

LETTERS TO THE EDITOR

Septic arthropathy complicating apatite associated destructive arthritis

Sir: We read with interest the account of septic arthropathy complicating apatite associated destructive arthritis (AADA) by Jones *et al* in this journal.¹ We report two cases affecting the shoulder, which illustrate the diagnostic difficulties that may arise between AADA and joint sepsis at first presentation.

CASE 1

A 79 year old man was seen in the rheumatology outpatients department with a six week history of pain and swelling in his right shoulder, which had deteriorated acutely after a fall two weeks previously. He had a past history of ischaemic heart disease and was taking ibuprofen, digoxin, and frusemide. On examination a large fluctuant swelling of the shoulder extending posteriorly over the right deltoid and scapula was seen. The shoulder was cool but swollen and tender with limited movement. An x ray examination of the joint initially seemed to support the clinical diagnosis of Milwaukee shoulder with areas of abnormal lucency and sclerosis in the humeral head. Attempted aspiration of the joint was unsuccessful but a sample from the scapular swelling contained frank pus. On microscopy numerous pus cells and Gram positive cocci were seen. Culture yielded a pure growth of *Staphylococcus aureus*.

He was treated with intravenous flucloxacillin 1 g four times a day and gentamicin 80 mg twice a day. Despite these antibiotics the collection reaccumulated and was aspirated twice more. After two weeks' treatment blood cultures were positive with the same organism. At this time he was noted to have a murmur consistent with mitral regurgitation, and an echocardiogram showed aortic stenosis and thickening of the mitral valve but no definite vegetations. A presumptive diagnosis of endocarditis was made and he was treated for a further four weeks with flucloxacillin 1 g four times a day and gentamicin according to serum concentrations, intravenously. He was discharged after three months having made a good recovery.

CASE 2

A 54 year old man was admitted with severe hypertension and rapidly deteriorating renal function. A diagnosis of malignant hypertension was made and he required haemodialysis for a short period. A few days after admission he developed a swollen painful left shoulder with a large effusion. All movements were limited by pain. An x ray examination showed rarification of the head of the humerus but no other changes. A diagnosis of Milwaukee shoulder was considered. The joint was aspirated and drained. On microscopy a large number of pus cells were seen, but no organisms or crystals, and cultures were sterile. He was given intravenous flucloxacillin 1 g four times a day and benzylpenicillin 2 MU four times a day for two days until the cultures were known to be sterile.

The effusion reaccumulated and was drained twice more with similar microscopic and culture results. Three weeks later he became feverish and increased shoulder swelling with an associated leucocytosis developed. Blood cultures and further shoulder aspirates grew *Staphylococcus aureus*.

The shoulder was then surgically drained and two weeks' intravenous treatment with flucloxacillin 1 g four times a day and gentamicin 80 mg three times a day was given, followed by two weeks' oral flucloxacillin 1 g four times a day.

Ten days after stopping antibiotics he developed a painless fluctuant swelling within the left biceps muscle. Aspiration yielded pus, which grew a pure culture of *Staphylococcus aureus*. The collection was surgically drained and after a further two weeks of oral flucloxacillin 1 g four times a day he made a good recovery.

DISCUSSION

In both these patients a diagnosis of Milwaukee shoulder was considered and, interestingly, both developed 'tracking' pus from the infected joint as described in the article by Jones *et al* in relation to the hip joint. The similarity of clinical features between AADA and joint sepsis make a diagnosis of AADA complicated by sepsis even more difficult. Subtle radiographic features indicated the final diagnosis in both cases. From a practical and clinical viewpoint we suggest that antibiotic treatment for 'most likely' organisms should be started where doubt remains as to whether the final diagnosis is destructive arthropathy alone or complicated by the presence of infection, as this may be life saving. Finally, infection in joints often takes some time to resolve and formal surgical drainage may be required in addition to antibiotic treatment.

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- 1 Jones A, Henderson M J, Berman P, Doherty M. Septic arthritis complicating apatite associated destructive arthropathy. *Ann Rheum Dis* 1990; 49: 1005-7.

Degradation of human cartilage by cytokines in vitro

Sir: In a recent issue of this journal Hollander *et al* reported that the cytokines interleukin 1 and tumour necrosis factor α were unable to degrade human articular cartilage on their own (in concentrations ranging from 0.1 to 10 ng/ml).¹ They suggested that these cytokines in synovial fluid can only act on human cartilage synergistically with some other component(s) of synovial fluid.

Previously, we published data showing that interleukin 1 can induce a significant loss of glycosaminoglycans from human articular cartilage.² The cartilage we used was taken within 24 hours of necropsy from the non-weightbearing part of the humeral head of donors, aged 0-78 years. The culture system we used was, in our opinion, essentially the same as the one used by Hollander *et al*. We used Dulbecco's modified Eagle's medium instead of RPMI, 10% instead of 5% human AB serum, and we added ascorbate (150

$\mu\text{g/ml}$). We found a glycosaminoglycan loss in the presence of 0.1 ng/ml interleukin 1 of 14% or 18% (depending on the age group), $p < 0.01$ or $p < 0.05$ respectively. This was found after a culture period of eight days, however, which is considerably longer than the two days used by Hollander *et al*.¹

For tumour necrosis factor α (16 ng/ml) we have recently found that after four days of culture no significant loss of glycosaminoglycan from the cartilage occurred, but after eight days with tumour necrosis factor α we noted a loss of about 25% compared with controls cultured without this factor.³

In their recent publication in *Clinical and Experimental Immunology* Hollander *et al* confirmed that even after six days interleukin 1 and tumour necrosis factor α , alone and in combination, still had no effect on the glycosaminoglycan loss of human articular cartilage.⁴ We suggest that in view of our data six days might also be too short a culture period to demonstrate the catabolic effects of these cytokines.

With respect to the suggestion of Hollander *et al* that interleukin 1 and tumour necrosis factor α only cause cartilage glycosaminoglycan loss in synergism with some other factor, we recently showed that interleukin 1 induces the production of interleukin 6 in human articular cartilage and that interleukin 1 requires this interleukin 6 to inhibit the cartilage glycosaminoglycan synthesis.⁵ For tumour necrosis factor α , however, we found that although it induces the production of interleukin 6 in human articular cartilage, inhibition of glycosaminoglycan synthesis induced by tumour necrosis factor α is independent of the presence of interleukin 6.³

Thus in our culture system with human articular cartilage both interleukin 1 and tumour necrosis factor α are able to cause a loss of cartilage glycosaminoglycans by inhibiting glycosaminoglycan synthesis while glycosaminoglycan release remains unchanged, but the mechanisms are apparently different.

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- 1 Hollander A P, Atkins R M, Eastwood D M, Dieppe P A, Elson C J. Degradation of human cartilage by synovial fluid but not cytokines in vitro. *Ann Rheum Dis* 1991; 50: 57-8.
- 2 Niefeld J J, Wilbrink B, Den Otter W, Huber J, Huber-Bruning O. The effect of human interleukin 1 on proteoglycan metabolism in human and porcine cartilage explants. *J Rheumatol* 1990; 17: 818-26.
- 3 Wilbrink B, Niefeld J J, Den Otter W, Van Roy J L A M, Bijlsma J W J, Huber-Bruning O. Role of TNF α , in relation to IL-1 and IL-6 in the proteoglycan turnover of human articular cartilage. *Br J Rheumatol* 1991; 30: 265-71.
- 4 Hollander A P, Atkins R M, Eastwood D M, Dieppe P A, Elson C J. Human cartilage is degraded by rheumatoid arthritis synovial fluid but not by recombinant cytokines in vitro. *Clin Exp Immunol* 1991; 83: 52-7.
- 5 Niefeld J J, Wilbrink B, Helle M, *et al*. Interleukin-1-induced interleukin-6 is required for the inhibition of proteoglycan synthesis by interleukin-1 in human articular cartilage. *Arthritis Rheum* 1990; 33: 1695-701.