Poststreptococcal reactive arthritis: clinical course and outcome in 15 patients

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Patients with Group A beta-hemolytic streptococcal infection and articular disease, who do not fulfill the modified Jones criteria for diagnosis of acute rheumatic fever (ARF), have been classified as having poststreptococcal reactive arthritis (PSRA). We reviewed the clinical characteristics, laboratory findings and outcome of 15 patients with PSRA. None of these patients had clinical evidence of carditis. The pattern of joint involvement was variable and included arthritis in five patients and arthralgia in the remaining ten patients. Nine patients were treated with salicylates for one to 16 weeks; the others recovered spontaneously. Usually, the patients with arthralgia responded promptly to salicylates, while the response was poor in patients with arthritis. One patient with monoarthritis developed carditis nine months after his first arthritis attack. Another patient presenting with monoarthritis later had two additional episodes of poststreptococcal reactive arthralgia.

It seems there is a wide spectrum of poststreptococcal rheumatic diseases, and patients with PSRA are also at risk for cardiac disease; therefore, prophylatic antibiotic therapy should be considered in these patients.

Key words: poststreptococcal reactive arthritis/arthralgia, childhood.

Patients developing articular disease following group A beta-hemolytic streptococcal (GABHS) infection who do not meet the modified Jones criteria for diagnosis of acute rheumatic fever (ARF) are defined as poststreptococcal reactive arthritis (PSRA). PSRA is not a well-defined clinical entity as yet. Like ARF, patients with PSRA also have the risk of developing carditis. The objective of this study was to analyze the clinical course and laboratory features as well as the outcome of patients who had articular manifestations (arthritis or arthralgia) and evidence of streptococcal infection. It was also our aim to review the literature and to determine the risk for subsequent development of rheumatic heart disease.

Material and Methods

This is a retrospective study of 15 patients with a diagnosis of poststreptococcal reactive arthritis/arthralgia seen at the Children's Hospital of Ankara University. Between January 1995 and July 1998, 18 children were seen with a diagnosis of PSRA, but only 15 were available for follow-up; the others were excluded from the study. Eight of the patients were female; mean age was 8.8 years (range, 4 to 12 years). All had rheumatologic symptoms following a proven GABHS infection, but none of them fulfilled the modified Jones criteria for a diagnosis of ARF. None of them had a prior history of ARF or arthritis/arthralgia. Laboratory investigations were done for all patients, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antistreptolysin O titer (ASO), throat culture, and white blood cell count, and to some patients complements (C3, C4), antinuclear antibody, and rheumatoid factor. Chest roentgenogram and 12 lead electrocardiogram were performed in 11 patients and echocardiogram in four patients. Fourteen of 15 patients were outpatients; only one of them was hospitalized. Mean follow-up duration was 17 months (range 4 to 35 months).

Results

Demographic characteristics and clinical and laboratory findings of 15 patients are summarized in Table I. Throat culture and/or ASO titration (at the beginning of arthritis and 2 to 3 weeks after) revealed streptococcal infection in all patients; however, only ten of them had a previous history of sore throat. Among the ten patients with antecedent pharyngitis (one patient had scarlet fever), only three patients had received antibiotic therapy. None of these patients had clinical evidence of carditis, chorea, erythema marginatum or subcutaneous nodules. Duration between pharyngitis and joint symptoms varied from four days to 14 days (mean 8.8 days). The pattern of joint involvement was variable and included arthritis in five patients (4 monoarthritis, 1 polyarthritis) and arthralgia in the remaining 10 patients. Polyarthritis and polyarthralgia were migratory or additive in nature. Large joints, primarily the knees, were affected; ankle, wrist, and hip were the other major joints involved. Small joints of hands and only one had arthritis of the metacarpophalangeal joints. Septic arthritis was excluded by joint aspiration in one patient with monoarthritis (Case 9). Chest roentgenograms and electrocardiograms were normal in 11 children tested. Cardiac evaluation with echocardiogram was performed in four patients and found normal.

Throat culture was positive for GABHS in four of 12 children tested. Serial ASO titer was elevated in all patients (800 to 3200 Todd Unit). ESR was elevated in all patients (mean 66.5 mm/hr; range 40 to 120) and RP was positive in all children. Twelve of 15 patients had elevated white blood cell counts with relative neutrophilia. Complements (C3, C4) were in normal limits in four, and rheumatoid factor and antinuclear antibody were negative in 11 children tested. HLA B27 was negative in one child tested (Case 9).

Four patients who had positive throat culture were treated with penicillin. Nine patients were treated with salicylates for one to 16 weeks (mean 3.2 weeks); the others recovered spontaneously. Seven of the nine patients (most of them had arthralgia). recovered rapidly in a few days; however, two patients with arthritis responded slowly to aspirin, hence therapy was prolonged in these patients. The ESR remained elevated for a mean of 15.2 days, range six to 37 days. Six of 15 patients were put on penicillin prophylaxis.

One patient (Case 9) with monoarthritis developed carditis nine months after his arthritis attack. This 11-year-old boy initially presented with pain in his right hip without fever. He had pharyngitis and fever one week before arthritis, but did not receive antibiotic

Table I. Demographic, Clinical and Laboratory Findings of 15 Patients with PSRA

Patient	Sex	Age (years)	Articular involvement	Fever	Antecedent pharyngitis	Positive throat culture	ASO (TU)	ESR (mm/hr)	Theray (Aspirin)	Duration of recovery	Prophylaxis	Outcome
1	F	9	Arthralgia	–	+	+	1200	120	+	in a few days	+	–
2	F	9	Monoarthritis	+	+(Ab)	–	800	45	–	in a few days	+	–
3	M	4	Arthralgia	–	+	–	800	65	+	in a few days	–	arthralgia
4	F	7	Monoarthritis	+	–	+	800	40	+	4 weeks	–	–
5	F	6	Arthralgia	+	–	–	1600	87	–	in a few days	+	–
6	M	11	Arthralgia	–	–	ND	800	70	–	in a few days	–	–
7	F	7	Arthralgia	–	Scarlet fever	–	800	110	–	in a few days	–	–
8	M	12	Polyarthritis	–	+	–	800	46	+	5 weeks	+	–
9	M	11	Monoarthritis	–	+	–	800	110	+	in a few days	–	carditis
10	M	8	Arthralgia	–	+(Ab)	–	3200	45	+	in a few days	–	–
11	M	8	Arthralgia	–	–	+	800	58	+	in a few days	+	–
12	F	10	Arthralgia	–	–	ND	800	44	–	in a few days	–	–
13	F	10	Arthralgia	–	+(Ab)	+	800	50	+	in a few days	+	–
14	M	10	Arthralgia	–	+	ND	800	53	+	in a few days	–	–
15	F	11	Monoarthritis	–	+	–	800	55	–	in a few days	–	–

PSRA : poststreptococcal reactive arthritis.
F : female.
M : male.
(–) : absence.
(+) : presence.
Ab : received antibiotic therapy.
ND : not done.
ASO : antistreptolysin O titer.
ESR : erythrocyte sedimentation rate.

therapy. The throat culture revealed no pathogenic microorganism but ASO titer elevated in the course of time, suggesting antecedent GABHS infection. His cardiac evaluation was normal. He was initially considered as juvenile rheumatoid arthritis or PSRA and was started on therapy with aspirin (80 mg/kg/day). Arthralgia resolved rapidly but ESR remained high until the 28th day of therapy. Nine months after discharge he presented with fever and dyspnea. ASO titer was 1600 TU, ESR was 85 mm/hr, and CRP was 3 (+). Echocardiogram revealed carditis with mitral and aortic insufficiency. He was treated with prednisone and is now on penicillin prophylaxis. One year later, control echocardiogram was found normal. Another patient (Case 3) presenting with monoarthritis later had two additional episodes of poststreptococcal arthralgia. These two patients had not received prophylactic antibiotic therapy after their first attcks. The remaining 13 children had no further complications during the follow-up duration. Case 2, who also presented with monoarthritis, was the sister of Case 9, who developed carditis.

Discussion

In 1945, Rantz et al.[1] wrote that "... rheumatic fever is a part of the whole complex involved in the poststreptococcal state." Since then a lot of reports have revealed the broad spectrum of poststreptococcal rheumatic manifestations extending from ARF with or without carditis to poststreptococcal rheumatic syndrome with either arthriis or arthralgia and systemic symptoms[2-7]. It is known that poststreptococcal rheumatic symptos also include extraarticular clinical manifestations, such as vasculitis and polymyalgia[8,9].

In 1959, Crea and Mortimer[10] reported 18 cases who developed arthritis within The first 10 days after the onset of scarlet fever[10]. In the long term follow-up, a clinical presentation suggesting ARF developed in 10 of these patients. None of them had received penicilin prophylaxis. The authors concluded that "scarlatinal arthritis" is a part of the spectrum of ARF.

The term PSRA was first put forth by Goldsmith and Long[11] in a presentation to the American Rheumatism Association in 1982. They described 12 children with prolonged rheumatologic symptoms following a streptococcal infection. They reported that arthritis in their series persisted for 10 to 28 days (mean 20 days) and that most of the chidren had significant arthralgias for 25 to 150 days (mean 75 days). None of them had carditis. All patients were given aspirin but responded slowly; however, all eventually recovered completely. The authors separated this clinical entity form ARF because of unusually prolonged joint manifestations and poor response to aspirin. They suggested that this clinical progress resembled the reactive arthritis following certain enteric infections.

De Cunto[12] et al. Reviewed 12 chidren with PSRA/ arthralgia in 1988. As with the others, none of them had carditis, and none were gven prophylactic penicillin. One of these patients developed classic ARF (with mitral and aortic insufficiency) 18 months after the first arthritis attack. In addition, four of 12 children had recurrent attacks of arthritis/arthralgia. The authors pointed out the short duration between respiratory infection and joint symptoms (7-10 days) but, on the contrary, response to aspirin was good in their series. Fink[13] explained the role of the streptococcus in PSRA and said that it is a form of ARF, but differs by the early development of arthritis after pharyngitis, by the more prolonged arthritis or arthralgia and by a less dramatic response to aspirin.

We presented 15 patients with PSRA who had various clinical and laboratory findings. The period between pharyngitis and joint symptoms was shorter than that of ARF, which is compatible with the previous reports. Most had arthralgia and elevated acute phase reactants. Only one patient had migratory polyarthritis but had no other criteria for ARF. Four patients had monoarthritis which is not compatible with ARF. Fever was present in only three patients. ESR was high and ASO titers were also elevated in all the patients. Most of the patients with arthralgia responded promptly to salicylates. Only two of 15 patients in our series had a less dramatic response to aspirin, which is one of the important properties of PSRA reported previously.

There are may causes of acute arthritis in children, such as acute septic arthritis, viral arthritis, other reactive arthritis, acute onset rheumatic diseases such as juvenile chromic arthritis, and the other seronegative spondyloarthropathies. PSRA should be borne in mind in any patient presenting with acute onset

arthralgia or arthritis whether including one or more joint. Throat culture and serial serologic testing for GABHS should be performed immediately. The importance of accurate diagnosis is to provide long-term antibiotic prophylaxis to prevent recurrent attacks in RAF. Whether or not all patients with articular symptoms related to a GABHS infection should be started on penicillin prophylaxis remains an unanswered problem. Herold et al.[14] suggested that it is premature to advocate long term prophylaxis for all patients presenting with arthritis/arthralgia in association with a GABHS infection, and recommended individualized management for patients. On the other hand, previous reports have shown the risk for developing carditis in these patients in the follow-up period[12]. We also presented one patient who developed carditis nine months after his previous arthritis attack. The rate of recurrence in PSRA reported as 25-41 percent in the literature[7,12]. Only two of our nine patients who were not on penicillin prophylaxis presented with a recurrence of either arthralgia or carditis (22%). Thus, carditis developed in one (11%), whereas this was reported as eight percent in De Cunto' s series[12]. Hicks and Yim[15] reported the incidence of carditis in PSRA as 40 percent at the 1990 meeting of the American College of Rheumatology. Similarly, Kurahara[16] reported a rate of 35 percent for developing carditis in children with PSRA. In our opinion, this data justifies the use of prophylaxis.

Both ARF and PSRA occur after GABHS infection, but the precise relationship between them remains unclear. The pathogenesis of PSRA and related carditis is not well identified at present; perhaps it is an autoimmune disease such as ARF. It is also known that there is a genetic predisposition for development of ARF[17,18], and recent researches demonstrated genetic similarities in these two entities. Further research would possibly clarify the relationship between bacteria and host properties in disease expression, and the risk factors for developing carditis. Until these factors are determined, prophylactic antibiotic therapy will continue to be discussed in PSRA.

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