Case reports and a Review of post infective arthritis

O. Elneima*, A. Pratt+, D. Ashok#
***F1, +SpR, #Consultant**
Rheumatology Department
University Hospital of North Durham
dayavathi.ashok@cddft.nhs.uk

Abstract

Post-infective inflammatory arthritis is a common problem seen in medical admissions and defined as an arthritis that follows an identifiable infection, but does not have the features of joint sepsis. In this review we report two cases of post-infective arthritis, the first a case of post streptococcal reactive arthritis (PSRA) in a 66 year old male with discussion based on the differences between PSRA and acute rheumatic fever (ARF) in adults; the second a case of post meningococcal inflammatory arthritis with discussion on the different presentations and pathogenesis of post meningococcal immune complex-mediated inflammatory arthritis.

Case 1: Report

A 66 year old male presented with a transient sore throat followed by a three week history of profound fatigue, accompanied by left wrist swelling and discomfort. The past medical history included asthma, hypothyroidism and carcinoma of the larynx treated three years previously with chemo-radiotherapy. Examination revealed a temperature of 38.6^{o}C, tachycardia and hypotension. He had a diffuse, petecheal, non-blanching rash in both lower limbs and the abdomen. Synovitis of the left wrist and proximal interphalangeal joints of the hands was apparent, with moderate bilateral knee effusions.

Blood results revealed a prominent acute phase response (CRP on admission 391), acute renal failure in keeping with clinical dehydration, and a normal complement C3 level but reduced C4 (remaining immunology negative). Left wrist aspirate was negative for gram stain and culture, but a group A β-haemolytic *Streptococcus* was cultured from the peripheral blood. Radiographs showed early degenerative change and no bony destruction. Anti-Streptolysin O (ASO) serum titre was 400 (normal 160-200) and a throat swab was negative. He was started on intravenous co-amoxiclav and clarithromycin, which was later changed to flucloxacillin. He had no peripheral stigmata of infective endocarditis and trans-thoracic and trans-oesophageal echocardiograms showed no evidence of vegetations. CT scan of the chest, abdomen and pelvis failed to identify an occult infective source.

The patient made steady progress with an improvement in his joint symptoms and was discharged with a further rheumatology follow-up in six weeks, after which he required a short course of steroids for controlling his inflammatory joint symptoms.

Case 1: Discussion: Acute Rheumatic Fever and "Post-Streptococcal Reactive Arthritis"

Streptococci are Gram-positive bacteria classified according to the haemolysis pattern they produce on blood agar, with complete lysis of red blood cells around colonies being a feature of the "β haemolytic" variety. A causative link between ARF and antecedent group A streptococcal infection of the pharynx is provided by compelling epidemiological evidence. Whilst disease pathogenesis is incompletely understood, being influenced by both host and pathogen factors, a type II hypersensitivity reaction is thought to be responsible, whereby host antibodies raised against antigenic epitopes cross-react with host elements – for example the heart – causing autoimmune inflammation and tissue damage.

With a peak incidence in childhood, the most common feature in ARF is a painful migratory arthritis, which is present in approximately 80% of patients. Large joints such as knees, ankles, elbows, or shoulders are typically affected, but monoarthritis at presentation is described in up to

25% of patients. Carditis may be the presenting feature and is the most lethal manifestation. Sydenham's chorea was once a common late-onset clinical manifestation but is now rare. The Jones criteria provide diagnostic guidelines for clinical diagnosis and require two major or one major and two minor criteria and evidence of prior streptococcal infection (throat culture positive for the bacteria, positive rapid antigen detection test results, or elevated antistreptolysin O titre [ASOT])[1]. Major and minor criteria are outlined in Box 1.

Major criteria
Carditis—tissue inflammation or new changing murmur
Polyarthritis—migratory pain in limb joints
Chorea—abrupt, purposeless movements with or without emotional changes
Erythema marginatum—non-pruritic rash, spares face
Subcutaneous nodules—painless, firm, on bones or tendons
Minor criteria
Fever
Arthralgia
Previous acute rheumatic fever or rheumatic heart disease
Acute-phase reactants—erythrocyte sedimentation rate, C-reactive protein, leukocytosis
Electrocardiogram—prolonged PR interval
Evidence of streptococcal infection
Throat culture positive for the bacteria
Positive rapid antigen detection test results
Elevated anti-streptolysin O titre
Scarlet fever

Box 1. *Jones criteria for diagnosing acute rheumatic fever: Diagnosis requires two major, or one major and two minor criteria and evidence of streptococcal infection or chorea alone*[1].

In adults, presentations of streptococcal reactive disease are well recognised, but characteristically differ in respect of clinical features compared with those of "classical" childhood ARF – for example, a lower prevalence of carditis is seen in adults. Reflecting this, the term *post-streptococcal arthritis* (PSRA) was first coined in 1959 and described more fully in 19822,3. Joint involvement in PSRA is typically non-migratory, particularly affecting the large joints of the lower limb. As distinct from ARF, mono-, oligo- and polyarthritis are equally represented, and are less responsive to Aspirin or other NSAIDs[2,3,4]. Extra-articular manifestations, such as tenosynovitis, polytendonitis and enthesitis are often seen in these patients and may be the only manifestations[5].

In 1997, clinical and serological criteria for the diagnosis of PSRA were proposed[6]. Key features are an acute-onset, non-migratory arthritis following a protracted course, which is poorly responsive to aspirin or NSAIDs; clear evidence of antecedent streptococcal infection is required, and the presence of major Jones criteria manifestations is not required (though may sometimes be present[3]). PSRA should therefore be considered as a part of the differential diagnosis in patients with lower extremity arthritis and those with arthritis, including those not fulfilling the Jones criteria for ARF[7,8,9]. At present it is not possible to estimate the incidence of ARF or PSRA in UK in adults as it is unlikely that this explanation for a monoarthritis or polyarthritis is considered in all presenting patients even when are seen by a specialist.

Case 2: Report

A previously fit 19 year old female student presented with a one day history of headache, abdominal pain and generalized weakness. Examination revealed pyrexia (39^{o}C), scattered pale-red non-blanching purpura and signs of meningeal irritation. She was fully alert with a GCS of 15. Blood tests identified a leukocytosis

(neutrophils 17.8) and raised acute phase reactants (eg CRP 342). An urgent CT head suggested an increased intracranial pressure, and lumbar puncture was consequently deferred. Blood culture identified *Neisseria meningitides* and she was started on intravenous ceftriaxone. Five days later she complained of right leg pain followed by increasing discomfort in the left knee and right elbow. A clinical evaluation revealed a picture of asymmetrical large joints oligo-arthritis. Left knee aspiration revealed a turbid synovial fluid which was negative for gram stain and organisms. She had negative repeat blood culture at this stage. Polymerase chain reaction (PCR) from the knee aspirate subsequently identified the presence meningococcus DNA.

The clinical picture was felt to be in keeping with an "allergic meningococcal" or "Type 3 post-meningococcal" arthritis *(see discussion)*, rather than metastatic infection. After a series of discussions between the medical team and microbiologist colleagues, she was commenced on 20mg oral prednisolone. Within 48 hours a remarkable improvement in her joint symptoms was seen. She was discharged home six days later with a reducing dose of steroids and she made a full recovery after six weeks.

Case 2: Discussion: Meningococcus-associated arthritis

The association between meningococcal infection and arthritis is well known and was described as early as 1919 by Herrick and Pankhurst[10]. The articular manifestations of meningococcal infection can be divided into three types. Type 1 is characterized by trivial arthralgias masked by the symptoms of the meningitis, type 2 includes septic arthritis preceding or occurring with systemic meningitis and sensitive to the antibiotics, and type 3 is the post-meningococcal arthritis with sterile articular fluid refractory to antibiotics[11]. This latter *allergic* meningococcal arthritis is considered to be the result of a type III "immune complex-mediated" hypersensitivity reaction according to the classification of Gell and Coombs. Antigen-antibody immune complexes form, characteristically four to ten days post menigococcal infection, and are deposited in tissue, leading to complement activation and the consequent infiltration of inflammatory cells in a so-called "Arthus reaction"[12,13]. Other occasionally seen post-meningococcal sequelae such as pericarditis, myositis, cutaneous and ocular changes are thought to reflect similar pathology[14].

Typically, patients with type 3 meningococcal arthritis experience symptoms in large joints such as the knee about three days after the start of the illness while the joint effusion develops within the next 24 hours[13,14]. The symptoms and the signs generally improve within three or four days, leaving the joint slightly tender but mobile. NSAIDS usually relieve the pain but the antibiotics don't appear to affect the disease course[10]. Many studies have suggested similarities between post-meningococcal arthritis and post-gonococcal arthritis, and management principles are the same. Systemic corticosteroids are valuable where severe symptoms arise from several joints, with a short course of oral prednisolone 10-30 mg daily usually being sufficient. Disease modifying drugs such as sulphasalazine and methotrexate are indicated where disabling symptoms persist for three months or more, or evidence of erosive joint damage is present[15,16]. Risk factors for post meningococcal arthritis include severe infection, serogroup C infections, and age, with the peak incidence being amongst adolescents and adults.

Conclusions

The two cases described, which were encountered within the space of a month, highlight presentations of post-infective arthritis that do not fall readily into the "classical" definition of HLA-B27-associated reactive arthritis, but should nevertheless be recognisable to the

general physician. In acute monoarthritis, joint aspirations and culture remain vital diagnostic procedures. Treatment of established post infectious arthritis with antibiotics is probably ineffective. A prompt diagnosis of these post infectious arthritides and appropriate treatment may prevent requirement for prolonged antibiotic treatment.

The development of sophisticated techniques for bacterial detection in joint fluid samples from patients with reactive arthritis has led to reappraisal of the exciting concepts of pathogenesis.

References.

1. Guidelines for the diagnosis of rheumatic fever. Jones Criteria, 1992 update. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. JAMA. 1992 Oct 21;268(15):2069-73. [Medline]
2. Grover V, Dibner R, Polyarthritis following a streptococcal infection, a doctor's dilemma in treatment: a case report. Cases J. 2009 Dec 3; 2:9140.
3. Deighton C., Beta haemolytic streptococci and reactive arthritis in adults.Ann Rheum Dis. 1993 Jun; 52(6):475-82.
4. Aviles RJ, Ramakrishna G, Mohr DN, Michet CJ Jr. Poststreptococcal reactive arthritis in adults: a case series Mayo Clin Proc. 2000 Feb;75(2):144-7.
5. Sarakbi HA, Hammoudeh M, Kanjar I, Al-Emadi S, Mahdy S, Siam A. Poststreptococcal reactive arthritis and the association with tendonitis, tenosynovitis, and enthesitis. J Clin Rheumatol. 2010 Jan; 16(1):3-6
6. Ayoub EM, Ahmed S. Update on complications of group A streptococcal infections. Current Problems in Pediatric. 1997; 27(3):90–101.
7. Koçak G, Imamoğlu A, Tutar HE, Atalay S, Türkay S. Poststreptococcal reactive arthritis: clinical course and outcome in 15 patients. Turk J Pediatr. 2000 Apr-Jun; 42(2):101-4
8. Shulman ST, Ayoub EM. Poststreptococcal reactive arthritis. Curr Opin Rheumatol. 2002 Sep; 14(5):562-5.
9. Logan D, McKee PJ. Poststreptococcal reactive arthritis. J Am Podiatr Med Assoc. 2006 Jul-Aug; 96(4):362-6
10. Whittle HC, Abdullahi MT, Fakunle FA, Greenwood BM, Bryceson AD, Parry EH, Turk JL. Allergic complications of meningococcal disease. I. Clinical aspects.Br Med J. 1973 Jun 30;2(5869):733-7.
11. Doury P, Cristau P, Pattin S, Schwartz J, Roue R. Post-meningococcal rheumatism (apropos of 3 cases)]. Rev Rhum Mal Osteoartic. 1977 Dec; 44(12):715-20.
12. Christensen C. Meningococcal infection and arthritis. Ugeskr Laeger [Danish]1990 May 7; 152(19):1357-9.
13. Goedvolk CA, von Rosenstiel IA, Bos AP. Immune complex associated complications in the subacute phase of meningococcal disease: incidence and literature review. Arch Dis Child. 2003 Oct; 88(10):927-30.
14. Schaad UB. Arthritis in disease due to Neisseria meningitidis Rev Infect Dis. 1980 Nov-Dec;2(6):880-8.
15. United Kingdom National Guideline on the management of Sexually Acquired Reactive Arthritis 2008. The British Association for sexual health and HIV www.bashh.org
16. Keat A, McHale J. infection and arthritis. Rheumatic Diseases Collected reports 2005(4) 15-20.