this can happen several years after or before the onset and can delay the diagnosis and treatment [2, 3, 9]. The audiovestibular prognosis depends on steroid treatment within the first month of the symptoms [3], but hearing loss may progress to profound bilateral deafness if the patient has repeated attacks [3–5]. Our patient’s initial ocular symptoms occurred 4 yrs before her hearing loss. This was the clue leading to diagnosis and appropriate treatment with corticosteroids, for the acute episode, and immunomodulation to maintain the success. Although 37% of patients with atypical Cogan’s syndrome progress to bilateral deafness [2], despite systemic corticosteroids and immunomodulation, our patient’s auditory acuity remained stable after a 2-yr treatment with corticosteroids, methotrexate and ciclosporin. In addition, systemic treatment did not modify the prognosis of the keratopathy due to her advanced initial presentation.

Severe keratopathy can be the end-stage of corneal compromise in Cogan’s syndrome and may present in childhood as the main manifestation. A multi-disciplinary approach is necessary to be successful at early diagnosis and treatment.

Rheumatology

<table>
<thead>
<tr>
<th>Key message</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Severe keratopathy in paediatric Cogan’s syndrome may present as the main manifestation.</td>
</tr>
</tbody>
</table>

Acknowledgements

H.M.-O. and G.F.-P. were supported by a grant from the Carolina Foundation, Ministry of Foreign Affairs, Spain.

The authors have declared no conflict of interest.

H. MARTÍNEZ-OSORIO, G. FUENTES-PAÉZ, M. CALONGE
The Ocular Immunology Unit, Institute of Ophthalmobiology (IOBA), University of Valladolid, Valladolid, Spain
Accepted 3 August 2006

Correspondence to: Margarita Calonge, MD, IOBA, Facultad de Medicina, Universidad de Valladolid, Ramón y Cajal 7, E-47005, Valladolid, Spain. E-mail: calonge@ioba.med.uva.es


Rheumatology 2006;45:1577–1578
doi:10.1093/rheumatology/kel344
Advance Access publication 13 October 2006

Atorvastatin for chronic synovitis due to massive intra-articular cholesterol monohydrate deposition in long-standing rheumatoid arthritis

Sir, Crystal-induced arthritis is quite common in rheumatology, particularly negatively birefringent needles due to monosodium urate and positively birefringent rhomboids due to calcium pyrophosphate. Negatively birefringent plates with notched corners are due to cholesterol monohydrate but only rarely occur or are under-recognized; it is a challenge for clinicians to correctly diagnose these [1, 2]. Which therapy is to be considered once cholesterol plates have been diagnosed remains unclear from literature.

A 51-yr-old female with unremarkable lipid profile presented with exacerbation of rheumatoid arthritis (RA) and a particularly painful synovitis of knee and shoulder. RA had been diagnosed 15 yrs earlier. Several disease-modifying anti-rheumatic drugs had previously been prescribed as monotherapy and as combination therapy (dual, but not triple): oral methotrexate (MTX with folic acid supplementation), sulphasalazine (SSZ) and hydroxychloroquine (HCQ), all without significant efficacy. Tolerance problems with MTX made her discontinue the MTX and continue SSZ monotherapy. Despite high disease activity, 28 joint count (DAS28) 5.1, she complied to SSZ for several years. Puncture of the right shoulder and left knee revealed a voluminous white colloidal fluid [1]. Micro-organisms were excluded. Polarization microscopy revealed cholesterol monohydrate plates. Treatment options aiming primarily at reducing total bulk of intra-articular cholesterol, and secondly at reducing DAS28, were considered; see Table 1. Failure on both end points was seen during 8 weeks of follow-up using weekly parenteral MTX 10 mg (without tolerance problems). Following intra-articular injection of 40 mg methylprednisolone acetate, a large voluminous increase of synovial fluid was produced, again loaded with cholesterol plates. It was only when atorvastatine 20 mg daily was started that the cholesterol bulk completely resolved; see Table 1. Possibly MTX in part, but particularly atorvastatine, should be held responsible for the resolution of the large bulk of intra-articular cholesterol.

Data from literature on treatment options of cholesterol crystal synovitis are lacking. Cases with cholesterol crystal deposition have only sporadically been reported in the literature [2]. If deposition occurs in rheumatoid diseases, then it occurs most frequently in structures with synovial lining and without concomitant hyperlipidaemia. General interest of immunologists/rheumatologists in statins has increased over the last years. Trial of Atorvastatin in RA (TARA) has drawn attention to the pivotal role statins may play in chronic rheumatoid inflammation [3]. Interestingly, statins have next to anti-cholesterol, also immunomodulatory and anti-inflammatory properties. They appear to act as direct repressors of class II major histocompatibility complex (MHC)-mediated T-cell activation while not affecting constitutive expression of class II MHC in dendritic cells and B-lymphocytes [4]. Statins selectively block β2 integrin and lymphocyte-function-associated antigen I (LFA-1)
by binding to a novel allosteric site within LFA-1 [5]. Another beneficial effect of statins may be the switch from Th1 to Th2 cytokines, as demonstrated for atorvastatin in a murine model [6]. Statins reduce CD40 expression in atheroma-associated cells in atherosclerotic lesions in situ in treated patients [7]. Fluvastatin has recently been shown to induce apoptosis in vitro in RA synoviocytes through a mitochondrial and caspase-3-dependent pathway and by inhibition of the geranylgeranylation pathway [8]. One may speculate that some of these previously proven mechanisms of action may be of relevance in the presented case.

Cholesterol crystalloids may appear as negatively birefringent, large, flat rectangular plates with notched corners, ranging from 8 to 100 μm, consisting of monohydrate cholesterol. These are thermodynamically stable and not easily cleared. This case lends support to the hypothesis that locoregional monohydrate cholesterol production or one of the aforementioned mechanisms (suppression of class II MHC or Th1–Th2 switch) play a pivotal role in the aetiopathogenesis of cholesterol synovitis, as cholesterol synovitis can be inhibited by atorvastatin in humans.

The authors have declared no conflicts of interest.

T. L. TH. A. JANSEN
Department of Rheumatology, Medical Centre Leeuwarden, POB 888, 8901 BR Leeuwarden, The Netherlands
Accepted 5 September 2006
Correspondence to: T. L. Th. A. Jansen, Department of Rheumatology, Medical Centre Leeuwarden, POB 888, 8901 BR Leeuwarden, The Netherlands. E-mail: T.Jansen@znb.nl


Rheumatology 2006;45:1578–1580
doi:10.1093/rheumatology/kel334
Advance Access publication 3 November 2006

Unilateral polymyalgia rheumatica with contralateral sympathetic dystrophy syndrome: A case of asymmetrical involvement due to pre-existing peripheral palsy

SIR, We describe the case of a man with pre-existing peripheral palsy who developed polymyalgia rheumatica (PMR); he was spared arthritis in the affected limb but experienced reflex sympathetic dystrophy syndrome (rSDS) in the paretic arm.

A 72-year-old man was admitted to our hospital because of nocturnal pain in his right shoulder and the pelvic girdle, with long-lasting morning stiffness, mild fever and weight loss. The pain in his buttocks and thighs was so severe that it limited his ability to stand and walk. His knee reflex responses were symmetrically reduced, and he was admitted to the Neurological Department with suspected paraparesis. The shoulder pain was not taken into account because the patient reported a diagnosis of rotator cuff tendinitis that had been made some days before by another physician.

The patient's history included left axilla irradiation performed 30 yrs ago because of a ‘lymphogranuloma’, which led to brachial plexus damage and peripheral palsy in the arm; the lymphoma did not relapse and the patient did not receive any other treatment.

Table 1. Time points of shoulder punctures, and correlation of total intra-articular cholesterol with three therapeutic interventions (bold)

<table>
<thead>
<tr>
<th>T (weeks)</th>
<th>0</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSZ</td>
<td>2 g/dy</td>
<td>starta</td>
<td>1 g/dy</td>
<td>cont</td>
<td>1 g/dy</td>
<td>cont</td>
</tr>
<tr>
<td>MTX</td>
<td>10 mg sc</td>
<td>start</td>
<td>10 mg sc</td>
<td>cont</td>
<td>10 mg sc</td>
<td>cont</td>
</tr>
<tr>
<td>MPA ia</td>
<td>0</td>
<td>0</td>
<td>40 mg</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Shoulder puncture results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume SF (ml)</td>
<td>80</td>
<td>50</td>
<td>30</td>
<td>130</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Leucocyte count (10⁹/l)</td>
<td>2.6</td>
<td>5.3</td>
<td>5.4</td>
<td>5.0</td>
<td>2.2</td>
<td>0</td>
</tr>
<tr>
<td>Cholesterol (mM)</td>
<td>7.8</td>
<td>7.4</td>
<td>7.8</td>
<td>12.9</td>
<td>5.9</td>
<td>0</td>
</tr>
<tr>
<td>Outcome parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF cholesterol (μmol)</td>
<td>624</td>
<td>370</td>
<td>234</td>
<td>1677</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>DAS₂₈</td>
<td>5.1</td>
<td>3.3</td>
<td>3.3</td>
<td>3.1</td>
<td>2.7</td>
<td>1.9</td>
</tr>
</tbody>
</table>

aStarting and subsequently continuing methotrexate (MTX), b intra-articular methylprednisolone acetate (MPA ia) injection, c starting and subsequently continuing atorvastatin treatment.

Disease activity of RA is measured according to validated scoring method applying 28 joint counts; interpretation: high disease activity when DAS₂₈ > 5.1; low activity when DAS₂₈ < 3.2. g/dy = grams per day; cont = continue; sc = subcutaneous; ia = intra-articular; SF = synovial fluid.