CHOLESTEROL CRYSTALS IN SHOULDER SYNOVIAL FLUID

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SUMMARY

Samples of 1945 synovial fluids have been examined from patients with a wide variety of joint disorders. Typical cholesterol crystals were seen in only 14 of these samples, all from the shoulders of six patients with severe rheumatoid arthritis and persistent shoulder effusions.

KEY WORDS: Cholesterol crystals, Shoulder, Rheumatoid arthritis.

Cholesterol crystals in body effusions have been recognized for more than a century [1]. Their presence in synovial fluid was first reported by Ropes and Bauer in 1953 [2]. They were positively identified by Zuckner et al. [3] in 1964 and since then there have been several further reports. Most cases reported have had rheumatoid arthritis (RA) but they have also been found in other conditions including osteoarthritis [4] and ankylosing spondylitis [5].

We present a review of joint effusions containing such crystals and propose that the anatomical site of joint involvement is a very important factor in their pathogenesis in joint effusions.

METHODS AND MATERIALS

Findings in all the articular synovial fluid (SF) samples received over a 4-year period were reviewed. Altogether, 1945 samples were examined of which 27% were from RA patients, 22% from other inflammatory arthropathies (including crystal arthropathies) and 34% from osteoarthritis patients. In most other cases the diagnosis was either unknown or not recorded. The RA samples came predominantly from the knee (66%) and shoulder (22%) joints but other sites such as the elbow (4%) and the wrist (1%) were also represented. Multiple samples from both the knee and shoulder joints were available in many RA patients. Bursal and tendon sheath aspirates were not included in the study.

Cholesterol crystals were considered present if polarized light microscopy showed the typical flat pleomorphic plates often with a chip out of one corner [6] (Fig. 1). In all cases the crystals were also soluble in ethanol, indicating lipid.

RESULTS

There were 14 samples (from six patients) in which the typical crystals were identified. Details of the patients and the SF are shown in the Table. All the patients had severe erosive nodular RA in a typical polyarticular distribution. Rheumatoid factor was positive in high titre in all but one case (patient no. 4).

The shoulder was the joint from which the crystals were isolated in all cases. None occurred in the knee or other locations.

Clinically, the involved shoulder was the most symptomatic joint in four patients. It was both painful and severely restricted in all cases with a large anterior effusion present in most (Fig. 2). The shoulder radiographs showed severe erosive changes in all cases (Fig. 3). In the four patients from whom multiple samples were available crystals were detected in the same joint at each
TABLE

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Disease duration (years)</th>
<th>Extra-articular features</th>
<th>Shoulder</th>
<th>SF WCC</th>
<th>No. samples</th>
<th>Duration of cholesterol effusions (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>62</td>
<td>23</td>
<td>Nil</td>
<td>Right</td>
<td>low</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>57</td>
<td>18</td>
<td>Nil</td>
<td>Right</td>
<td>low</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>75</td>
<td>12</td>
<td>Nil</td>
<td>Left</td>
<td>low</td>
<td>3</td>
<td>1.5</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>72</td>
<td>8</td>
<td>Nil</td>
<td>Right</td>
<td>1.0×10⁹/l</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>45</td>
<td>12</td>
<td>Heart valve granuloma</td>
<td>Right</td>
<td>low</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>63</td>
<td>13</td>
<td>Lung fibrosis</td>
<td>Right</td>
<td>low</td>
<td>1</td>
<td>—</td>
</tr>
</tbody>
</table>

WCC = white cell count.

subsequent aspiration. In no case has the cholesterol effusion resolved.

**DISCUSSION**

We have confirmed that articular SF cholesterol crystals are found almost exclusively in patients with long-standing nodular erosive RA. We have shown that in such patients the shoulder is much more likely to contain the crystals than the knee or other joints commonly aspirated. This suggests that their expression is in large part due to modification of disease expression by the conditions prevailing in a particular anatomical site.

The anatomical and biomechanical features of the shoulder joint are unique and are certainly very different to those in the knee. It is probable, therefore, that RA involving the shoulder would have many local effects which would be quite different to those of disease in the knee or other joints. Local factors have been implicated in the pathogenesis of cholesterol crystals. Bland et al.
[7] suggested impaired lymphatic drainage of the joint. Zuckner et al. [3] suggested that deficient removal of red blood cells after local intra-articular haemorrhage is important although blood staining has not been a feature of fluids containing the crystals in this series or other reported cases. As cell membranes are thought to provide a source of cholesterol in such effusions, these, or other, local factors could act by causing an accumulation of cell debris thus providing a suitable substrate for the formation of cholesterol crystals. Clearly other factors must also play a part in their formation in SF. The finding of cholesterol crystals in chronic bursae and calf cysts [3, 5] also implicates local factors such as reduced drainage, and it was striking that all our patients had persistent large effusions in the affected shoulders.

There is some evidence in experimental animals that the crystals may cause a low-grade inflammation [3, 7, 8]. Zuckner and colleagues suggested that this may be self-perpetuating by inducing 'chronicity of the pathological state'. There are however few data to support this in man and further work is required. In our patients there was nothing to suggest that the crystals played any role in the pathogenesis of the joint disease.

It is well recognized that crystals such as monosodium urate and calcium pyrophosphate dihydrate favour certain joints as sites for their formation. Our data suggest that the shoulder joint is the particular site favoured for the formation of cholesterol crystals in RA patients. It is likely therefore that their detection in the shoulder joint merely reflects this predilection in chronic severe RA and probably carries no other clinical or pathological significance.

ACKNOWLEDGEMENTS

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REFERENCES

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INDICATIONS
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DOSAGE
Usually 1 daily. If required, 1 twice daily. Take with food.

CONTRAINDICATIONS
Active peptic ulcer; history of GI lesions; patients with nasal polyps associated with angioneurotic oedema; hypersensitivity to indomethacin, acetylsalicylic acid or other NSAIDs; pregnancy; lactation; children.

PRECAUTIONS
Use with particular care in the elderly, in impaired liver or renal function, and in patients with a history of psychiatric disorders, epilepsy, or Parkinsonism. If GI symptoms occur, weigh benefits against risks of continuing. If GI bleeding occurs, discontinue. May mask the signs and symptoms of infection. If headache, with or without dizziness or lightheadedness, develops and persists despite dose reduction, discontinue. Possible ocular effects may occur after prolonged therapy. Monitor the prothrombin time when adding 'Indocid' to the treatment of patients on anticoagulants or with coagulation defects.

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Product Licence Number:
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CONTRA-INDICATIONS: Active peptic ulceration, history of peptic ulceration, perforation.

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SIDE-EFFECTS: Surjan is generally well tolerated. Gastro-intestinal reactions which have been reported include dyspepsia, nausea, abdominal pain, vomiting, anorexia, indigestion, heartburn, bloating, constipation, diarrhea, flatulence, diarrhea. Peptic ulcers, gastro-intestinal bleeding and perforation have occasionally been reported but in exceptional cases may have been associated with fatalities. Headache and drowsiness have occasionally been reported, as have skin reactions which include rash, photo-sensitivity, urticaria, pruritus, angioedema and anaphylaxis.

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LEGAL CATEGORY: POM.

BASIC NHS PRICES: Surjan 300mg £14.83 per pack of 60. Surjan 200mg £13.76 per pack of 100.

PRODUCT LICENCE NUMBERS: Surjan 300mg tablets 0190/0109. Surjan 200mg tablets 0190/0127.

DATE OF PREPARATION: November 1996.