Staphylococcus aureus triggered reactive arthritis

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Abstract

Objectives—To report two patients who developed reactive arthritis in association with *Staphylococcus aureus* infection.

Methods—A review of the case notes of two patients.

Results—Two adult female patients have developed sterile arthritis in association with *Staph aureus* infection. The first patient has had two episodes of arthritis; the first followed olecranon bursitis, the second followed infection of a central venous catheter used for dialysis. The second patient developed sterile arthritis while being treated for pyomyositis. Both patients had a self limited arthritis and were HLA-B27 negative.

Conclusion—Reactive arthritis may rarely follow *Staph aureus* infection. HLA-B27 negativity may be associated with a self limited arthritis in these cases.

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Reactive arthritis is a sterile joint inflammation induced by infection elsewhere in the body. Many organisms may trigger the condition;^{1–3} *Staphylococcus aureus* is not usually considered one of them, though some case reports have described a sterile arthritis in association with staphylococcal infection.^{4–7} Many of the previously reported cases developed arthritis in association with toxic shock syndrome.^{4–7}

We report two patients who developed reactive arthritis in association with *Staph aureus* infection, neither of whom had toxic shock syndrome.

Case reports

PATIENT 1

A 45 year old lady was diagnosed as having end stage renal failure secondary to IgG multiple myeloma. In addition to regular haemodialysis, her treatment included monthly courses of prednisolone and melphalan. She was referred to the Rheumatology team in July 1992 because of pain and swelling in the right elbow region, of one week's duration and associated with fever and chills. Examination revealed a tender, warm cystic swelling consistent with olecranon bursitis, and both blood culture and culture of the aspirate from the olecranon bursa grew *Staph aureus*. Her haemoglobin (Hb) was 86 g/l, leucocyte count $9.4 \times 10^9/l$ with 78% neutrophils and 20% lymphocytes, and platelets $410 \times 10^9/l$.

The patient was treated with intravenous cloxacillin 1 g six hourly for two weeks and the

swelling was surgically drained under local anaesthesia. Her recovery was rapid. One week later she started to complain of right knee pain. She was afebrile and had no previous history of right knee injury. Examination revealed synovitis of her right knee and the aspirate culture was negative, while microscopy revealed no crystals. Other laboratory findings were Hb 100 g/l, leucocyte count $5.8 \times 10^9/l$ with 55% neutrophils and 40% lymphocytes. Erythrocyte sedimentation rate (ESR) was 76 mm in the first hour, platelets $314 \times 10^9/l$, blood urea 36 mol/l, creatinine 705 $\mu\text{mol/l}$, and urate 0.49 mmol/l. The corrected serum calcium concentration of 2.21 mmol/l was normal for our laboratory, but IgG was increased to 38.6 g/l (normal range 8–15 g/l).

The patient was treated with an intra-articular injection of methyl prednisolone and with sulindac and she recovered in about 10 days.

In December 1992 she developed bilateral knee synovitis. Two weeks previously she had had a *Staph aureus* infection of a subclavian catheter and her treatment included intravenous vancomycin 1 g (one dose) and intravenous gentamicin 100 mg three times weekly after dialysis, in addition to removal of the subclavian catheter. Examination revealed synovitis of the knee, more prominent on the right side. Synovial fluid aspirate from the right knee revealed a turbid fluid having a leucocyte count of $45 \times 10^9/l$, with 90% neutrophils. Culture of the fluid was sterile. Microscopy revealed no crystals. Other investigations revealed Hb 80 g/l, white blood count $5.8 \times 10^9/l$ with 70% neutrophils, and ESR 60 mm in the first hour. Rheumatoid factor (RF), antinuclear antibody (ANA), anti-DNA, anti-streptolysin O (ASO) titre and HLA-B27 were normal or negative. Radiography of the knees revealed soft tissue swelling with no erosions or joint space narrowing. Treatment with sulindac led to resolution of the synovitis over a two week period and the patient has had no recurrence.

PATIENT 2

A previously healthy 32 year old lady presented in September 1992 complaining of pain involving the right thigh and left arm, of five days duration and associated with fever and chills. She denied any history of recent trauma or receiving injections. Her temperature was 38.5°C. Local examination revealed hardening of the skin over the right thigh anteriorly and the left arm anterolaterally, with swelling and tenderness. Hb was 120 g/l, white blood count

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$19 \times 10^9/l$ with 85% neutrophils, and ESR 58 mm in the first hour. Radiography revealed no bone or joint changes, but computed tomography scan revealed diffuse swelling with oedema of the right quadriceps and left deltoid muscles. Culture of a needle aspirate from the right quadriceps yielded heavy growth of *Staph aureus*; blood culture was negative. The patient was diagnosed as having multifocal pyomyositis, and intravenous cloxacillin 8 g/day was started. On the sixth day in hospital, although her muscles started to improve she complained of bilateral knee pain and examination revealed the presence of knee synovitis with effusion. Aspiration of the left knee yielded a dark, straw coloured fluid which was sterile on culture. The leucocyte count was $34 \times 10^9/l$ with 80% neutrophils; no crystals were found on microscopy. RF, ANA, ASO titre, anti-DNA, and HLA-B27 were negative or normal. Naproxen was added to her treatment regimen and she responded well in about two weeks. On follow up two months later she was symptom-free, with no clinical evidence of muscle or joint disease.

Discussion

Reactive arthritis (ReA) refers to acute non-purulent arthritis that follows infection elsewhere in the body and the term has been used primarily to refer to arthritis that follows enteric or urogenital infections and occurs predominantly in individuals with histocompatibility antigen HLA-B27. The pathogens that trigger reactive arthritis are now believed to include *Borrelia burgdorferi*² and HIV.³

Staphylococcus aureus is not usually implicated in this condition. Staphylococcal septicaemia, while frequently associated with arthralgia, has rarely been associated with a sterile arthritis though it not infrequently results in septic arthritis. As 30% of the population are long term and 50% of the population are intermittent carriers of the organism,⁸ *Staph aureus* associated non-purulent arthritis would appear to be rare.

Arthritis in relation to *Staph aureus* infection was reported more than a decade ago as a manifestation of toxic shock syndrome.^{6,7} Arthritis seems to be very rare in this syndrome, with no mention of it in several large series.⁹⁻¹² In the reported cases the arthritis occurred at the time of septicaemia and was considered to be a manifestation of the disease, and not reactive arthritis. Foley-Nolan *et al* reported an HLA-B27 patient who developed chronic synovitis following *Staph aureus* toxic shock syndrome.⁷ The authors proposed that certain phage types of *Staph aureus* can trigger reactive arthritis in genetically susceptible individuals. This case demonstrates that occasionally the arthritis associated with toxic shock syndrome may resemble reactive arthritis.

Identifying the triggering infection in reactive arthritis is not always easy, as it is unusual for the triggering infection to persist throughout the time of onset of reactive

arthritis; cultures often become negative and an increase in antibody titre is not found.¹ Valtonen *et al*¹ found serological evidence of *Staph aureus* infection in two of 50 consecutive cases of reactive arthritis. On the basis of a high anti-teichoic acid antibody titre in those two patients, he suggested that the organism is one of the triggering agents in reactive arthritis. However, it should be stressed that positivity to anti-teichoic acid antibodies may be difficult to interpret¹³ and this limits the usefulness of anti-teichoic acid antibodies as markers of previous staphylococcal infection in the absence of blood or aspirate culture.

Our two patients had had arthritis for which no alternative explanation other than reactive arthritis was found, despite a full programme of investigations as described. The temporal relationship with *Staph aureus* infection was strong, particularly in the first patient, who developed recurrence of arthritis following a new episode of *Staph aureus* infection. The second case might have resulted from bacteraemia at the time of needle aspiration of the infected muscle, with secondary seeding in the knees. However, the facts that she had a negative synovial aspirate and blood culture, and that her arthritis improved so quickly without needing further drainage, make this unlikely.

The duration of the arthritis in our two patients was short and their disease was relatively mild. Both patients were negative for HLA-B27, which might explain the mild course of the disease. Leirisalo *et al* found that HLA-B27 may not be obligatory for the development of reactive arthritis, but it might increase the severity of the disease and its late sequelae.¹⁴ Kvien *et al* found a large proportion of patients characterised by a self limiting arthritic disease without detectable triggering agents. In contrast to the group of patients with chlamydia induced arthritis and enteropathic arthritis, no association with HLA-B27 was found.¹⁵

In conclusion, *Staphylococcus aureus* may be one of the pathogens that may rarely trigger reactive arthritis. The arthritic disease seems to be mild in HLA-B27 negative individuals.

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