Chronic Large Joint Synovitis in Systemic Lupus Erythematosus: Finding What You Look For

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Systemic lupus erythematosus, Synovitis, Musculoskeletal TB, Osteonecrosis

Case Report
Systemic Lupus Erythematosus (SLE) patients commonly have musculoskeletal complaints. We describe two SLE patients with persistent knee pain and swelling that were initially mistaken for inflammatory arthritis.

Case 1
A 30-year-Black African female was diagnosed with SLE when she presented with a Coombs positive haemolytic anaemia, lymphopenia, polyarthritis, oral ulcers and a malar rash. Her antinuclear antigen (ANA) was positive, she had hypocomplementaemia and she was HIV negative. She was commenced on oral corticosteroids (initially high dose 60 mg/day and later weaned to 15 mg daily), chloroquine sulphate and azathioprine. Her blood counts and SLE symptoms improved. Four months after diagnosis, she developed a right knee monoarthritis. Despite intra-articular steroid injections, nonsteroidal anti-inflammatories, her knee symptoms persisted. Plain X-rays of the knees and chest were unremarkable, but she had an elevated C-reactive protein (14 mg/l) and very high ESR (88 mm/h). Over the next four months, three joint aspirations were Gram and Ziehl-Neelsen stain and culture negative. A synovial biopsy submitted for histology revealed necrotising granulomatous inflammation. The positive Ziehl-Neelson stain for acid-fast bacilli confirmed the diagnosis of osteoarticular Mycobacterium tuberculosis infection (Figure 1). She had no history of previous tuberculosis (TB), and there was no evidence of extra-pulmonary disease elsewhere. Her knee swelling and symptoms resolved within 3 months of commencing anti-TB treatment, and this therapy was continued for 18 months.

Case 2
A 30-year-old female of mixed racial ancestry was diagnosed with SLE when she presented with a Coombs positive haemolytic anaemia, lymphopenia, polyarthritis, oral ulcers and a malar rash. Her antinuclear antigen (ANA) was positive, she had hypocomplementaemia and she was HIV negative. She was treated with intravenous solumedrol 500 mg daily for 3 days followed by oral corticosteroids at 60 mg daily which were tapered to 15 mg daily over 4 months, chloroquine sulphate and mycophenolate mofetil. Within 4 months, her SLE was inactive but she complained of a painful right knee. On examination, she had bilateral knee effusions, but no synovitis of any other joint. She was commenced on oral corticosteroids at 60 mg daily which were tapered to 15 mg daily over 4 months, chloroquine sulphate and mycophenolate mofetil. Within 4 months, her SLE was inactive but she complained of a painful right knee. On examination, she had bilateral knee effusions, but no synovitis of any other joint. The knee was aspirated on two occasions, and the serous fluid was shown to be a Type 2 inflammatory fluid (slightly turbid with a white cell count 2000-10000, 20-70% neutrophils), with negative bacterial and fungal cultures. Intra-articular steroids were unhelpful, and symptoms and swelling continued for the next four months. Plain radiographs showed a fragmented medial epicondyle of the right knee (Figure 1) and MRI of the right knee demonstrated a joint effusion, large bony infa rcts with surrounding oedema in the medial and lateral femoral condyles, proximal tibia and patella lesions. She was ANA and dsDNA positive, HIV negative, and had no antiphospholipid antibodies. She was treated with intravenous solumedrol 500 mg daily for 3 days followed by oral corticosteroids at 60 mg daily which were tapered to 15 mg daily over 4 months, chloroquine sulphate and mycophenolate mofetil. Within 4 months, her SLE was inactive but she complained of a painful right knee. On examination, she had bilateral knee effusions, but no synovitis of any other joint. The knee was aspirated on two occasions, and the serous fluid was shown to be a Type 2 inflammatory fluid (slightly turbid with a white cell count 2000-10000, 20-70% neutrophils), with negative bacterial and fungal cultures. Intra-articular steroids were unhelpful, and symptoms and swelling continued for the next four months. Plain radiographs showed a fragmented medial epicondyle of the right knee (Figure 1) and MRI of the right knee demonstrated a joint effusion, large bony infa rcts with surrounding oedema in the medial and lateral femoral condyles, proximal tibia and patella
Osteonecrosis is a common complication of SLE, affecting large weight bearing joints such as the hip and knee and the spine. Patients with SLE may be at particular risk of osteonecrosis (ON) of at least one other large joint, commonly the other knee (82%) or hip (67%) [12]. The aetiology of ON in SLE patients is multifactorial, with high inflammatory markers, corticosteroid therapy, other immunosuppressive therapies, lymphopenia, nephritis and inflammatory arthritis [8,9].

Osteonecrosis (ON) is a common complication of SLE, affecting 2-30% of patients [10]. Although the hip is the most common site, knee ON is well described. In a series of knee ON patients, Navaez describes gradual or sudden onset of pain, with tenderness and the presence of an effusion in 81% of patients [11]. Multiple sites of ON are frequently seen. In a series of 136 patients with knee ON, 74% had knee ON is well described. In a series of knee ON patients, Navaez describes gradual or sudden onset of pain, with tenderness and the presence of an effusion in 81% of patients [11]. Multiple sites of ON are frequently seen. In a series of 136 patients with knee ON, 74% had ON of at least one other large joint, commonly the other knee (82%) or hip (67%) [12]. The aetiology of ON in SLE patients is multifactorial, and predisposing factors include glucocorticoid therapy, vasculitis, lymphopenia, nephritis and inflammatory arthritis [8,9].

Table 1: Differential diagnosis of arthritis in SLE patient.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>SITES</th>
<th>CLINICAL</th>
<th>RISK FACTORS</th>
<th>INVESTIGATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory arthritis</td>
<td>Hand joints, knee, frequently symmetrical.</td>
<td>Frequently presenting problem. May be associated with flare in other organs.</td>
<td>No clear association with ESR, C3, and SLEDAI score.</td>
<td></td>
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<tr>
<td>Septic arthritis</td>
<td>Hip, knee (frequently multiple sites)</td>
<td>Acute onset, hot effusion</td>
<td>Corticosteroid therapy, inflammatory arthritis, osteonecrosis</td>
<td>High CRP, Joint aspiration: type 3 inflammatory fluid (turbid or frank pus, white cell count &gt; 50,000, &gt; 70% of which are neutrophils), positive culture.</td>
</tr>
<tr>
<td>Osteo-articular Mycobacterium Tuberculosis infection</td>
<td>Spine, Hip, Knee, Wrist</td>
<td>Insidious onset, possible constitutional symptoms</td>
<td>Corticosteroid therapy, other immunosuppressive therapies, lymphopenia, nephritis, inflammatory arthritis</td>
<td>High inflammatory markers. Synovial fluid Gene x-pert and TB culture, synovial biopsy.</td>
</tr>
<tr>
<td>Osteonecrosis</td>
<td>Hip, knee (frequently multiple sites)</td>
<td>Cold effusion</td>
<td>High dose corticosteroid therapy, vasculitis, coagulopathy, antiphospholipid antibodies, Raynaud's phenomenon</td>
<td>X-ray may be abnormal if advanced, frequently normal in early stages. MRI is investigation of choice.</td>
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</tbody>
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ESR: Erythrocyte Sedimentation Rate, SLEDAI score: SLE Disease Activity Score, CRP: C - Reactive Protein, TB: Tuberculosis, MRI: Magnetic Resonance Image
Raynaud's phenomenon, antiphospholipid antibodies and high disease activity [13,14]. Early disease may respond to core decompression surgery or to bisphosphonate therapy although large randomised control studies are lacking [15,16]. Advanced cases, such as our patient, where the knee joint is destroyed require arthroplasty.

In both the cases described, there was considerable diagnostic delay despite follow-up at a specialist centre. The expense and invasiveness of synovial biopsy and histology or MRI studies to make either diagnosis frequently underlie this delay. However, awareness of the differential diagnosis and appropriate investigation of a persistent large joint swelling is critical to make a timeous diagnosis in order to prevent joint destruction. In addition, these two cases also highlight the devastating side effects of prolonged high-dose corticosteroids. This risk of corticosteroid-induced damage is increasingly recognized in SLE patients and best practice is to use moderate doses for the shortest possible time [17].

In summary, a painful, swollen joint in a SLE patient should prompt consideration of a cause other than inflammatory arthritis. In particular, persistent pain and swelling, and involvement of a large joint, are important clues to a “non-SLE arthritis” and should prompt investigations for other causes, in particular septic arthritis and osteonecrosis. Remember, “You only find what you look for, and you only look for what you know”.

Ethical Statement

Written informed consent was obtained from the patients for publication of this case report and accompanying images.

References