

Original Article

Post-streptococcal Reactive Arthritis (PSRA): Clinical Features and Risk of Carditis

Adel Mohammed al-Wahadneh¹, Imad Abed-al-hameed Khriesat²¹Department of Pediatrics, King Hussein Medical Center, Royal Medical Services, Amman, Jordan²Department of Pediatric Cardiology, King Hussein Medical Center, Royal Medical Services, Amman, Jordan

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ABSTRACT

Background: Post-streptococcal reactive arthritis (PSRA) is a poorly understood clinical syndrome in which oligo- or polyarthritis occurs following a group A streptococcal pharyngitis. There is lack of universally accepted guidelines for diagnosis and management of these patients. Long-term data regarding risk of carditis within this population are insufficient.

Objectives: To study the clinical features, risk of subsequent carditis and the need for prophylactic antibiotics in this population.

Patients and Methods: Forty-five patients with the diagnosis of PSRA were identified at the pediatric immunology clinic in King Hussein Medical Center, Jordan between January 1999 and April 2003. They all had evidence of preceding streptococcal infection and joint disease at initial presentation. However, none fulfilled the updated revised Jones criteria for diagnosis of acute rheumatic fever (ARF). Common viral causes of reactive arthritis were excluded and all patients had cardiac evaluation at presentation. Follow up was for a minimum of two years, focusing on clinical recurrences

and the clinical and/or echocardiographic evidence of carditis.

Results: Forty patients, 21 male and 19 female, aged between six and 17 years with a mean age of 10 years were included in the follow up study. All patients had persistent arthritis lasting 2-6 weeks at presentation, which did not respond to conventional therapy with salicylates. Symmetrical polyarthritis of large joints was predominant. Small and axial joints were involved in 45% and 33% cases respectively. Cardiac evaluation at initial presentation was normal. They all had evidence of preceding group A streptococcal infection. During follow up, four patients developed evidence of carditis with recurrence of arthritis. They were found to be non-compliant with prophylactic antimicrobials.

Conclusion: Post-streptococcal reactive arthritis may be considered a separate entity from acute rheumatic fever. However, because of the risk of subsequent carditis in certain percentage of patients, we recommend long-term antimicrobials prophylaxis as advised for patients with acute rheumatic fever.

KEY WORDS: arthritis, carditis, poststreptococcal, reactive

INTRODUCTION

Acute rheumatic fever (ARF) is a common and serious public health problem in developing countries and remains a great challenge for both developed and developing countries^[1-6]. Anxieties were renewed when outbreaks were reported in several areas around the United States^[7]. The original Jones criteria for diagnosis of ARF, first introduced in 1944, have been modified four times and updated revised criteria have been published in 1992^[4]. Arthritis that follows Group A *Beta Hemolytic Streptococcus* (GABHS) infection in patients whose illness otherwise does not meet the Jones criteria for diagnosis of ARF, were first described by Crea and Mortimer in 1959^[8]. No additional reports were published until 1982 when Goldsmith and Long described twelve patients with the same arthritis and they were the first authors who designated this syndrome as Post-

streptococcal Reactive Arthritis (PSRA)^[9]. We describe a group of children developing an illness characterized by reactive arthritis and with the evidence of recent streptococcal infection. These patients did not fulfill the updated Jones criteria for diagnosis of ARF. With the resurgence of GABHS infection, their non-suppurative sequelae, and the difficulty in differentiating between PSRA and ARF, in this report, we focus on clinical features, risk of subsequent carditis and the need for long-term antimicrobial prophylaxis.

PATIENTS AND METHODS

Forty-five children with a diagnosis of PSRA were identified at a pediatric immunology clinic at King Hussein Medical center (KHMC) between January 1999 and April 2003. Forty patients were available for follow up. They all had evidence of recent Group A beta hemolytic streptococcal

Address correspondence to:

Dr. Adel M. Al-wahadneh MD, Pediatric Immunologist, Department of Pediatrics, King Hussein Medical Center, Royal Medical Services, P.O.Box: Amman (11115) P.O.Box (150 719) Jordan. Tel: 00 962 6 5815 161, Fax: 00 962 6 565 232 6. E- Mail: awah88@hotmail.com

Table 1
Characteristics of arthritis at initial presentation

Characteristics	n (%)	Characteristics	n (%)
Total number of patients	40 (100)	Small joints	18 (45)
Flitting	0 (0)	Symmetrical involvement	34 (85)
Persistent	40 (100)	Asymmetrical involvement	6 (15)
Monoarthritis	4 (10)	Axial skeleton	13 (33)
Oligoarthritis (<5)	30 (75)	Poor response to ASA	40 (100)
Polyarthritis (>4)	7 (15)	Favorable-NSAID response	40 (100)
Large joints	40 (100)	Erosions	0 (0)

ASA: Acetylsalicylic acid, NSAID: nonsteroidal anti-inflammatory drug

(GABHS) infection and joint disease at initial presentation. However, none fulfilled the modified Jones criteria for ARF. Laboratory investigations including antistreptolysin-O titer (ASOT), erythrocyte sedimentation rate (ESR-Westergren) and C-reactive protein (CRP) were done for all patients. Latex Agglutination method was used for both ASOT and CRP assay. The cut-off point for positive interpretation was 200 IU for ASOT and 6 mg/L for CRP. ESR above 20 mm/hr (Westergren) was considered abnormal. All patients were examined initially in consultation with a pediatric cardiologist. We re-evaluated patients three-monthly during the first year, then six-monthly for a minimum of two years. At each visit, we recorded any recurrence of arthritis or arthralgia. Echocardiogram was done in all patients to rule out carditis. Diagnosis of primary episode of carditis was based on the presence of significant apical systolic and basal diastolic murmurs, pericarditis and /or unexplained congestive heart failure. Silent carditis was diagnosed in the presence of echocardiographic evidence of valvular involvement when a clinically detectable carditis was absent. All patients with previously diagnosed ARF or arthritis were excluded. Serological viral studies including Epstein Barr Virus (EBV), Cytomegalovirus (CMV), Rubella and hepatitis (B, C, A) were done in all patients. All patients were started on monthly long-acting Benzathine penicillin with at least one week of Acetylsalicylic acid (ASA). We used naproxen when response to ASA was not satisfactory.

RESULTS

Forty patients were included in the study, aged six to 17 years with mean age of ten years. Twenty-one were male and 19 female, with a male to female ratio of 1 : 0.9. All patients had persistent arthritis for 2-6 weeks at initial presentation. The characteristics of their arthritis are shown in Table 1. We found that arthritis responded less promptly to acetyl salicylic acid (ASA) than other NSAIDs like naproxen. No patient had carditis, erythema marginatum, chorea or subcutaneous nodules.

Table 2
Results of laboratory investigations at initial presentation

Laboratory test	n (%)	Laboratory test	n (%)
Leukocytosis	36 (90)	ANA(>1:80)	0 (0)
ASOT (>200)	40 (100)	EBV-VCA-IgM	0 (0)
ESR (>20)	40 (100)	Rubella-IgM	0 (0)
CRP(>6)	40 (100)	Abnormal total Ig	0 (0)
Abnormal CXR	0 (0)	Abnormal SIJ-XR	0 (0)
Abnormal Echocardiogram	0 (0)	Positive throat culture for GABHS	2 (6)*
HLA-B27	2 (5)	Positive culture joint aspiration	0 (0)

* 30 patient only had throat swab culture

ASOT: antistreptolysin-O antibody titer, ESR: erythrocyte sedimentation rate, CXR: chest X-ray, HLA: human leukocyte antigen, ANA: antinuclear antibody, EBV: Epstein Barr virus, VCA: viral capsid antigen, IgM: immunoglobulin, SIJ-XR: sacroiliac joint X-ray, GABHS: group A beta hemolytic streptococcus

Fever (38.5 °C - 40.0 °C orally) was observed in 38 (95%) patients. All patients gave a history of acute pharyngitis at least two weeks before presentation. Family history of ARF was positive in 13 (32%) patients. Results of laboratory investigations at initial presentation are shown in Table 2. Notably, all patients had ASOT values ranging between 400-1600 IU, (mean 520 ± 20.5), CRP 24-96 mg/L (mean 39 ± 30.5) and ESR 55-120 mm/hr (mean 50 ± 43.8). The four patients with monoarthritis who had their joints aspirated for possibility of septic arthritis failed to grow any bacterial organism. Over two years of follow-up, eight patients had at least one relapse. All had arthritis, four had carditis; three with mitral regurgitation (MR) and one with both MR and aortic regurgitation (AR). None of them had cardiomegaly or heart failure. No patient had other major criteria of ARF. ASOT, ESR and CRP were elevated in all patients while none grew GABHS in their throat swabs.

DISCUSSION

The occurrence of arthritis after GABHS infection in children who did not fulfill the criteria for the diagnosis of ARF was described by Crea and Mortimer in 1959 as scarlitinal arthritis^[8,10]. Goldsmith and Long described 12 patients with arthritis and streptococcal disease^[9]. These patients had prolonged joint manifestations, poor response to aspirin and did not have ARF. The term PSRA describes a reactive arthritis preceded by pharyngeal streptococcal infection 1-2 weeks earlier^[11]. In 1997, Ayoub and Ahmed proposed diagnostic criteria for the diagnosis of PSRA^[12]. Arthritis has no specific pattern^[11]. The response to aspirin or non-steroidal anti-inflammatory drugs (NSAID) may be poor or slower than in ARF^[11,13]. The arthritis in our patients also had no characteristic pattern (Table 1). It was predominantly non-migratory with small joint involvement seen in

Table 3

Analysis of the eight patients with recurrent attacks during the two year follow-up

Patient	1	2	3	4	5	6	7	8
Sex	M	M	M	M	M	M	M	M
Age(Year)	7	11	9	10	12	14	8	7
Carditis	+	+	+	-	+	-	-	-
Arthritis	+	+	+	+	+	-	+	+
Fever	+	+	+	+	+	+	+	+
Pharyngitis	+	+	+	+	+	+	+	+
Throat C/S	-	-	-	-	-	-	-	-
ASOT	H	H	H	H	H	H	H	H
ESR/CRP	H	H	H	H	H	H	H	H
ANA	-	-	-	-	-	-	-	-
FHx	+	+	-	+	-	-	+	-

M: male, H: high, +: present, -: absent

45% and axial skeleton involved in 33% cases. This was consistent with another report where the axial skeleton was involved in 24% patients^[14]. Patients in our series with axial skeleton involvement presented with pain at the dorso-lumbar junction or lumbar spine and limitation of lumbar spine motion and were found to have normal radiograph of the sacroiliac joints (Table 2). Although not diagnostic for sacroilitis, the clinical history was suggestive of involvement of the axial spine and/or sacroiliac joints. They responded poorly to ASA and continued to have arthritis and/or arthralgia for more than two weeks on aspirin treatment, and this was concordant with other reports^[11,14,15]. Based on its designation, GABHS infection is the inciting cause for this form of arthritis and evidence for such an infection should be documented in all patients^[16]. In contrast to ARF, where throat cultures or rapid antigen detection tests are positive in only one third of patients, they are positive in 75% patients with PSRA^[14,16]. This difference can be attributed to the shorter latency period (<10 days) in PSRA^[14,16]. All our patients had history of pharyngitis or upper respiratory tract infection, but GABHS was isolated in only two patients out of 30 on whom throat swab culture was done. This low frequency was discordant with higher frequency reported by others^[11,14]. Effective antimicrobial therapy or spontaneous clearance can explain this low frequency of positive throat cultures^[16]. However serological evidence of antecedent GABHS infection obtained by ASO test were present in all of our patients. The few available reports show that the leukocyte count in PSRA is normal in the majority of patients. However the ESR is elevated in 75% cases^[14,16]. Somewhat surprisingly we found high leukocyte count in our series. The disease course over two years of follow-up excluded other possible diseases manifesting

Table 4

The incidence of pharyngitis in the children in different countries

Country	Pharyngitis No. of patients	GABHS pharyngitis %	Year
Egypt	156	19	1973
Kuwait	465	22	1984
Kuwait	4109	24	1992
USA	5500	23	1974
India	284	14	1961

Adapted from reference 17

with leukocytosis like Still's disease. We reported reasonably larger number of patients with PSRA than other researchers in the developed countries, which may be due to higher incidence of GABHS among our population compared with that in the developed world (Table 4). This can also be partially explained by the fact that King Hussein Medical Center in Jordan is a national referral center serving about 800,000 children. None of our patients had evidence of carditis at initial presentation, but over two years follow up, three of them developed clinical and one developed silent carditis. Of note, all patients with carditis were male and aged less than 11 years. Family history of ARF and/or rheumatic carditis was positive in two patients with carditis. All eight patients who had relapsed were non-compliant with antimicrobial prophylaxis. Majeed *et al* reported that 8% of patients with acute rheumatic fever without carditis in the first episode developed carditis during the second attack^[14]. Apparently the risk of carditis in PSRA during a second episode is almost similar to ARF^[17-19]. The long-term risk of carditis following PSRA has not been determined, although several reports of carditis occur with subsequent recurrences of PSRA in children^[17-19]. Silent carditis was also reported in children who were previously diagnosed with PSRA^[20]. Although our series is small to comment on risk factors of carditis it raises the need for large-scale studies focusing on risk factors of carditis in patients with PSRA^[19,20].

In conclusion, in the presence of some overlap of clinical features of PSRA and ARF, the diagnosis of PSRA should be considered in children with acute arthritis. Evidence of streptococcal infection should be sought by throat swab culture and serological testing. Long-term follow up with cardiac evaluation including echocardiogram is warranted. Further large-scale studies to delineate the risk factors for development of carditis are needed. Until these are better delineated, antimicrobial prophylaxis similar to that in rheumatic fever is recommended in patients with PSRA.

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