Successful treatment of SAPHO syndrome with infliximab: report of two cases

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The treatment of SAPHO syndrome is empirical and has recently been reviewed.[1–3] Non-steroidal anti-inflammatory drugs (NSAIDs) are the first choice but have limited efficacy. Second line drugs have been tried with mixed results. Positive effects with pamidronate, which partly works by blocking tumour necrosis factor α, have been reported.[3 4] Recently, Maksymowych *et al* suggested that pamidronate is also effective in spondarthritis, which shares manifestations and clinical associations with the SAPHO syndrome.[5 6] Infliximab, a chimeric anti-tumour necrosis factor α monoclonal IgG1 antibody, has recently been proved to be effective in the treatment of ankylosing spondylitis[7 8] and psoriatic arthritis.[7 9]

CASE REPORTS

In view of this information we treated two patients affected by refractory SAPHO syndrome with infliximab. Both patients had chest pain limiting normal activity despite adequate treatment with NSAIDs and second line treatment was unsuccessful. Both patients received three intravenous infusions of infliximab (5 mg/kg) at weeks 0, 2, and 6 and were evaluated at baseline, on days 3, 7, and 14, and then every two weeks.

Patient 1

The first patient was a 35 year old man who had had severe acne and painful osteitis of the left clavicle for 17 years. His family history showed that his mother had psoriasis and his brother had had one episode of acute anterior uveitis. Locus B HLA typing of the patient disclosed the B18 antigen. His disease had been treated with NSAIDs for 12 years. In 1996 he was given cyclosporin at a dose of 3 mg/kg/day, with some benefits for the chest pain only. The drug was stopped after two years owing to a loss of efficacy. In the following months long term antibiotic treatment with azithromycin, which has been suggested to be efficacious in SAPHO syndrome,[10] was tried without any results.

When we decided to start infliximab treatment the patient had had severe pain of his left clavicle for three months despite treatment with nimesulide, the best alternative NSAID for our patient, at a dose of 400 mg/day. The left clavicle was swollen, warm, and tender and florid acne was present on his face and posterior chest wall. Laboratory evaluation was normal except for a C reactive protein (CRP) of 13.5 mg/l (normal <5). Three days after the first infusion the chest wall pain disappeared and the patient was able to stop NSAID treatment. Swelling and tenderness on the left clavicle remitted and the CRP returned to normal. Severe acne dramatically improved in one week. Chest wall pain, swelling and tenderness, and acne reappeared two months after the third infusion when we decided to proceed with a fourth infusion. The CRP was normal. Again a complete remission of the symptoms was seen in three days. The disease has remained in remission so far, two and a half months after the fourth infusion. Infliximab treatment was well tolerated, with no side effects.

Patient 2

The second patient was a 52 year old man with SAPHO syndrome affecting the sternum, the sternoclavicular joints, the clavicles, and the first two ribs. He had no family history of SAPHO syndrome or spondarthritis. Locus B HLA typing was positive for B35 and B52. His disease began at the age of 42 with palmoplantar pustolosis, which disappeared after six months. Five years later a severe chest wall pain appeared, which was treated with various NSAIDs for 10 years. In 1996 and 1997 he was given sulfasalazine, methotrexate, and cyclosporin A at different times, with no improvement. In the six months before the start of infliximab treatment the patient took 150 mg/day diclofenac, with little result.

On the day on which the first infusion was given a physical examination showed tenderness and swelling on the manubrium sterni and both sternoclavicular joints. The only aspect of laboratory evaluation worthy of note was a CRP of 24 mg/l (normal <5). The day after the first infusion the chest wall pain disappeared and NSAIDs were discontinued. At the first visit, on day 3, a physical examination and CRP were normal. The disease remained in remission for two and a half months after the third infusion. Pain, swelling, and tenderness on the manubrium sterni and both sternoclavicular joints again disappeared in three days after the fourth infusion and have not reappeared so far, two months after the fourth infusion. No side effects of infliximab treatment were seen.

COMMENT

Our study suggests that infliximab is an effective drug in SAPHO syndrome. A larger, controlled, double blind study is required, which should also establish whether improvement of bone scan or magnetic resonance imaging parallels the clinical remission.

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Muscle involvement in childhood sarcoidosis and need for muscle biopsy

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Sarcoidosis is a multisystem disorder with protean manifestations in childhood.[1] We report on a child with prominent muscular symptoms at presentation. Muscle involvement in childhood sarcoidosis has been described in only two previous reports to our knowledge.[2 3] We believe that muscle biopsy has a valuable role in aiding the diagnosis of childhood sarcoidosis even in children with no clinical symptoms of muscle involvement.

CASE REPORT

A 10.5 year old girl presented with a nine weeks' history of fever, red eyes, loss of appetite, malaise, florid widespread rash, weakness, and lymphadenopathy. She attended a district general hospital and was diagnosed to have a mycoplasma chest infection and treated with antibiotics. She failed to respond despite three courses of erythromycin and had persistent conjunctivitis, florid rash over her trunk, erythema nodosum over her legs, and weight loss and was therefore referred to our tertiary rheumatology unit.

On review, she was pale, miserable, tired with muscle wasting, weakness, and lymphadenopathy. A complete investigation was carried out and haematological tests showed haemoglobin 102 g/l (normal 114–140 g/l) and white cell count 10.2 (normal 4–11). Her biochemical profile was normal and liver functions showed alanine aminotransferase 263 IU/l (normal 0–45 IU/l). Her autoantibody profile was negative, and inflammatory markers like C reactive protein 190 mg/l (normal <60 mg/l) and erythrocyte sedimentation rate 92 mm/1st h (normal <5 mm/1st h) were raised. Her lactate dehydrogenase 884 IU/l (normal ≤620 IU/l), serum angiotensin converting enzyme 133 IU/l (normal 15–55 IU/l), and antistreptolysin O titre >800 (normal <200) were all raised. Her creatine kinase was normal. Her chest *x* ray examination disclosed bilateral hilar lymphadenopathy with some pulmonary interstitial changes. An echocardiogram, cranial magnetic resonance imaging (MRI), magnetic resonance angiography, dimercaptosuccinic acid (DMSA) scan, and abdominal ultrasound were normal. Her muscle biopsy showed non-caseating, non-necrotising granulomas in fibrous septa and within muscle fascicles. In areas there were granulomas surrounding muscle fibres, the latter showing degenerative features (fig 1). The epitheloid granulomas had some admixed lymphocytes and giant cells. Skin biopsy showed granulomas in debris and subcutaneous tissues. A Mantoux test, gastric washings, and urine examination for acid fast bacilli were negative and bone marrow aspiration was normal. Ocular examination showed evidence of uveitis.

A diagnosis of sarcoidosis was made based on clinical and histological features and treatment was started with high dose methylprednisolone at 30 mg/kg/dose, followed by oral prednisolone. During the course of illness, she developed a tender liver and raised transaminases suggestive of hepatic disease.

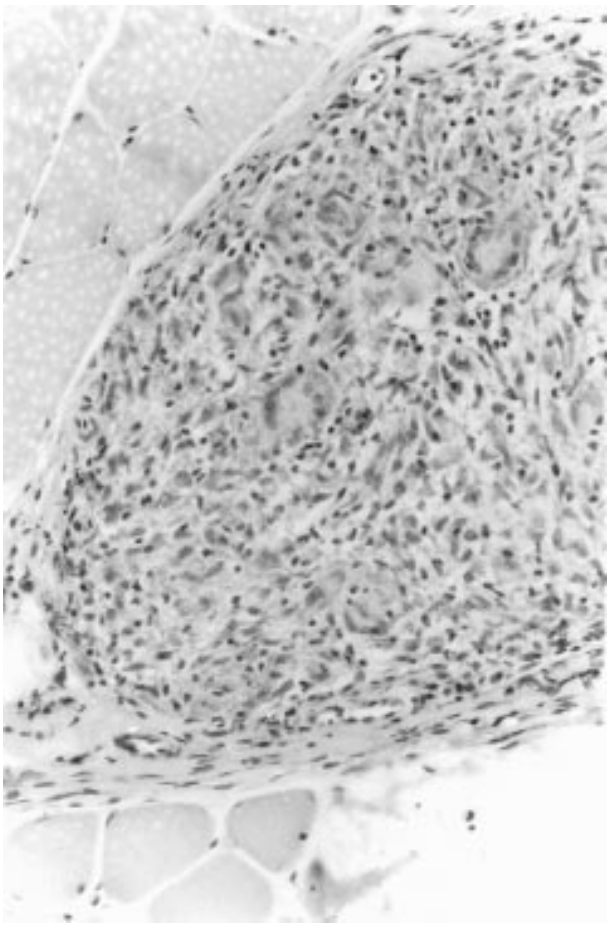

Figure 1 Muscle biopsy specimen showing well defined non-caseating granuloma. Magnification ×40, haematoxylin and eosin.

Currently she is in remission with no symptoms and has been weaned off steroids completely. No symptoms have recurred during the past three years of follow up.