission and three are disabled with acute disease requiring splintage, occasional aspirin and restriction of activities.

Complications. Three of the five boys in this series of 22 children developed chronic iridocyclitis, three months, two years and five years after the onset of MJRA. All three showed Grade III synovial changes. The tests for antinuclear antibodies were positive and for rheumatoid factor negative in two boys, and this position was reversed in the third boy.

Serological testing. The tests for antinuclear antibodies were positive (greater than 1/16 dilution) in five out of 16 children tested. The Rheumaton test was positive in five of 20 children tested but R₃ was positive (1/128) in only one of these. Immunoglobulins and complement levels were within normal limits in 16 children.

As shown in Table III, of the five children with antinuclear antibodies (four with negative Rheumaton and one positive) two boys developed classic iridocyclitis two and five years after onset of the disease. Of the seven children whose disease progressed to other joints, the tests for antinuclear antibodies were positive in three. A positive Rheumaton test with or without a confirmatory positive R₃ bore no prognostic significance during the period of follow-up. Of the five children with a positive Rheumaton test, the only child with a positive R₃ showed radiological progression and she continues to have active disease.

Radiological evidence. Table IV correlates the original radiological change with other features. Five children with a normal radiograph at onset of the disease showed no progression or complications at follow-up. However, of the 17 children with Grade I or II radiographic changes such as swelling of soft tissue, pauciarticular osteoporosis and periosteal new bone formation, within some cases the addition of narrowing of the joint space and overgrowth of the epiphysis, the disease progressed to involve other joints in seven patients though neither the length of history nor the synovial histology was significantly different from the remainder.
DISCUSSION

Monarticular juvenile rheumatoid arthritis (MJRA) often presents a diagnostic problem and its outcome cannot be predicted. In our series the knee was the predominant joint affected, then the ankle, wrist, hip and metatarsophalangeal joint in that order. Other authors have also noted the frequency of involvement of knee, ankle and wrist (Griffin, Tachdjian and Green 1963; Bywaters and Ansell 1965).

We found no way of predicting which child with monarthritis would develop involvement of other joints. In seven children other joints became involved within three and a half years of the onset of the disease. Grokoest, Snyder and Schlaeger (1962) reported that in 39 per cent of 110 patients with juvenile rheumatoid arthritis (JRA) the disease had commenced with one joint only, but that other joints had become involved within a month in a number of cases. Similarly Edström (1958) noted that 32 per cent of his 161 cases of JRA presented with monarthritis and that six per cent remained monarticular.

Bywaters and Ansell (1965) studied 33 children with MJRA. At follow-up (mean 6.5 years) the disease was confined to one joint in 14 children, had progressed to involve one or two other joints (pauciarticular) in seven and had become generalised, with at least four joints involved, in the rest. Of the 19 cases which progressed, 15 did so within the first year. The Rose–Waaler test was positive in only one of the 33, a girl of 11 years who developed polyarthritis. Six children developed uveitis.

Uveitis has been well recognised in the last decade as a serious complication of JRA. Bywaters and Ansell (1965) observed this complication in 18 per cent of those with monarthritis, in contrast to an overall incidence of 8.9 per cent. In our series three children (13.5 per cent), all boys, developed eye complications. Of these, two had antinuclear antibodies. In another two children with antinuclear antibodies the possibility remains that eye complications may occur later in life. It therefore seems important that children, especially boys, with MJRA and antinuclear antibodies should have periodic ophthalmic assessment as early treatment is essential.

There was poor correlation between the histological grade and the outcome of the disease as judged by involvement of other joints and the functional status. Our experience suggests that in about one third of cases of MJRA synovial biopsy is also unhelpful in diagnosis. The value of an open biopsy as part of the initial investigation of a case of monarthritis lies in the exclusion of other diseases such as tuberculosis.

REFERENCES