Poststreptococcal Reactive Arthritis: Diagnostic Challenges

Colleen Chun, MD; Daniel J Kingsbury, MD

E-pub: 10/18/2019  https://doi.org/10.7812/TPP/18.304

ABSTRACT

Poststreptococcal reactive arthritis (PSRA) is associated with prior group A β-hemolytic streptococcal (GABHS) infection and has a reported annual incidence of 1 to 2 cases per 100,000 persons, approximately twice that of acute rheumatic fever (ARF) in the US. Children who present with reactive arthritis are not uncommon in a busy general pediatric practice in the US, whereas children who present with ARF are very rare. Distinguishing PSRA from ARF can be challenging because the symptoms and signs are similar, but the diseases differ in long-term therapy, follow-up evaluation, and prognosis. We review the diagnostic criteria for PSRA, the pertinent features of the 2015 ARF diagnostic guideline from the American Heart Association, and the major characteristics that differentiate PSRA from ARF.

INTRODUCTION

Poststreptococcal reactive arthritis (PSRA) is associated with prior group A β-hemolytic streptococcal (GABHS) infection and has a reported annual incidence of 1 to 2 cases per 100,000 persons, approximately twice that of acute rheumatic fever (ARF) in the US. In comparison, the incidence of reactive arthritis from bacterial enteric infections is 0.6 to 3.1 cases per 100,000 persons in Minnesota and Oregon,5 5.4 cases per 100,000 children younger than 16 years in Finland,4 and 9 cases per 100,000 children in Norway.1 Children presenting with reactive arthritis are not uncommon in a busy general pediatrics practice in the US, whereas children presenting with ARF are very rare. Distinguishing PSRA from ARF can be challenging because the symptoms and signs are similar but the diseases differ in long-term therapy, follow-up evaluation, and prognosis. We review the diagnostic criteria for PSRA, the pertinent features of the 2015 ARF diagnostic guideline from the American Heart Association, and the major characteristics that differentiate PSRA from ARF.

DIAGNOSTIC GUIDELINES

Diagnostic criteria for PSRA include persistent, additive, nonmigratory acute arthritis in 1 or more joints, evidence of prior GABHS infection, and the lack of other major criteria for ARF.6 When considering the diagnosis of ARF, it is important to review the incidence-related differences in ARF diagnostic criteria published in 2015 by the American Heart Association.7 In addition to the revised Jones criteria, this update added new information about Doppler echocardiographic findings of carditis and incidence-related differences in diagnostic criteria adopted from the Australian ARF diagnostic guideline.8 The latter recommendation specifies that the Jones criteria for individuals at high risk for ARF differ somewhat from those for individuals at low risk. Individuals are considered at low risk if they live in a community with an annual ARF incidence of fewer than 2 cases per 100,000 school-aged children or an all-age rheumatic heart disease (RHD) prevalence of 1 case or fewer per 1000 persons per year. Individuals are considered at high risk for ARF if they live in a community with an annual ARF incidence of more than 30 cases per 100,000 among 5- to 14-year-olds or an all-age RHD prevalence of more than 2 per 1000 persons per year. Criteria for those at moderate risk are less well defined. For patients from communities at greater than low risk, polyarthritis and acute monarthralgia are considered major Jones criteria, and monarthralgia is a minor criterion. These criteria are in contrast to the diagnostic criteria used in the US, where the incidence of ARF is low and polyarthritis remains a minor criterion (Figure 1).

Although ARF incidence is low in the developed countries of Europe and North America, the rates of ARF and RHD in Aboriginal Australians (153–380 cases per 100,000 among 5– to 14-year-olds), Maoris, Pacific Islanders in New Zealand, and Pacific Island nations are some of the highest in the world. The prevalence of RHD is also high in the Indian subcontinent, sub-Saharan Africa, Latin America, the Middle East, and Northern Africa.8

MUSCULOSKELETAL FEATURES

Carditis has been reported in 5.8% of PSRA cases among children9 and can occur without a cardiac murmur.10 The onset of PSRA-related carditis has been reported 1 to 18 months after the arthritis appears.11 In contrast, 50% to 70% of ARF cases have carditis at initial presentation,12 and it is rare for RHD to manifest more than 1 week after arthritis onset.3

There are a few published case series with late echocardiographic follow-up studies of patients with PSRA, and fewer studies include whether patients reported cardiac symptoms of lightheadedness,

Author Affiliations
1 Pediatric Infectious Diseases, Department of Pediatrics, Northwest Permanente, Portland, OR
2 Pediatric Rheumatology, Department of Pediatrics, Randall Children’s Hospital at Legacy Emanuel, Portland, OR

Corresponding Author
Colleen Chun, MD (dscrmntg@gmail.com)

Keywords: acute rheumatic fever, poststreptococcal carditis, poststreptococcal reactive arthritis, prior group Aβ-hemolytic streptococcal infection, reactive arthritis
The 2009 Federation criteria for echocardiographic findings did not meet 2012 World Heart Federation criteria for echocardiographic diagnosis of ARF carditis. Among 40 children with PSRA in Jordan, none had diagnostic criteria for echocardiographic evidence of valvular involvement without murmur, pericarditis, or heart failure.

An unpublished case of a school-aged patient with suspected PSRA had normal echocardiography results and completed 10 days of penicillin treatment. Findings from the cardiac examination were normal at follow-up visits 12, 39, and 40 days after diagnosis. Sixty-one days after diagnosis, the patient had a new heart murmur, and results of a follow-up echocardiogram showed mild-to-moderate mitral insufficiency with leaflet thickening, mild aortic insufficiency, and mild left ventricular enlargement. The patient did not have cardiac symptoms, and acute-phase reactants were normal. Secondary prophylaxis with penicillin was restarted. Twelve months after diagnosis, the echocardiogram showed mild aortic and mitral insufficiency with complete resolution of the left ventricular enlargement.

Among 40 children with PSRA in Jordan, none had carditis at diagnosis; however, 4 patients who were nonadherent with antibiotic prophylaxis developed carditis during the first 2 years of follow-up accompanied by arthritis, elevated acute-phase reactants, and elevated antistreptolysin-O antibody titers. Three of the 4 patients had mitral insufficiency, and the fourth had mitral and aortic insufficiency. One of the 4 patients had silent carditis defined as echocardiographic evidence of valvular involvement without murmur, pericarditis, or heart failure.

Although many children with PSRA and delayed-onset carditis reportedly lacked cardiac symptoms, identifying the proportion of children with ARF and RHD without cardiac symptoms is limited by the literature. Studies of hospitalized patients with RHD tend to omit those without cardiac symptoms. Multiple studies of children in India and Africa diagnosed RHD solely on echocardiographic findings from large-scale screenings of children attending school; however, alternative explanations for the valvular abnormalities were not uniformly sought so the true sensitivity and specificity of the echocardiographic abnormalities to diagnose RHD remained unknown. Therefore, a direct comparison to the children diagnosed with PSRA who subsequently are diagnosed with carditis without cardiac symptoms is not possible.

The risk of carditis among adults diagnosed with PSRA differs from that of children. Two prospective studies from the Netherlands of adults with PSRA evaluated individuals for carditis. The 1999 study of 23 adults treated with antibiotic prophylaxis for 2 years and followed-up for 4 years did not find evidence of carditis. The 2009 study involved 75 adults who were not treated with antibiotic prophylaxis after PSRA diagnosis. After a median of 8.9 years of follow-up, 60 of the 75 individuals had follow-up echocardiographic studies, which did not reveal an increased incidence of valvular abnormalities compared with controls.

Possible explanations for the marked difference in carditis among adults include the following: 1) an age-related difference in carditis incidence among patients with PSRA, 2) the alternative diagnosis of reactive arthritis attributable to another bacteria or virus in an individual with unrelated persistently elevated levels of streptococcal antibodies, or 3) the alternative diagnosis of a different seronegative subacute-to-chronic arthritis.

**TREATMENT**

Patients with PSRA should be followed-up closely for at least 1 year with complete physical examinations. NSAID treatment should continue until the arthritis has resolved and acute-phase reactants become normal. Antibiotic treatment should be
prescribed to eradicate streptococci from the throat followed by secondary antibiotic prophylaxis. Secondary prophylaxis is recommended for 1 year for patients with PSRA with normal initial echocardiography results because of possible delayed onset of carditis. If carditis develops, the patient is typically classified as having ARF and should continue secondary antibiotic prophylaxis according to the current GABHS guideline. However, in contrast to ARF, the effectiveness of secondary prophylactic prophylaxis to prevent the occurrence or recurrence of PSRA carditis is not well studied.

CONCLUSIONS

PSRA should be part of the differential diagnosis for children and adults presenting with acute arthritis in 1 or more joints. On the basis of differences in disease presentation, clinical course, and response to NSAID therapy, PSRA and ARF appear to be separate entities. In addition, different genetic markers have been correlated with each disease: HLA-DRB1*01 with PSRA and HLA-DRB1*16 with ARF. Because the diagnosis of PSRA relies on sequential clinical findings that may not have occurred before a patient’s first office visit, there is risk of a missed diagnosis without careful follow-up.

There remain many unanswered questions about the usefulness of antibiotic prophylaxis with PSRA. The lack of carditis as a late-onset complication among adults without antibiotic prophylaxis raises the question of the effectiveness of prophylaxis in preventing late-onset carditis. Studies in children are inconclusive, and there is the additional concern about avoiding unnecessary antibiotic treatment. Until there are more prospective studies to better delineate the optimal treatment for and prognosis of PSRA, treatment recommendations will continue to resemble those for ARF. Additional studies of PSRA are needed that include follow-up echocardiograms and acute-phase reactant measurements at standardized intervals, serial screening for cardiac symptoms, and evaluation for concurrent viral causes with new-onset carditis. Such studies would help determine the optimal frequency of echocardiography surveillance for patients with PSRA.

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgments

Laura King, ELS, performed a primary copy edit.

How to Cite this Article


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