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Case Report

Differentiating post-streptococcal reactive arthritis from acute rheumatic fever: a case report and review of literature

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ABSTRACT

Differentiating between acute rheumatic fever (ARF) and post-streptococcal reactive arthritis (PSRA) is crucial because, despite their similar presentations, there are immunological and genetic differences between them, and these two illnesses require different treatment approaches. Here, we report a case of an 8-year-old male child who presented with multiple large joint swellings and with a dilemma in diagnosis and approach to management. An 8-year-old male child with no previous family history of arthritis presented with bilateral knee and ankle joint swelling for 15 days, affecting his range of movements significantly, associated with high-grade fever with no antecedent respiratory/ throat infection. Investigations showed raised inflammatory markers and elevated anti-streptolycin O (ASO) titer and anti-DNAse levels. Electrocardiogram (ECG) and 2 D echocardiography were normal. The possibilities of ARF and PSRA were considered. Antibiotics and anti-inflammatory medications were started. After a few weeks of poor response, there was an improvement with a reduction in pain and swelling. On follow up the child was normal with normal echocardiography. PSRA was diagnosed based on clinical findings and the absence of cardiac involvement. The child is still being regularly followed up with a plan to repeat echocardiography till 2 years after initial presentation to rule out ARF. Current data supports the concept that PSRA is distinct from ARF based on clinical symptoms, response to therapy, and the low incidence of cardiac involvement in PSRA. It is currently unclear if prophylactic antibiotic use is advised for PSRA patients or if carditis develops later in the course of the illness. There is a need for improved identification and diagnostic criteria for diagnosing PSRA to gain a clearer understanding of its occurrence, especially in developing countries, and to better differentiate it from ARF. There is a need for improved identification and diagnostic criteria for diagnosing PSRA to gain a clearer understanding of its occurrence, especially in developing countries, and to better differentiate it from ARF. There is also a need for randomized placebo-controlled trials to further investigate prophylaxis in PSRA, as there is presently insufficient data to support this approach.

Keywords: Post-streptococcal reactive arthritis, Acute rheumatic fever, Arthritis, Carditis

INTRODUCTION

Acute rheumatic fever (ARF) and post-streptococcal reactive arthritis (PSRA) are two clinical entities that are the result of a prior group a beta-hemolytic streptococcal (GABHS) infection. In India, the incidence and prevalence of ARF, a post-infectious, non-suppurative sequelae to pharyngeal infection, has gradually declined over the past few decades. Its incidence is now estimated to be around 50/100000 children annually in India.[1] Since PSRA was identified in the early 1980s, there has been discussion about whether it is a separate illness or a subset of ARF. The question of whether PSRA is a separate entity from ARF remains unanswered.[2] The incidence or prevalence of PSRA is unknown in India as it is particularly challenging to distinguish between PSRA and ARF because of the significant overlap in their symptoms, signs, and laboratory characteristics.[3] The clinical and laboratory findings outlined in the revised Jones criteria are used to diagnose ARF.[4] While Barash et al employed a

mathematical formula to diagnose PSRA, Ayoub et al used clinical and laboratory markers to distinguish PSRA from ARF.[5,6] Differentiating between PSRA and ARF is crucial because, despite their similar presentations, there are immunological and genetic differences between them, and these two illnesses require different treatment approaches. Here, we report a case of an 8-year-old male child who presented with multiple large joint swellings and with a dilemma in diagnosis and approach to management.

CASE REPORT

An 8-year-old male child presented with bilateral knee and ankle swelling (Figure 1), tenderness, and pain for 15 days affecting his range of movements significantly. There was also high-grade fever not associated with chills and rigors for 15 days with no antecedent respiratory/ throat infection. On examination, his vitals were normal. There was swelling of bilateral knee and ankle joints with redness and local rise in temperature. Possibilities of acute rheumatic fever, post streptococcal reactive arthritis and juvenile rheumatoid arthritis were considered. Radiography of knee and ankle were normal. Blood Investigations showed normal leukocyte count, with elevated erythrocyte sedimentation rate (ESR) (55 mm/hour), C reactive protein (CRP) (179.5 mg/dl) and thrombocytosis (650000/ul). Anti-streptolycin O (ASO) titer was elevated (781.80 IU/l), and anti-DNAse antibody (995) was raised. Throat swab culture was sent which showed no growth. Electrocardiography (ECG) and echocardiogram (2D echo) were normal. Antibiotics and non-steroidal anti-inflammatory (NSAID) medications were started. The initial response to NSAID was poor. After 2 weeks of therapy, there was a response, when the child showed significant improvement in mobility and reduction in pain and swelling. The diagnosis of post streptococcal reactive arthritis was made based on exclusion, as the patient had no migratory arthritis, and no evidence of carditis and did not meet the revised Jones criteria. Antibiotics were stopped and the child was discharged on Paracetamol with no other prophylactic antibiotics.

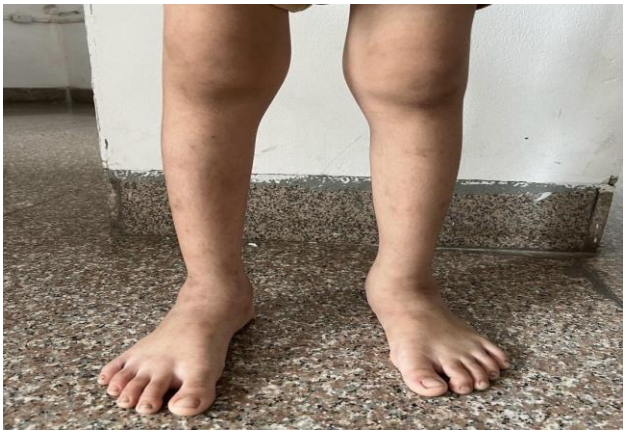

Figure 1: Bilateral knee and ankle joint swelling.

On follow up after 1 and 6 months, the child had improved further with no fever spikes and enhanced mobility with normal anti-inflammatory markers. ECG and 2D echo were also normal. The plan is to follow up the child for at least 2 years.

DISCUSSION

Our child, an eight-year-old boy, had multiple large joint involvement with additive effect, in addition to moderately elevated inflammatory markers and evidence of an antecedent GABHS infection. A moderate response to NSAIDs was observed, with no cardiac involvement. We believed that PSRA was a more likely diagnosis based on the clinical presentation and laboratory criteria available, and we managed the child accordingly.

In contrast to ARF, which typically has a single age distribution at 5 to 15 years with peak incidence around 12 years, PSRA has a bimodal age distribution with two peaks: one at 8–14 years of age and another at 27–34 years. ARF normally appears between 10 and 28 days after GABHS infection, while PSRA usually occurs 7 to 10 days after GABHS infection.[7] Our child presented on 14th day of illness with elevated ASO titer (781.80 IU/l). The relationship between class II HLA-DR antigens and PSRA and ARF has been the subject of several contradictory investigations. ARF is hypothesised to be an autoimmune reaction to GABHS infection, where host cells are attacked by HLA molecules presenting antigens that resemble both streptococcus and human tissue, called molecular mimicry. PSRA may also have a similar mechanism although not well established. ARF is believed to be an autoimmune response to GABHS infection, in which HLA molecules display antigens that resemble both streptococcus and human tissue, leading to the assault of host cells. This phenomenon is known as molecular mimicry. PSRA may also possess a comparable mechanism, although it is not yet fully understood.[8]

PSRA arthritis can affect large joints, small joints, or the axial skeleton. It tends to be persistent and additive. In ARF, arthritis is transient and migratory, typically involving the large joints. ARF arthritis has an acute presentation with severe pain and prompt response to NSAID therapy usually within 2 days and has a self-limited course. Even without treatment arthritis in ARF has a self-limiting course and resolves within 4 weeks with no long-term sequelae. PSRA arthritis lasts longer with a range of 1 week to 8 months and has mild to moderate response to NSAID therapy. In our case, only large joints were affected and the initial response to NSAID was poor. After 2 weeks of therapy, there was response with reduction in pain and swelling of large joints.

In addition, 35% of PSRA patients have been observed to have tenosynovitis. This condition can manifest as painful tendon nodules; these should not be mistaken for the subcutaneous nodules of ARF which are usually painless,

involve large joints, and are frequently associated with rheumatic heart disease (RHD).[9]

With a 50% to 70% frequency, carditis is one of the main symptoms of ARF that can affect the aortic, mitral, or both valves. Pancarditis is another unusual presentation of ARF.[4] Although a prominent characteristic of ARF is carditis, there is inconclusive information about cardiac involvement in PSRA. Carditis in PSRA patients has been documented in a small number of case reports and series, although the prevalence is low and the presentation usually occurs during the follow-up phase rather than at the initial presentation.[10] 2D echo of our patient was normal at time of presentation and during follow up also.

The Jones criteria, which were initially developed in 1944 and most recently updated in 2015, is universally accepted as the basis for the diagnosis of ARF. With a high sensitivity of 93% and a moderate specificity of 62%, the revised Jones criteria is the most accurate for diagnosing ARF; but also has its limitations due to its specificity.[11] There are currently no specific predefined criteria for PSRA. Ayoub et al attempted to establish a diagnostic criterion for PSRA, which relied on the failure to meet the modified Jones criteria for ARF.[6] This criterion was developed in 1997 and was based on the Jones criteria from 1994. More recently, Barash et al also attempted to create a mathematical formula based on ESR, CRP levels, days to the resolution of joint symptoms, and return of joint symptoms to distinguish PSRA from ARF.[2] However, these criteria were also established before the revised Jones criteria, and may not apply to the current situation. In our case, although child had large joint involvement, it was non migratory in nature. There was no cardiac involvement. On the basis of exclusion, PSRA was diagnosed.

To diagnose PSRA and ARF, it is imperative to have evidence of prior group A Streptococcus (GAS) infection. The most commonly utilized serological tests involve assessing elevated or increasing ASLO titers and anti-DNase-B titers. These titers may persist for months to years after the primary GAS infection. It is, however, noteworthy that these antibody levels are higher in school-age children compared to adults, thereby posing a diagnostic challenge. Compounding this issue is the lack of clear-cut threshold levels for these titers in the context of GAS infection.[12] In our child, there was no prior throat infection but only increased ASO titers (781), suggestive of GAS. With ongoing therapy, the titers normalised.

Anti-inflammatory medication for joint involvement, supportive therapy for carditis or other significant criteria, and antibiotic therapy based on penicillin for the eradication of GAS infection are all part of the acute treatment of ARF. Based on cardiac involvement, ARF necessitates prolonged secondary prophylaxis for a period of five to ten years or longer.[13] On the other hand, children with PSRA who get secondary prophylaxis are treated for one to two years following the beginning of symptoms, albeit the effectiveness of this treatment is questionable. A second echocardiography is performed 12 to 24 months after secondary prophylaxis is started. After a year, the presence of valvular disease indicates that the joint symptoms were caused by ARF, and this should prompt ongoing prophylaxis following ARF guidelines. If an echocardiography is performed again, and the results are normal, antibiotic prophylaxis can be stopped.[12] Our child was started on antibiotics and given for 14 days and given symptomatic treatment and was discharged on paracetamol. On follow-up, the child had improved with no fever spikes and normal ESR, CRP, and ASO titres. ECG and 2D echo were also normal.

CONCLUSION

Based on the currently available literature, we diagnosed an 8-year-old male child with PSRA and administered appropriate treatment. The child is currently under regular follow-up. Current data supports the concept that PSRA is distinct from ARF based on clinical symptoms, response to therapy, and the low incidence of cardiac involvement in PSRA. It is currently unclear if prophylactic antibiotic use is advised for PSRA patients or if carditis develops later in the course of the illness. There is a need for improved identification and diagnostic criteria for diagnosing PSRA to gain a clearer understanding of its occurrence, especially in developing countries, and to better differentiate it from ARF. There is also a need for randomized placebo-controlled trials to further investigate prophylaxis in PSRA, as there is presently insufficient data to support this approach.

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