Poststreptococcal Reactive Arthritis and the Association With Tendonitis, Tenosynovitis, and Enthesitis

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Aim: To study the clinical presentation of poststreptococcal reactive arthritis (PSRA) and its periarticular manifestation.

Methods: This is a retrospective study. The files of all patients diagnosed with PSRA between January 2004 and November 2007 were reviewed with a predetermined checklist. Patients were included if they met our study criteria for diagnosis of PSRA.

Results: A total of 33 files were reviewed; 26 of these patients (14 female, 12 male, Arab and Asian, aged 11–41 years) met our agreed protocol for the diagnosis of PSRA. The ethnic backgrounds of the patients were as follows: 18 patients were from Arab origins and 8 patients were Asians. Twenty-one patients (80%) had asymmetric complaints, whereas 5 patients (20%) had symmetrical complaints. Two patients (7.6%) had monoarthritis, 8 patients (30.76%) had oligoarthritis, and 11 patients (42.3%) had polyarthritis. Five patients (19.23%) had only polytendonitis, tenosynovitis, and/or enthesitis. Nine patients (34.61%) had tendonitis, tenosynovitis, or enthesitis alone or with arthritis/arthralgia. The average elevation of antistreptolysin antibodies titer was 624.8 and the average sedimentation rate 44 mm/H. The response to nonsteroidal antiinflammatory drugs was generally good (84.6%), being poor in only 4 patients (15.38%) who required treatment with corticosteroids. Prophylactic penicillin was given to 15 patients (57%). No patient had carditis on presentation or follow-up.

Conclusions: It is concluded that polytendonitis, tenosynovitis, and enthesitis are common presentations in PSRA and could be the only manifestation of poststreptococcal infection.

Key Words: reactive arthritis, *streptococcus*, tendonitis, tenosynovitis, enthesitis

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The term poststreptococcal reactive arthritis (PSRA) was first described by Goldsmith and Long who reported 12 patients with arthritis after documented group A streptococcal infection but failed to meet the Jones Criteria for the diagnosis of acute rheumatic fever (ARF).[1] Subsequently, more than 20 reports have been published describing the same entity; however, some authors think that this disease is just a different presentation of ARF.[2]

Only a few reports[3–9] have described the presence of tendonitis, tenosynovitis, and enthesitis along with arthritis in patients with PSRA. Most of these reports have described only 1 or 2 of their patients having one of the above periarticular manifestations. In 1 study, 6 of 17 patients developed palmar tenosynovitis along with their arthritis.[9]

The aim of this study is to describe the clinical picture of PSRA and its periarticular manifestations.

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MATERIALS AND METHODS

A retrospective study was made of all the files of patients with the diagnosis of PSRA seen between January 2004 and November 2007. Patients were included if they met our study criteria.

1. The patient had been diagnosed by a rheumatologist to have PSRA.
2. There was documented serologic evidence of a recent group A streptococcal infection.
3. There was negative serology for rheumatoid factor (RF) and antinuclear antibodies (ANA).
4. The patient did not meet the modified Jones criteria for the diagnosis of ARF.[10]
5. No alternative diagnosis was evident by the reviewing rheumatologist.

The data collected included gender, age at diagnosis, nationality, history of sore throat, duration between sore throat and onset of joint pain, history of fever, joints involved, additive versus migratory onset of arthritis, periarticular manifestations, skin rash, any symptoms of rheumatic fever, medical history, and heart murmur, sedimentation rate, C-reactive protein, antistreptolysin antibodies titer (ASO), repeat ASO titers (the first repeat titer following the first ASO measurement), throat culture, ANA, RF, electrocardiogram, echocardiogram, and the response to any treatment.

The files were reviewed for follow-up of up to 2 year regarding the course of the disease and the development of cardiac murmur.

RESULTS

Initially, the files of 33 patients were reviewed; 7 of these were excluded because 1 patient had a normal ASO, 1 had a positive RF titer (1:128), 1 patient did not have ANA or RF checked, and 4 had an alternative diagnosis when their files were reviewed or on follow-up. Twenty-six patients were left in the study, 14 females and 12 males (1:1.16) with ages ranging from 11 to 41 years (mean, 25.4 years), but 13 (50%) were under 24 years of age; 18 were of Arab origin (69.2%), 8 were Asian (30.8%). Nine of the Arabs were Qatari, 3 Egyptian, 2 Palestinian, 2 Sudanese, 1 Yemeni, and 1 Somali. Five of the Asians were Indian, 2 Pakistani, and 1 Bengali. The socioeconomic of our patients were 9 patients had high socioeconomic status, 9 had moderate socioeconomic status, and 8 had low socioeconomic status.

About 15 patients (57.6%) had a history of a sore throat and another had a history of recurrent tonsillitis, ie, 16 patients (61%) had a history of sore throat prior to their arthritis. The onset of joint pain was 2 weeks after the sore throat in 6 patients, 10 days in 1, 6 days in 2, 3 weeks in 1, 4 weeks in 1, and 6 weeks in another (Table 1). There was insufficient information to determine the interval in the remaining 4 patients.

Throat cultures were negative in 12 patients and were not done in14 patients. About 21 patients (80%) had asymmetric joint involvement, 5 (20%) had symmetrical joint involvement. Two patients (7.6%) had mono-arthritis, 8 (30.76%) had oligoarthritis, and 11 (42.3%) had polyarthritis. Nine patients (34.6%) had a

TABLE 1. The Demographic, Laboratory, and Clinical Characteristics of Patients With PSRA

Patient	Sex	Age	Time Between Sore Throat and Joint Pain	Initial ASO	Repeat ASO	Arthritis	Arthralgia	Periarticular Manifestation
1	M	15	NA	822	189	Yes	Yes	No
2	M	14	NA	718	673	Yes	Yes	No
3	F	11	3 wks	400	195	Yes	Yes	No
4	F	38	2 wks	1210	NA	Yes	Yes	No
5	M	27	6 wks	701	489	No	No	Bilateral knee tendonitis and plantar fasciitis
6	F	16	2 wks	1640	453	No	Yes	No
7	F	40	NA	173	182	No	Yes	Plantar fasciitis
8	F	40	4 wks	200	370	Yes	No	Achilles tendonitis and trochanteric bursitis
9	M	40	NA	786	730	No	Yes	No
10	M	12	2 wks	1090	1140	Yes	Yes	No
11	F	13	NA	502	NA	No	Yes	No
12	F	40	NA	535	464	No	Yes	No
13	F	14	NA	630	NA	Yes	Yes	No
14	F	21	2 wks	444	424	Yes	Yes	No
15	M	12	NA	745	661	Yes	Yes	No
16	F	19	NA	293	335	No	Yes	Patellar tendonitis/enthesitis
17	F	41	NA	186	NA	Yes	Yes	No
18	F	31	2 wks	452	266	No	No	Bilateral ankle tenosynovitis (medial)
19	M	35	NA	2680	782	No	No	Bilateral achilles tendonitis
20	F	13	2 wks	322	309	Yes	No	No
21	F	31	NA	507	428	No	No	Polyenthesitis at bilateral elbow, bilateral wrist, left ankle, right achilles' and posterior tibialis
22	M	38	NA	301	317	Yes	Yes	Posterior tibialis
23	M	41	NA	400	585	No	No	Plantar fasciitis, myalgia
24	M	29	10 d	774	716	No	Yes	No
25	M	16	6 d	791	1230	Yes	Yes	No
26	M	23	6 d	826	NA	Yes	Yes	No

NA indicates not available; wks, weeks; d, days.

history of additive arthritis, 1 had a history of migratory arthritis (patient 15, Table 1). No data were available for the others. Five patients (19.2%) had only tendonitis, enthesitis, and tenosynovitis; and of these, 1 had bilateral Achilles' tendonitis, 1 had bilateral polyenthesitis of the both elbows (lateral epicondylitis), both wrists (extensor carpi ulnaris tendon), left ankle (tibialis posterior), and right Achilles'; 1 had bilateral knee tendonitis and plantar fasciitis; 1 had bilateral medial ankle tenosynovitis; 1 had myalgia and bilateral plantar fasciitis. Nine patients (34.61%) had tendonitis, enthesitis, and tenosynovitis alone or with arthritis or arthralgia (Table 1). The joints involved were, knees in 17 patients (65.4%), ankles in 12 (46.2%), elbows in 8 (30.8%), wrists in 7 (26.9%), shoulders in 5 (19.2%), hips in 2 (7.7%), metacarpophalangeal in 2 (7.7%), metatarsophalangeal in 1 (3.8%), and low back pain in 1 (3.8%) (Fig. 1). Four patients (15%) had a history of skin rash, 3 had skin rash at the time of the physical examination, 2 had erythema nodosum (7.6%), and 1 patient had a purpuric rash.

Two patients had history of rheumatic fever as a child; one 10 years previously, and the other one had rheumatic fever as a child and received penicillin from age of 3 till the age of 15. The father of one patient had rheumatic fever with heart valve disease. One patient had jerky movement of the trunk at age of 11. Nine patients reported history of fever but only 5 of them had fever at the first presentation.

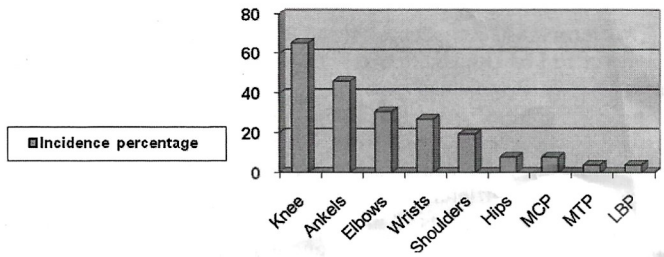

FIGURE 1. Incidence of joints involved.

In Hamad General Hospital the normal ASO titers according to age are considered to be from birth to 6 years, 0 to 99 IU/mL; from 6 to 12 years, 0 to 249 IU/mL; and from 12 to 120 years, 0 to 115 IU/mL; but in patients under review, the average ASO titer was 624.8 IU/mL (range, 173–2680). However, the ASO measurements were done at different intervals and frequencies for each case and examiner since, at that time, there was no agreed protocol.

There was a relationship between ASO titer and clinical characterization, and symptoms and relapses did correlate with increased ASO levels in 24 of 26 (92%) patients in whom ASO titer was repeated within 6 months and there was good correlation and

improvement of symptoms. The raised ASO titer fell down in 20 of the 24 patients, which coincided with improvement of symptoms, 4 of them had one or more episode of worsening of the symptoms and the ASO titer correlated to the disease activity. There was no correlation between the ASO titer and the symptoms in 2 patients. It was noted also that it took some patients up to 2 years for their ASO levels to come back to normal (patients 8 and 9 in Table 1).

The average sedimentation rate was 44 (range, 4–110) and the average C-reactive protein was 57.1 mmol/L (range, 0–322, responses to treatment with nonsteroidal antiinflammatory drugs (NSAIDs) were generally good, only 4 patients (15.4%) showing a poor response and needing treatment with corticosteroids. The NSAIDs used were naproxen (8 patients), diclofenac sodium (5 patients), meloxicam (6 patients), ibuprofen (2 patients), tenoxicam (1 patient), and diclofenac potassium (1 patient). A pregnant patient was not given any NSAIDs. Long-term penicillin injections were given to 15 patients (57%). No patient had carditis on presentation or follow-up; electrocardiogram was normal in 13 patients and was not done in the other 13. Echocardiology was performed in 15 patients. One patient had an aortic valve replacement (nonrheumatic by history diagnosed 31 years previously at the age of 11). No patient had glomerulonephritis on presentation or follow-up.

None of our patients who were included in the study had human leukocyte antigen (HLA) B27 checked, sacroiliac X ray was checked for 2 patients (patient number 7 and 22 in Table 1), and it were normal in both; however, among the patients who were excluded from the study because they did not meet our inclusion criteria, 3 of them had later in their presentation a clinical picture suggestive of spondyloarthropathies group (1 patient had sacroiliitis by magnetic resonance imaging the other one who was diagnosed later as psoriatic arthritis, had sacroiliac x-ray and HLA B27 but both were negative).

DISCUSSION

PSRA is a reactive arthritis that may affect children and adults after group A streptococcal infection of the throat. To differentiate it from ARF, some authors have proposed criteria for the diagnosis of PSRA similar to that proposed by Deighton[11] and the one proposed by Ayoub and Ahmed.[12]

Mackie and Keat[13] conducted a systematic search and reviewed 188 articles of PSRA and concluded that PSRA seems to be heterogeneous group of clinical entities, some of which share features with ARF and others with HLA B27-related spondyloarthropathies.[13] Patients may have PSRA without fulfilling the above proposed criteria.

A history of a prior sore throat was available in 61% of our patients. Jansen et al[14] found in a study of 23 patients with PSRA, 14 patients (61%) complained of a painful throat. They found also that the most commonly involved joints were knees, ankles, elbows, and the wrists. About 83% of their patients had asymmetric joint involvement similar to our findings. The duration between the sore throat and joint manifestation is usually less than 2 weeks, whereas it is about 3 weeks in ARF.[15] Most of our patients had less than a 2-week latent period although in 3 it was longer. In the review by Mackie and Keat,[13] the latent period was less than 2 weeks for most cases although a few had a longer latent period up to and beyond 35 days. Although usually 30% of patients with PSRA have positive throat culture for group A streptococcal infection, many of ours had negative cultures, possibly due to antibiotic treatment prior to culture; in such cases, sequential monitoring showing rising ASO titers is evidence of recent streptococcal infection[16] as was found in our study (Table 1).

Erythema nodosum occurred in 7% of our patients and is reported in up to 30% in some studies.[14] Vasculitis lesions have been observed also in PSRA; Gutierrez-Urena et al[5] noted 5 cases of PSRA that had biopsies showing leukocytoclastic changes. Only one patient in our study had a purpuric skin rash suggestive of leukocytoclastic vasculitis.

Monoarthritis could be the sole manifestation of PSRA and some authors consider it a differentiating aspect of PSRA since it does not occur in ARF.[14] It occurred in only 2 of our patients (7.6%). The average of monoarthritis in other studies is about 19%.[13] The arthritis in PSRA is characterized as nonmigratory, unlike that of ARF.[12,15] The nonmigratory history of the arthritis was not available in all of our patients either because it was not recorded or in 1 of our patient it was reported as migratory arthritis. A nonmigratory history of arthritis was found in about 80% of patients in articles reviewed by Mackie and Keat.[13]

Few reports have described periarticular manifestation; Young et al[3] described 1 patient with bilateral adductor enthesitis and bilateral supraspinatus tendonitis along with arthritis. De Cunto et al described 1 patient with tenosynovitis affecting the dorsum of the left foot along with arthritis.[4] Kobayashi et al described bilateral Achilles tendonitis with arthritis in 2 articles, including a patient case report.[6,7] Logan et al described a case of bilateral tenderness on palpation along the longitudinal arches of a foot.[17]

In a letter to the editor Roddy and Jones described a case of PSRA secondary to genital tract infection; the patient had peroneal tendonitis of the right ankle with arthritis.[8] Finally, 2 articles described palmar flexor tenosynovitis along with arthritis; the first described 4 patients,[5] and the second 6 patients.[9] Except the palmar flexor tendonitis/tenosynovitis cases, all the previous articles reported a limited number of patients with periarticular manifestations. None of these articles described the incidence of periarticular manifestations, namely tendonitis, enthesitis, and tenosynovitis alone without arthritis in PSRA.

In our study, 9 out 26 patients (34.6%) had tendonitis, tenosynovitis, and/or enthesitis. In 5 patients (20%), these manifestations occurred alone without concomitant arthritis. Our article is the first to describe the incidence of tendonitis, enthesitis, and tenosynovitis as the sole musculoskeletal manifestation of PSRA.

None of patients who were included in the study had HLA B27 checked and only 2 had Sacroiliac x-ray done which was normal. This was a retrospective study and patients who had positive HLA B27 would have been excluded because they fall under the category of seronegative spondyloarthropathy.

One of our patients (Patient 23, Table 1) had myalgia and with bilateral plantar fasciitis; we have found only 2 case reports of PSRA myalgia.[18,19] Harats et al[18] reported 3 patients with severe myalgia with only serological evidence of streptococcal infection and Jansen et al[19] reported 2 patients who had myalgia poststreptococcal infection with elevated ASO and positive throat culture.

One of our patients had family history of ARF, Al-Wahadneh and Khriesat,[20] found in a study of pediatric PSRA, 32% of their patients had a family history of ARF, this could represent genetic predisposition to these 2 diseases.

None of our patients had carditis on presentation and follow-up, while carditis could occur in >30% with a first attack of ARF[21] and up to 10% in pediatric PSRA.[22] The incidence of carditis in adult PSRA is extremely low,[9,13,23] so the prolonged prophylactic antibiotic treatment in an adult with PSRA is a matter of debate.[9,23] The American Heart Association currently recommends that individuals with PSRA be monitored closely for several months after the episode because of the potential for carditis. Prophylaxis is administered for up to 1 year and then is discontinued if there is no evidence of carditis.[24] Deighton recommended prophylactic therapy if a patient has a valve disease, those with a single severe extraarticular attack of PSRA, those with more than one attack of disabling reactive arthritis or enthesitis and those with a first degree relative with a history of rheumatic fever.[11] The recurrence of joint symptoms however occurred in fewer patients who received antibiotic prophylaxis.[13]

Many of our patients responded well to NSAID therapy. Although most studies indicate a poor response of PSRA to NSAIDs some articles (10, 17, and 18) reported patients with PSRA responded well to NSAIDs drug treatment. There are also reports (5, 17, and 18) of improvement after treatment with corticosteroids, which was the case in 4 of our patients.

The weakness of our study is that it was a retrospective study and some of the information was missing from some files. Additive versus migratory joint involvement history was not recorded in many files and throat culture was not done for many patients. The strength of our study is that it emphasizes the high incidence of periarticular manifestations and it is the first one to show that these manifestations could occur alone without concomitant arthritis. A prospective study is necessary to confirm our findings.

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