CASE REPORT

Successful treatment of resistant SAPHO syndrome with anti-TNF therapy

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SUMMARY

A 42-year-old Caucasian woman with SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) refractory to non-steroidal anti-inflammatory drugs, sulfasalazine, methotrexate, bisphosphonates and steroids was successfully treated with antitumour necrosis factor therapy (infliximab). This case was a diagnostic challenge leading to extensive investigations for infection and malignancy and delayed diagnosis for several years. We report the significant improvement in clinical, radiological and laboratory markers of disease activity on infliximab and the steroid sparing effect of such therapy.

BACKGROUND

SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) should be included in the differential diagnosis of seronegative arthropathies associated with aseptic osteitis/osteomyelitis. Antitumour necrosis factor (TNF) therapy in our experience is a useful therapy when clinicians are faced with refractory SAPHO syndrome.

CASE PRESENTATION

We report on the beneficial effect of infliximab in a 42-year-old woman with severe refractory SAPHO syndrome of over 10 years duration.

This patient initially presented to the orthopaedics department with low back pain and degenerative changes on lumbar spine x-ray. Treatment with analgesics, NSAIDs and physiotherapy was ineffective and she developed erosive gastritis secondary to NSAID treatment. Her MRI scan showed degenerative changes. Therapeutic trials of amitriptyline, gabapentin, opiates and diazepam were ineffective and facet joint steroid injections were beneficial for up to 4 months.

Six years from presentation, she developed cervical spine and right shoulder pain radiating to the right arm and sternoclavicular and sternocostal pain. x-Rays of the cervical spine were normal but blood tests revealed raised C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) at 30 and 42, respectively. An isotope bone scan raised the possibility of a lytic lesion in the shoulder and showed increased uptake in the spine, sternum and right humerus. An MRI scan of the shoulder showed a joint effusion with subacromial bursitis, bone oedema and a lytic lesion in the head of humerus. Extensive investigations to rule out an underlying malignancy were negative. Arthroscopic biopsies from the lesion in the shoulder showed chronic osteomyelitis and acute on chronic synovitis possibly secondary to osteomyelitis. Cultures from the biopsy

specimens were negative and a full septic screen was negative. However, the ESR was persistently elevated and had risen to 80 at that time.

The patient was then referred to rheumatology. At this time she reported recurrent swelling in the right knee and was noted to have a knee effusion on admission. She was tender over the sternoclavicular joints. Lumbar and cervical spine movements were significantly restricted but the degree of limitation was out of proportion to the findings on x-rays.

The history and examination findings were not consistent with a spondyloarthropathy or multisystem disease.

INVESTIGATIONS

Antinuclear antibody was positive at 1:160 homogenous, but antidouble-stranded DNA, extractable nuclear antigens, anticardiolipin antibodies, antineutrophil cytoplasmic antibodies and complement profile were repeatedly negative. Rheumatoid factor and human leucocyte antigen B27 were also negative. Her ESR and CRP remained elevated at 74 and 65, respectively and aspiration of the knee effusion yielded an inflammatory synovial fluid with negative cultures. Intra-articular steroids provided significant relief over 3 months duration. A repeat MRI with a special short inversion time inversion recovery image of the lumbar spine and sacroiliac joints showed in addition to degenerative changes evidence of bone oedema in some vertebrae but no sacroilitis was identified.

DIFFERENTIAL DIAGNOSIS

On the basis of the findings of synovitis of the shoulder and knee, inflammatory spinal disease with normal sacroiliac joints, costochondral and sternoclavicular involvement and aseptic osteitis, the possibility of SAPHO syndrome (without skin involvement) was considered.^{1 2}

TREATMENT

Treatment with a course of steroids (20 mg prednisolone/day) provided a dramatic response. Because of difficulty reducing the dose, a trial of sulphasalazine and subsequently methotrexate was considered but both proved ineffective. Treatment with zoledronic acid provided complete resolution of all spinal symptoms and restoration of spinal mobility but the effect only lasted for 4 weeks despite continued treatment with 10 mg of prednisolone and strong analgesics. Baseline bone markers before zoledronic acid therapy were checked. Serum CrossLaps (CTX), a bone resorption marker, was 0.133 (0.01–5.94) ng/ml, and serum TP1NP, a bone

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formation marker, was 9.22 (20.00–100.0) ng/ml. Repeat bone markers 6 months after zoledronic acid infusion revealed significantly suppressed turnover despite clinical relapse and as such it was not possible to repeat the infusion; CTX and TP1NP levels post-treatment were 0.018 and 9.94 ng/ml, respectively. A subsequent isotope bone scan was arranged and this confirmed progressive changes in the above-mentioned sites. The patient was then considered for infliximab therapy in combination with 10 mg of methotrexate weekly.

Infliximab treatment (5 mg/kg) given at weeks 0, 2, 4 then 8 weekly induced rapid remission of the osteoarticular symptoms.

OUTCOME AND FOLLOW-UP

At 6 weeks there was marked symptomatic improvement in the spinal and joint pain and stiffness, chest pain, general well-being and mobility and for the first time the patient was able to reduce her prednisolone below 10 mg without worsening symptoms. At 3 months she was receiving 3 mg of prednisolone daily and at 6 months she had managed to stop steroids altogether with maintained clinical remission. Objectively, there was no synovitis in the knee or the shoulder or tenderness over the sterno-clavicular joints. For assessment of spinal symptoms we used Bath ankylosing spondylitis indices, namely Bath Ankylosing Spondylitis Metrology Index, Functional Index, Disease Activity Index, Global Index and spinal pain by visual analogue scale. There was a substantial improvement in all indices at 3 months compared to baseline (table 1).

The patient was persistently anaemic before treatment with a haemoglobin ranging between 114 and 119 (120–160) g/l with persistently raised platelet count ranging between 459 and 532 ($140\text{--}400 \times 10^9/\text{l}$). Six months after infliximab her haemoglobin was 128 g/l with normal platelets. A repeat bone scan at 6 months showed that the increased uptake in the lumbar spine has totally faded. The uptake in the sternum, right shoulder and right knee had not changed but the conclusion was that the overall burden of tracer uptake had reduced in comparison to the pretreatment scan, suggesting a response to infliximab. The slow response might in part be related to the patient's intolerance to methotrexate because of severe nausea even on 7.5 mg weekly. The scan was taken before arrangements were made to administer methotrexate by subcutaneous route.

Table 1 Effect of infliximab on spinal symptoms of SAPHO

	Baseline	3 Months after infliximab
BASMI	5.2	4.0
BASFI	9.02	6.64
BASDAI	7.84	4.2
BAS-G	7.6	2.7
Spinal VAS	6.4	5.2

BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Functional Index; BASDAI, Disease Activity Index; BAS-G, Global Index; VAS, visual analogue scale.

DISCUSSION

This case report is our first experience of infliximab therapy in SAPHO syndrome. There is no consensus as to how best to treat SAPHO syndrome despite a number of case reports on the use of biologic agents^{3–4} with treatment protocols often similar to those of spondylarthropathies.^{5–6} Bisphosphonate therapy has been suggested as a first-line therapeutic option in many case reports^{5–8} but our patient had inadequate response to such therapy. Other drugs have been used in this condition such as NSAIDs, corticosteroids, sulfasalazine, methotrexate, ciclosporin, leflunomide and calcitonin with variable success rates.^{9–10} We believe that anti-TNF therapy is useful in patients with SAPHO syndrome and can be used early in severe refractory disease.

Learning points

- ▶ SAPHO (syndrome synovitis, acne, pustulosis, hyperostosis and osteitis) is a rare but debilitating illness.
- ▶ Consider SAPHO syndrome in the differential diagnosis of seronegative arthropathies associated with aseptic osteitis or osteomyelitis (ask/look for acne, pustulosis and hyperostosis).
- ▶ Antitumour necrosis factor therapy can be very useful in refractory SAPHO syndrome.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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