

Streptococcal Infections: Differences between Post-Streptococcal Reactive Arthritis and Acute Rheumatic Fever

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Abstract

Microbial infections have long been empirically known to be associated with arthritic conditions. Among them, Post-Streptococcal Reactive Arthritis (PSReA), a condition occurring following upper respiratory tract inflammation caused by streptococcal infection, has been reported to be different from Acute Rheumatic Fever (ARF), although the differences and distinctions between the two remain unclear. PSReA laboratory findings and symptoms are said to resemble those of ARF but, in case of PSReA, increases in inflammatory response and erythrocyte sedimentation rate in blood tests are often unnoticeable. Whereas ARF is rarely seen in adults and its age of onset is mainly associated with childhood, PSReA has a bimodal peak incidence, in childhood and adulthood, and the onset of arthralgia occurs earlier than in ARF. While arthritis in ARF have been essentially reported to affect only large joints, in PSReA, the pattern of joint involvement, besides large joints, includes also small joints (e.g., fingers). Moreover, one of the main differences between the two diseases is that, while in PSReA arthritis is typically "non-migratory", in ARF, arthritic symptoms are characterized by a "migratory" pattern. Although, unlike ARF, cardiac complications are not known to occur in PSReA, otorhinolaryngologists should take this condition into account when dealing with cases of streptococcal tonsillitis/pharyngitis, which are frequently encountered in routine medical practice.

Keywords: Post-streptococcal reactive arthritis; Acute rheumatic fever; Acute tonsillitis; Streptococcal infection

About the Study

Streptococcal pharyngitis and tonsillitis are frequently encountered not only in otorhinolaryngologic practice, but also in general internal medicine and pediatric care. Complications associated with streptococcal infection include Acute Rheumatic Fever (ARF) and post-streptococcal acute glomerulonephritis and, although they are not frequently encountered, many medical institutions routinely perform various diagnostic tests (e.g., pharyngeal swab culture test, rapid antigen detection test for group-A Streptococcus and urinary antigen test) to identify them. However, an additional pathological condition, aside from those mentioned above, arising after streptococcal infection is called Post-Streptococcal Reactive Arthritis (PSReA).

PSReA has been defined as inflammatory arthritis associated with a recent upper respiratory tract infection caused by streptococcal infection in a patient who does not fulfill the diagnostic criteria for ARF. While PSReA cases have been occasionally reported in internal medicine and pediatrics, few cases have been reported, to date, in the otorhinolaryngology literature. In this paper we discuss the similarities and differences between PSReA and ARF based on literature reports.

Originally defined as sterile arthritis associated with microbial infection that affects body parts other than joints [1], reactive arthritis had been previously described by Shichikawa et al. as "subacute rheumatoid arthritis"[2]. On the other hand, in 1982, by Goldsmith and Long identified a transient arthritis occurring after upper respiratory tract inflammation caused by streptococcal infection in children as "Post-Streptococcal Reactive Arthritis (PSReA)" [3]. Although PSReA has been defined as a "persistent inflammatory arthritis

occurring after a streptococcal infection in patients who do not meet the diagnostic criteria for Acute Rheumatic Fever (ARF)", the differences and distinctions between the two remain unclear [4,5].

PSReA develops within 10 days of the streptococcal infection; affects large joints such as knees, ankles, and wrists; and is characterized by poor responsiveness to NSAIDs and salicylates, and prolonged and recurrent joint manifestations [6]. Kobayashi et al., previously reported that although antibacterial and anti-inflammatory drugs were often administered in the acute stage of the disease, improvement of early symptoms was not observed in many cases and that, eventually, in some cases, tonsillectomy effectively cured the disease [7].

Characteristics of subacute rheumatoid arthritis

- i) Male/female ratio: 1:2; most common among younger adults (age: 20–30 years) Arthritis appears after the symptoms of infectious diseases, especially tonsillitis, have disappeared.
- ii) Polyarthritis persists from a few weeks to 2 years.
- iii) Oligoarthritis mostly affects knee and ankle joints; involvement of elbow and wrist joints is infrequent.
- iv) No extra-articular manifestations are observed; no cardiac involvement is observed.
- v) Waalar-Rose and RA tests are negative. ASO titer is elevated initially but becomes negative during the course of the disease.
- vi) No significant radiographic findings are observed. ASO, anti-Streptococcus Group O IgG antibody; RA, rheumatoid arthritis (Shichikawa et al. (1967) Clinical Orthopaedic Surgery 2: 19. In Japanese) (Table 1).

	PSReA	ARF
Male/female differences	No clear description	Most common among females
Age of onset	Bimodal age distribution with peaks at 8-14 years and 21-37 years	Unimodal age distribution with a single peak at approximately 12 years
Time from prior infection to onset of disease	8-14 days (mean: 10 days)	Approximately 3 weeks
Characteristics of arthritis	Non-migratory	Migratory
Affected joints	Primarily affects large joints (in order of decreasing frequency): knees, ankles, wrists, and hips. In a 10-30% case, it also affects small joints such as fingers.	Primarily affects only large joints
Response to NSAIDs	Poor compared to ARF	Relatively good
Other	Streptococcus positivity rate of pharyngeal swab culture is high	Streptococcus positivity rate of pharyngeal swab culture is low
ARF: Acute Rheumatic Fever; PSReA: Post-Streptococcal Reactive Arthritis		

Table 1: Differences between post-streptococcal reactive arthritis and acute rheumatic fever.

Generally, the immunoglobulin G neutralizing antibody titer against group A Streptococcus (ASO titer) starts to increase approximately 1-2 weeks following group A streptococcal infection, reaching a peak approximately 3-5 weeks later, and then gradually decreases returning to the pre-infection level approximately 2-3 months later. However, as a significant increase in antibody titer may not be observed in individuals on antibiotic treatment, it is important to take into account the time of infection and collect paired serum samples because a single measurement is not sufficient to determine the titer. Anti-cardiolipin antibodies and HLA-B27 antigen are detected in a large proportion of patients with PSReA [8,9]. In 2004, Mackie et al., summarized the results of an analysis of PSReA and ARF cases, the majority of which were PSReA cases, including children and adults, and described many similarities and differences between PSReA and ARF, while leaving unresolved the question on whether a strict distinction should be made between the two [10]. While ARF is most commonly seen among children aged 5-15 years but rarely among adults, age distribution in PSReA is characterized by a bimodal pattern, with a peak at ages 8-14 years and another at ages 21-37 years. In addition, the time of onset in ARF is about 3 weeks after streptococcal infection, while in PSReA is shorter, averaging approximately 10 days. The most common joints involved in PSReA are the large joints (in order of decreasing frequency): knees, ankles, wrists and hips, but in 10-30% cases involvement of small joints such as fingers is also observed. Moreover, in more than 80% of the reported cases, arthritis is "non-migratory". This is thought to be one of the major differences between PSReA and ARF, in which, arthritic symptoms are characterized by a "migratory" pattern. Although limited to pediatric cases, Tutar et al., and Sato et al., reported, in 2002 and 2017, respectively, the results of two detailed comparative studies conducted on large samples of patients with PSReA or ARF [5,11]. NSAIDs are used for the symptomatic treatment of PSReA although

the response is generally poor. While it has been reported that in some cases tonsillectomy was found to be ultimately effective in treating the symptoms of PSReA, the recurrence rate after tonsillectomy, and the criteria for determining whether tonsillectomy is the appropriate treatment in cases of PSReA, have not been reported.

Future Prospective

When examining a patient with streptococcal tonsillitis or pharyngitis, it is not difficult to recall complications such as ARF or PSAGN after streptococcal infection, but it is unlikely that PSReA will always be considered in the examination. In our department, we have experienced a case of streptococcal tonsillitis in which the patient did not meet the diagnostic criteria for ARF based on the timing of the disease, changes in blood test findings, and appearance of arthralgia and skin symptoms, and was later diagnosed as PSReA. The differences between PSReA and ARF based on the reports of Mackie et al., Tutar et al., and Sato et al., are summarized in Table 1 [5,10,11]. The "subacute rheumatoid arthritis" identified by Shichikawa et al., shares several of the characteristics found in adult patients with PSReA [2]. In conclusion, it is important to be aware that streptococcal infections in adults and children can cause PSReA in addition to ARF and post-streptococcal acute glomerulonephritis.

Authorship statement

Oyake K and Kobayashi S were involved in searching literatures reported in the past and its interpretation.

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Conflicts of interest

No conflict of interest to declare.

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