Cartilage macromolecules in knee joint synovial fluid. Markers of the disease course in patients with acute oligoarthritis

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Abstract

Objective—To investigate the development of chronic joint symptoms in patients presenting with acute oligoarthritis including knee joint synovitis with effusion and explore whether prognostic information can be derived from initial synovial fluid concentrations of aggrecan and cartilage oligomeric matrix protein (COMP) for development of chronic joint symptoms.

Methods—Retrospective follow up of 25 patients identified in a bank of knee joint synovial fluids collected consecutively from patients presenting with knee joint synovitis and symptoms from at most three additional joints and in whom no diagnosis could be established at presentation.

Results—The 10 patients who developed chronic joint symptoms were characterised by lower knee joint synovial fluid concentrations of aggrecan as well as lower aggrecan/COMP ratios (p<0.001) than the 15 patients who had a transient arthritis. No other clinical or laboratory differences between the groups were apparent at the time of presentation.

Conclusions—The synovial fluid content of aggrecan is a potential tool in acute arthritis for distinguishing patients with a benign disease course from those who will develop a chronic joint disorder.

Arthritis with acute onset frequently presents a diagnostic challenge in rheumatology. After identifying the rare cases of septic arthritis and the cases of crystal induced arthritis, most of the remaining patients will initially be diagnosed as having undifferentiated non-infectious inflammatory arthritis. In some of these patients the disease course will reveal the diagnosis, whereas in others the diagnosis will remain unknown. In some patients the acute arthritis will resolve completely while others will develop a chronic joint disorder for example, rheumatoid arthritis (RA). Conventional clinical or laboratory variables often fail to reveal the diagnosis in the acute phase, or predict the subsequent course of the arthritis. Thus, it is not possible to give the patient reliable prognostic information and importantly, it is impossible to initiate aggressive treatment in cases prone to rapid functional or structural deterioration resulting from a chronic joint disease. As it is increasingly believed that such early treatment is beneficial the lack of diagnostic and prognostic instruments applicable in the acute stage may preclude potentially preventive treatment.

Synovial fluid analyses of joint matrix macromolecules represent a novel tool for the study of tissue involvement in arthritis. Promising results regarding the diagnostic and prognostic utility of such measurements have been obtained. Notably, in acute stages of reactive arthritis and crystal induced arthropathies with normal radiographic appearance of the knee joints, high concentrations of aggregan, the large aggregating cartilage proteoglycan, have been found in synovial fluid. The concentrations in these conditions significantly exceeded the values found in RA patients with normal knee joint radiographs and a duration of synovitis comparable with that in reactive arthritis. Subsequently, as the joint symptoms subsided in the patients with reactive arthritis, decreasing synovial fluid concentrations of aggregan were found. In RA, the synovial fluid aggregan concentrations are highest in patients with radiographically well preserved joints and lower values are found in stages with pronounced joint damage. In contrast, the synovial fluid content of another primarily cartilage derived macromolecule, cartilage oligomeric matrix protein (COMP), does not appear to vary considerably in different phases of reactive arthritis or RA. The ratio between the concentrations of these markers in synovial fluid has been used to reduce the confounding effect of variations in amounts of retrievable fluid, regardless of the fact that the clearance rates of the molecules may vary.

In this retrospective study we have investigated the development of chronic joint symptoms in patients initially presenting with acute oligoarthritis including a synovitis of the knee joint requiring joint fluid aspiration and where a diagnosis could not be established at presentation using clinical or routinely used laboratory variables. Furthermore, we explored the concentration in synovial fluid of aggregan and COMP, as possible predictors of persisting arthritis.

Methods

Patients
A computer search of a bank of synovial fluid samples collected consecutively from patients in whom arthrocentesis had been performed...
Table 1 Characteristics of patients with transient arthritis (n=15) and chronic arthritis (n=10). The figures denote median (range).

<table>
<thead>
<tr>
<th>Final diagnosis (number of patients)</th>
<th>Transient arthritis</th>
<th>Chronic arthritis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligoarthritis</td>
<td>11</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Gout</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Seronegative large joint arthritis</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>41 (25–75)</td>
<td>50 (34–75)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>8/7</td>
<td>4/6</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of synovitis (months)</td>
<td>0.5 (0.03–2)</td>
<td>0.75 (0.25–5)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of swollen joints</td>
<td>1 (1–3)</td>
<td>2 (1–4)</td>
<td>NS</td>
</tr>
<tr>
<td>ESR (mm/1st hour)</td>
<td>20 (5–27)</td>
<td>20 (5–50)</td>
<td>NS</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>136 (106–153)</td>
<td>134 (100–150)</td>
<td>NS</td>
</tr>
<tr>
<td>SF-aggrecan (µg/ml)</td>
<td>182.5 (78.2–328.8)</td>
<td>71.3 (26.3–166.9)</td>
<td>0.0007</td>
</tr>
<tr>
<td>SF-COMP (µg/ml)</td>
<td>111.7 (54.1–226.8)</td>
<td>98.9 (38.3–199.8)</td>
<td>NS</td>
</tr>
<tr>
<td>SF-aggrecan/COMP concentration ratio</td>
<td>1.7 (0.8–3.9)</td>
<td>0.8 (0.4–1.0)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Results

At the initial computer search we found 80 patients who at the time of joint fluid aspiration had been diagnosed as having knee joint arthritis of unknown cause with a duration of synovitis not exceeding six months. By examining their charts it was found that 36 patients already at the time of aspiration had an established diagnosis. In 14 cases there was a history of previous joint symptoms. Three patients had died and were not possible to evaluate. In one patient the arthritis was considered to be result from a loose body and in another case the arthritis was probably a paramalignant reaction. These patients were not studied further.

The remaining 25 patients were further studied and could be separated in two groups according to the final diagnosis as shown in table 1. Thus we were able to identify one group (n = 15) with transient arthritis and one group (n = 10) with chronic joint symptoms.

Table 1 also shows a comparison of some of the features of the patients with transient arthritis and chronic arthritis, respectively, at the time of joint fluid aspiration. No significant difference between the groups were found for the clinical variables, erythrocyte sedimentation rate or haemoglobin concentration. In contrast, the synovial fluid concentrations of aggrecan were significantly higher in the patients with transient arthritis (fig 1). The COMP concentrations did not differ between the groups. To reduce the variability resulting from varying amounts of synovial fluid present in the different joints we also calculated the ratios between the aggrecan and COMP concentrations. The ratios were significantly
Cartilage macromolecules in knee joint synovial fluid

Vdi confounding factor if there were considerable concentrations for comparisons might be a to develop a chronic joint disorder. The use of with a benign, resolving course and those prone possible way of di aggrecan in synovial fluid in the acute stage is a

This retrospective follow up of patients who
diagnosis was possible were su...
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