Poststreptococcal reactive arthritis

Sir: We read with interest the recent paper by Arnold and Tyndall1 and support the authors’ views that poststreptococcal reactive arthritis should not be confused with rheumatic fever or endocarditis. We would, however, like to extend their description of poststreptococcal arthritis to include severe leathery and malaise, a relapsing nature, and the presence of cryoglobulins. Our second case exemplifies the prostration that may characterise this condition.

CASE 1

A 28 year old man underwent uneventful arthroscopy to investigate a previously injured left knee. A day after the operation he was febrile with severe pain in the operated knee, and examination showed the knee to be warm and tender with an effusion. Treatment with ampicillin and flucloxacillin was started, but these were replaced by naproxen when the knee aspirate proved sterile. Four days later he complained of pain in wrists, elbows, and right shoulder, all of which were swollen with joint line tenderness. A maculopapular rash was noted over buttocks and legs and his fever had recurred. Investigations showed erythrocyte sedimentation rate 59 mm/h, C reactive protein 77 mg/l (normal range (NR) <5 mg/l), anti-streptolysin O titre 1200 U/ml (NR<200 U/ml). Further questioning disclosed that two weeks before admission, as part of his general practitioner’s investigations of severe pharyngitis with fever, malaise, and arthritis/arthralgias, a throat swab had grown haemolytic streptococci. Furthermore, he gave a history of four previous hospital admissions over 10 years with similar symptoms, after which he had malaise for up to six months. Immunological investigations showed the presence of immune complexes by an anticomplementary method and a cryoglobulin was detected at a concentration of 150 mg/l (NR<50 mg/l) comprising polyclonal IgG, IgA, and C3. Serum C3 and C4 were normal, though evidence of in vivo complement activation was obtained by the finding of raised plasma C3 degradation products (C3dg). No autoantibodies were detected. He was treated with penicillin and indomethacin, which led to resolution of his joint symptoms, though his rash took a few days to fade. He was subsequently lost to follow up.

CASE 2

A 26 year old man presented with a two week history of severe sore throat. On the day before admission he developed two lesions of erythema nodosum on his right forearm and pain in his left wrist and left shoulder with tenderness and sore testicles. He had been given antibiotics with little effect and had required regular analgesics. He recounted similar illnesses 12 and 16 years previously, though testicular swelling was a new feature. He was in hospital for seven months during one of these episodes and was treated with corticosteroids for two years. He had undergone tonsillectomy at the age of 9. On examination his face was waxed, wrists were tender, and there was bilateral cervical lymphadenopathy. His left first metacarpophalangeal joint was swollen.

Clinical investigations showed a neutrophil leucocytosis of 23 x 10^9/l with an erythrocyte sedimentation rate of 33 mm/h. Renal and liver function tests were normal and blood, throat, and urine cultures were sterile. Anti-streptolysin O titre was raised at 800 U/ml (NR<200 U/ml), a standard viral screen was negative, and serum C reactive protein was 314 mg/ml.

He was treated with intravenous benzylpenicillin with little effect. Therefore, hydroxychloroquine 100 mg intravenously every day was then started with rapid improvement.

Immunological investigation after commencement of steroids showed normal concentrations of C3, C4, C3dg, IgG, IgA, and IgM, and no autoantibodies were detected. A cryoglobulin was detected measuring 100 mg/l comprising polyclonal IgG, IgA, and IgM. Treatment with prednisolone 40 mg was then started in a reducing dose schedule with prophylactic penicillin. Rapid reduction of his steroid daily dose at 30 mg led to a prompt recurrence of his symptoms. A further increase in dose with slow reduction to zero over the subsequent weeks led to a full recovery.

Discussion

Like the patients of Arnold et al., both our patients may have had post-streptococcal arthritis with significant increase of antistreptococcal antibodies and C reactive protein, but in only the first case was bacteriological evidence obtained. Both patients had been extensively investigated during previous attacks without a precise diagnosis being made. Both were distressed by their disease and, in particular, patient 2 was so prostrated by his problems that polyarthritus and related investigations were considered. The recurrent episodes are highlighted by both cases and in the second this was after a lapse of 12 years. Patient 2 presented with a variety of facets, including his dramatic trismus, which led to mouth opening being gauged in a nasogastric tube for feeding. Severe myalgia after streptococcal upper respiratory tract infection characterised by incapacitating muscle pain and tenderness affecting both proximal and distal muscles without increase of muscle enzyme has been described by Harats et al. These authors, however, tried to classify this problem in terms of 'minor streptococcal disease' within the spectrum of rheumatic fever, but we agree that it is difficult to define this type of streptococcal problem should not be confused with rheumatic fever, which is not a circulating immune complex disease. Patient 2 also had bilateral epididymo-orchitis, and we are unaware of this being associated with cryoglobulinemia. Precipitation of the cryoglobulin by the cooler temperatures within the scrotum might have been a factor in its development. Arnold and Tyndall do not mention the presence or absence of cryoglobulinemia, but this should be suspected with symptoms such as severe leathery and arthralgia/arthritis when associated with a rash which is non-pustular in nature, appears in crops or even purpuric. Cryoglobulinemia associated with streptococcal infection has been described in infective endocarditis and also after immunisation of rabbits with group B streptococci. Cryoglobulinaemia was not a feature of our patients, nor of those of Arnold and Tyndall, though evidence of complement activation, presumed cryoglobulinaemia (reaction of cryoglobulins) was reported in our first case by the increased C3dg concentration.

We agree with Arnold and Tyndall that although serological investigations are common, streptococcal infection associated with joint disease is very uncommon and unless it is considered, cases will be overlooked. They described the arthritis as 'reactive', however, in view of the presence of circulating immune complexes (cryoglobulins) in our patients this is inappropriate. Perhaps a better descriptive name for this group of conditions would be 'arthritis and poststreptococcal cryoglobulinemia'.

patients. Cryoglobulinaemia was not suspected in our patients in the absence of suggestive clinical phenomena and therefore cryoglobulins were not assayed. Further study of such patients may clarify the relevance of the finding of mixed cryoglobulinaemia to the pathogenesis of the arthropathy. The importance of serial serological testing of several streptococcal antibodies is emphasized.

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Association between gold induced skin rash and remission in patients with rheumatoid arthritis

Sir: The recent article by Drs Caspi, Tishler, and Yaron entitled ‘Association between gold induced skin rash and remission in patients with rheumatoid arthritis’ states that this observation is ‘previously undescribed’. In fact this association was described by one of us more than 30 years ago; it was published initially in abstract form in this very journal, and subsequently in more detail as part of a review article. The second author of this letter discussed the association in a recent letter to Arthritis and Rheumatism.

It is gratifying that this observation has remained valid over three decades. Our experience agrees with that of the authors: toxicity induced remissions are limited to dermatisis, and are not found with renal, pulmonary, or haematological reactions to gold. Although our earlier experience was limited to sodium aurothiglucose, as was that of the authors of the present paper, in later years we have seen the same response to sodium aurothiomalate on many occasions (unpublished).

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Serum osteocalcin concentrations in patients with rheumatoid arthritis

Sir: In the recent study of Pietschmann et al., normal osteocalcin values in patients were reported, suggesting a normal rate of bone formation in these patients.

These data disagree with other studies, in which both increased and decreased serum concentrations of osteocalcin in patients with rheumatoid arthritis were reported. It was suggested by the authors that their differences might be related to the use of remission inducing drugs.

As most of the patients were women with an average age of 53 we wonder if patients were also matched for menopausal status. It is well known that osteocalcin is influenced by age, sex, and menopausal status. I strongly believe that before definite conclusions can be drawn about serum osteocalcin and bone formation in rheumatoid arthritis we should have larger studies in which every patient ideally should be matched with a control of the same age, sex, and menopausal status.

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