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CASE REPORT

Post-streptococcal reactive arthritis: where are we now

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SUMMARY

A 35-year-old man presented with polyarthritis and constitutional symptoms, and a recent history of multiple tick bites and skin rash on trekking holiday. He did not respond to oral doxycycline and cephalexin for presumed Lyme's disease. Further investigation confirmed strongly positive streptococcal serology. There was absence of clinical or echocardiography evidence of heart involvement and immunological screening for inflammatory arthritis was negative. In the absence of other major Jones criteria for acute rheumatic fever, besides polyarthritis and the serological evidence of a recent streptococcal infection, a diagnosis of post-streptococcal reactive arthritis (PSRA) was also made. He responded well to penicillin therapy and has been started on oral penicillin prophylaxis as per available guidance. As streptococcal infections in the adult population are increasingly reported, it is a timely opportunity to revisit PSRA, and develop comprehensive treatment and antibiotic prophylaxis guidelines.

BACKGROUND

Post-streptococcal reactive arthritis (PSRA) is well described, but no diagnostic criteria have been agreed on, and there are no guidelines for management or duration of subsequent penicillin prophylaxis. The case presented here illustrates the non-specific nature of the presenting symptoms, with discussion of its management.

CASE PRESENTATION

A 35-year-old Asian man, born in the UK, developed polyarthritis for 3 weeks following a holiday in Scotland. His holiday involved mountain climbing on the mainland, and he reported multiple tick bites and a non-specific rash around the right elbow a week prior to the onset of his joint symptoms. The joint pain was associated with night sweats, malaise and fatigue and weight loss of 5 kg in 3 weeks. The rash resolved spontaneously over 2 weeks and was not witnessed by any healthcare professional. He denied a preceding infection and had no symptoms of sore throat, gastrointestinal or genitourinary infection. There was no medical history of joint pain, uveitis, psoriasis or inflammatory back pain. Family history was not significant. A presumptive diagnosis of acute Lyme syndrome was made by his general practitioner, and he was prescribed 3 weeks of twice daily oral doxycycline 100 mg and subsequently 1 week of oral cephalexin pending referral to rheumatology. There was no improvement in joint and constitutional symptoms after completion of 4 weeks of oral antibiotics.

INVESTIGATIONS

Examination in rheumatology clinic confirmed widespread active synovitis in the small joints of hands and feet, along with wrist, elbows, knees and ankles synovitis. Shoulder and hip examination confirmed tender joints with globally restricted movement. There was no skin rash, no lymphadenopathy and he was afebrile. Cardiovascular, respiratory, abdominal and neurological examination was normal. Blood investigations revealed C reactive protein (CRP) 67 mg/L (0–10), erythrocyte sedimentation rate (ESR) 42 mm/hour (0–12), rheumatoid factor (RF)-negative, anti-cyclic citrullinated peptide (CCP)-negative, antinuclear antibody-negative and human leucocyte antigen (HLA-B27)-negative, and normal serum electrolytes, liver and renal function. Despite the tick bite history, no supportive serology for Lyme disease was identified. *Borrelia burgdorferi* serology 6 and 10 weeks after start of symptoms was negative. Serology for hepatitis B and C, HIV, syphilis, Epstein-Barr virus, cytomegalovirus, parvo virus and rubella virus were negative. Throat culture was not undertaken as it was thought that in absence of pharyngitis symptoms and post 4 weeks of oral antibiotics, the diagnostic yield would be low. Serology for other atypical viral and bacterial infections was negative. Antistreptolysin O (A.S.O) titre was 800 IU/mL and anti-DNase B level was 1600 u/mL. Urine was normal. Blood cultures were negative after 48 hours. An ECG and cardiac two-dimensional echo were within normal limits.

DIFFERENTIAL DIAGNOSIS

- ▶ PSRA;
- ▶ Lyme arthritis;
- ▶ Postinfective (viral/bacterial);
- ▶ Spondyloarthropathy: seronegative arthritis (reactive, psoriatic, enteropathic, spondyloarthritis);
- ▶ Acute rheumatic fever (ARF);
- ▶ Rheumatoid arthritis.

TREATMENT

He was prescribed penicillin V 500 mg two times a day for 10 days, with a tapering course of oral prednisolone.

OUTCOME AND FOLLOW-UP

He responded well to treatment with resolution of his polyarthritis and constitutional symptoms. Cardiovascular and neurological examination remained normal. He was started on penicillin V 250 mg twice daily for prophylaxis and prednisolone was tapered over the next 4 weeks, with no



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recurrence of his joint symptoms. Repeat blood samples taken 6 weeks later showed CRP 2 and ESR 2, antistreptococcal titres 400 IU/mL (decreasing) and anti-DNAse B levels of 1600 u/mL (stable). He was asymptomatic in the 12-week follow-up, without evidence of polyarthritis or carditis.

DISCUSSION

The strongly positive streptococcal serology, despite no symptoms of pharyngitis, is indicative of group A streptococcal infection and in this case, PSRA. Lyme arthritis was considered as differential with history of tick bite but negative serologies 6 and 10 weeks after first symptoms make Lyme disease unlikely. Persistent polyarthritis for more than 6 weeks makes postinfection arthritis (viral or bacterial) unlikely. In the presence of strongly positive streptococcal serology and absence of RF and anti-CCP antibodies, rheumatoid arthritis is an unlikely diagnosis. Seronegative arthritis, such as reactive arthritis, enteropathic arthritis, peripheral spondyloarthritis and psoriatic arthritis, were also considered in the differential diagnosis, but the lack of gastrointestinal or genitourinary symptoms, no history and clinical signs of psoriasis, and no history of uveitis and inflammatory back pain went against the possibility of seronegative arthritis. Scarlet fever and invasive Group A streptococcus infections are increasingly being recognised in the UK in the past 5 years. The streptococcal infection presents most commonly in adults with a median age of 62 years (<1–105-year).¹ ARF and PSRA are two sequels of streptococcal infection with significant differences (table 1).

Post-streptococcal arthritis without cardiac involvement was first reported in 1959.² Since then, the separate entity of PSRA has been further developed to reduce overdiagnosis of patients with ARF without cardiac involvement. The term PSRA was first suggested by Goldsmith and Long in 1982.³ ARF and PSRA differ demographically. ARF shows single peak at 12 years, while PSRA shows a bimodal peak between 8–14 years and 21–37 years. Gender appears not to be of relevance in either ARF or PSRA.⁴ Ayoub *et al*⁵ have proposed diagnostic criteria for PSRA. PSRA is diagnosed in patients with polyarthritis who have a recent evidence of streptococcal infection and no other major Jones criteria. The arthritis in ARF and PSRA have different presentation. PSRA develops within 10 days of streptococcal infection; this arthritis is non-migratory and non-responsive to aspirin/non-steroidal anti-inflammatory drugs, and is usually of

a longer duration (more than 2 months). The arthritis associated with ARF is migratory, responds well to aspirin/NSAIDs and usually improves in 2–3 weeks.^{6–8} In adults, reactive arthritis secondary to recent streptococcal infection is more likely to be missed as pharyngitis is not a common initial presentation of streptococcal infection.^{6 7 9} The expressions of HLA DRB1*01 and HLA DRB1*16 alleles are increased in PSRA and ARF, respectively. HLA-B27 expression is not raised in patients with PSRA, suggesting its pathogenesis is more similar to ARF than reactive arthritis.¹⁰ Increased expression of alloantigen D8/17 on B lymphocytes has also been demonstrated giving weight to the argument that those individuals susceptible to ARF and PSRA share the same genetic susceptibility.¹¹

The risk of carditis after PSRA in children is ~8%, but remains unclear in adults. van Bommel *et al*¹² suggested no increased risk of carditis after median follow-up of 8.9 years, and advised no long-term prophylaxis. This was also reflected in a long-term follow-up case series from Mayo Clinic.¹³ There are strategies for primary and secondary prevention of carditis in ARF, but the need for chemoprophylaxis after PSRA is still debated. However the American Heart Association recommends 1 year of secondary prophylaxis with clinical monitoring for carditis.^{8 14}

Our case highlights the need of considering PSRA as one of the differentials for acute polyarthritis in adults and raises a number of unanswered questions about the management of PSRA. Most of the data of PSRA has come from paediatric follow-up studies, and adult inception cohort studies are lacking. There is no agreement about the need for and duration of penicillin prophylaxis. Giving 1–2 years of antibiotics prophylaxis to an adult without clear evidence is counterintuitive, particularly in view of increasing antibiotic resistance. As streptococcal infections in the adult population are increasingly reported, it is a timely opportunity to revisit PSRA and develop comprehensive treatment and antibiotic prophylaxis guidelines.

Learning points

- ▶ Post-streptococcal reactive arthritis (PSRA) has now emerged as a different clinical entity to acute rheumatic fever.
- ▶ PSRA should be considered as one of the differentials for acute polyarthritis in adults.
- ▶ There is no agreement about the need and duration of penicillin prophylaxis for PSRA in current literature.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Table 1 Differences between ARF and PSRA

	ARF	PSRA
Age	Single peak at 12 years	Bimodal peaks 8–14 years and 21–37 years
Genetics	Increased expression of HLA DRB1*16 alleles	Increased expression of HLA DRB1*01 alleles
Gender	No difference	No difference
Arthritis	2–3 weeks post-streptococcal infection migratory, flitting, large joints improves in 2–3 weeks, self-limiting	7–10 days post-streptococcal infection non-migratory, additive, small joints, axial, large joints median duration 2 months or more, can be recurrent
Treatment	Good response to Aspirin or NSAIDs	Moderate response to Aspirin/NSAIDs

ARF, acute rheumatic fever; HLA, human leucocyte antigen; NSAIDs, non-steroidal anti-inflammatory drugs; PSRA, post-streptococcal reactive arthritis.

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