

Post streptococcal reactive arthritis in children: varied presentations, differentiation from acute rheumatic fever and antibiotic prophylaxis

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Abstract

Post streptococcal reactive arthritis (PSRA) refers to inflammation of one or more joints soon after streptococcal throat infection without a demonstrable presence of the organisms in the joint. We present here, two children with very different forms of PSRA. While the first child had axial and appendicular joint involvement in non-migratory pattern that persisted for a long time with intermittent exacerbation without carditis and with no preceding clinically apparent throat infection, the second child presented with throat infections followed by involvement of knee joints alone in episodic and migratory patterns with disease free intervals in between, but with evidence of mild carditis. Clinical suspicion and close attention to the differentiating features from acute rheumatic fever (ARF) are necessary to arrive at the appropriate diagnosis which could at times be challenging. The need for long term follow up is emphasized as the former child was noted to evolve into enthesitis related arthritis. Presented is a review of differentiating features between ARF and PSRA and the role of antibiotic prophylaxis.

Key words- Arthritis, post infectious, Antibiotic prophylaxis, Carditis, Acute rheumatic fever, Enthesitis related arthritis, Juvenile

Background

Reactive arthritides are inflammatory arthropathies where joint and extra articular manifestations follow an extra articular infection with arthritogenic bacteria like Chlamydia, Shigella and Campylobacter [1]. With frequent human leukocyte antigen (HLA) B27 positivity, they present as lower limb, asymmetrical oligoarthritis. Group A beta hemolytic streptococcal (GAS) infection of the throat causes several immune mediated diseases like acute rheumatic fever (ARF) and post streptococcal reactive arthritis (PSRA). Although considered part of the same spectrum, they differ in presentation, immunology, therapy and prognosis, making differentiation necessary [2].

Case 1: A 15-year-old boy with no previous personal or family history of arthritis presented with bilateral knee and ankle arthritis with severe low spine pain, preventing him from standing or walking. He had high fever, chills and rigors but no antecedent respiratory or gastrointestinal infections. Investigations showed normal leucocyte count, elevated erythrocyte sedimentation rate (ESR) (120mm after one hour), positive C-reactive protein (CRP) and thrombocytosis (420000/mm³). Antistreptolysin O (ASO) titre was elevated (500IU/l) but throat swab culture was sterile. Electrocardiogram (ECG) and echocardiography (ECHO) were normal. Anti nuclear antibody (ANA) and rheumatoid factor (RF) were negative. Possibilities of ARF, PSRA and seronegative spondyloarthropathy were considered. Aspirin with

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antibiotics proved futile while naproxen for 2 weeks elicited partial response. Oral prednisolone elicited dramatic response and was tapered, with re-introduction of aspirin for 14 weeks with penicillin prophylaxis. Child then received naproxen for mild arthralgia and plantar fasciitis. A mild relapse six months later responded to steroids. He was noted to

be HLA B27 positive. Repeat ECHO scan was normal but sacro-ilitis was evident. A diagnosis of enthesitis related arthritis was made. His eye examination was normal. Naproxen was restarted and could later be stopped with resumption of good quality of life for the past 2.5 years of follow up.

Case 2: A 9 year old boy suffered sore throat, followed three days later by severe and debilitating arthritis of right and left knees sequentially without fever. He responded to antibiotics and anti inflammatory drugs given by his doctor. Two months later, he had recurrence of bilateral knee joint arthritis three days following pharyngitis with elevated CRP (29mg/dl) and ASO (600IU/l) without carditis. He was treated for acute rheumatic fever, responded and put on oral penicillin prophylaxis, compliance to which was poor. Two and five months after the first recurrence, child suffered similar manifestations, each time after 4-5 days of a sore throat. Several months after his fourth episode, he presented in an asymptomatic state to us for evaluation, when normal ESR, CRP and ASO and throat swab culture were noted. But echocardiography revealed mitral valvulitis. On retrospective review of his records, a diagnosis of post streptococcal reactive arthritis seemed more likely, with late development of carditis, unlike the acute phase carditis noted in acute rheumatic fever. Child was continued on regular penicillin prophylaxis and followed up for 2 years when he had a mild relapse but responded well and then remained healthy.

Discussion

Acute rheumatic fever is conventionally diagnosed using modified Jones criteria [3] while Gewtitz et al proposed modifications emphasizing ECHO input [4]. PSRA was suspected in those not fulfilling these criteria after streptococcal infection.

Table-1: Diagnostic criteria [5] for PSRA.

A. Characteristics of the arthritis
1. Acute-onset arthritis, symmetrical or asymmetrical, usually non-migratory, can affect any joint
2. Persistent or recurrent
3. Poorly responsive to aspirin or non steroidal anti-inflammatory drugs
B. Evidence of antecedent group A streptococcal infection
C. Does not fulfill the modified Jones criteria for the diagnosis of acute rheumatic fever

PSRA vs ARF:

Table- 2: Differentiating points between acute rheumatic fever and post streptococcal reactive arthritis.

Characteristic	Acute rheumatic fever	Post streptococcal reactive arthritis
Age	5-15 years	Bimodal: 8-14 years and 21-37 years
Latency period after streptococcal infection	2-3 weeks	7-10 days
Migratory arthritis	Yes	No
Involved joints	Usually large joints only	Large, small and axial joints
Joint involvement	Transient	Persistent or recurrent
Carditis frequency	Occurs in about 60%	Occurs in about 6%
Carditis onset	During acute phase	Several months later, if occurs
HLA B27 positivity	None	Some patients with axial involvement
Genetic markers	DRB1*01	DRB1*16
Acute phase reactants elevation	Marked	Moderate
Positive evidence of preceding streptococcal infection	30%	75%
Response to aspirin	Dramatic	Not dramatic
Erythema nodosum or erythema multiforme[6]	Sporadic occurrence	Noted more frequently

Secondary prophylaxis guidelines provided by the World Health Organization (WHO) for ARF may be followed in children who had satisfied modified Jones criteria in their acute phase with overlapping features of ARF and PSRA (case 1) or those with PSRA who develop carditis subsequently (case 2). Uncertainty exists regarding prophylaxis with American Heart Association advocating stopping it after one year in well patients without carditis in acute phase [7]. Presence of non group A streptococcal infections, as indicated by higher ratios of ASO titer to anti DNAase B titer have been associated with lesser incidence of carditis and so recommended to decide about prophylaxis but are yet to be validated[8].

Challenges in the presented cases: The first child with polyarthritis (one major manifestation), fever and elevated acute phase reactants (two minor manifestations) would qualify for the diagnosis of acute rheumatic fever. However, presence of axial skeletal involvement, non-migratory persistent arthritis, absence of carditis, normal leukocyte count and lack of dramatic response to aspirin favour the diagnosis of PSRA rather than ARF. Owing to the risk of carditis following a possible relapse, it is preferable to continue penicillin prophylaxis for 5 years as per WHO guidelines. Polytenosynovitis, tenosynovitis and enthesitis have been documented in PSRA and so were not contradictory to the initial consideration [9]. However, on follow up, owing to a chronic lingering course and enthesitis in this adolescent boy with subsequent HLA B27 positivity and sacro-ilitis, revision of diagnosis to enthesitis related arthritis was made and child treated for the same currently.

The second child whose diagnosis was delayed, developed carditis seven months after the acute episode. This has been noted to occur in about 5.8% of PSRA patients[10]. With appropriate anti-inflammatory drugs, arthralgia completely resolved in this child. On a compliant oral penicillin prophylaxis, he didn't experience a relapse for the past 1.5 years. Children who develop recurrent break through arthritis despite oral penicillin prophylaxis should be considered for intramuscular injections of benzathine penicillin, as recurrence rates are less[11], but couldn't be adopted in this child due to consent refusal. Prophylaxis in this child must be continued until 25 years of age.

Conclusion

Post streptococcal reactive arthritis presents a diagnostic challenge, especially in its differentiation from acute rheumatic fever. The most important factors that would help in deciding about the antibiotic prophylaxis would be the presence or absence of co-existent carditis and fulfillment of modified Jones criteria in the acute phase of illness. In those with carditis and in those who have features overlapping with ARF, it is preferable to follow the WHO guidelines for antibiotic prophylaxis for ARF patients until convincing data on this aspect are available. Long term follow up is essential to monitor evolving pattern of joint diseases.

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Abbreviations

PSRA: Post streptococcal reactive arthritis, **ARF:** Acute rheumatic fever, **HLA:** Human leucocyte antigen, **GAS:** Group A beta hemolytic streptococcus, **ESR:** Erythrocyte sedimentation rate, **CRP:** C reactive protein, **ASO:** Anti streptolysin O, **ECG:** Electrocardiogram, **ECHO:** Echo-cardiography, **ANA:** Anti nuclear antibody, **RF:** Rheumatoid factor, **WHO:** World health organization, **DNAase:** Deoxyribonuclease

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