PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**ACUTE REHEUMATIC FEVER.**" These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Acute Rheumatic Fever

Developed by Mahabba Smoka and Dr. Dax Rumsey for PedsCases.com.
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Introduction:

Hi everyone, my name is Mahabba Smoka and I am a medical student at the University of Alberta in Edmonton, Canada. This podcast aims to provide you with an approach to Acute Rheumatic Fever – or ARF for short. It was created in collaboration with Dr. Dax Rumsey, a Pediatric Rheumatologist at the University of Alberta and Stollery Children's Hospital in Edmonton, Canada. We hope you find it useful to your learning!
By the end of the ARF PedsCase, you should be able to:

1. Define ARF and identify the classification criteria thereof
2. Describe the epidemiology and etiology of ARF
3. Recognize the clinical presentation of ARF and formulate a differential diagnosis
4. Discuss pertinent investigations
5. Distinguish between primary and secondary management of patients with ARF

The Case

Let's start off with a case! You are working at a general pediatric community clinic and a 7-year-old girl presents with her father. The patient's father reports that he has noticed his daughter fidgeting constantly and making jerky movements with her arms and legs. She also has a low-grade fever and has been experiencing aches in her knees and ankles that seem to come and go. On history, you learn that the patient is a healthy girl with an unremarkable medical history, although she did complain of a sore throat about a month ago. You perform a physical exam. On inspection, you see an erythematous rash on her abdomen. On auscultation, you hear a holosystolic murmur in the area of the apex of the heart which radiates to the axilla. Based on the history and physical exam, you suspect that this patient has ARF.
How are you going to confirm her diagnosis and manage her accordingly?

Definition and Criteria for Diagnosis

ARF is a childhood inflammatory disease that can affect multiple organ systems and is triggered by a preceding infection of the tonsils and/or pharynx with Group A β-Hemolytic Streptococcus (GAS). There is a 2-3 week latency period between the initial infection with GAS and the resulting clinical picture of ARF. The diagnosis of ARF is not based on a single definitive test but on a combination of clinical and laboratory findings that satisfy the classification criteria known as the Jones Criteria. A patient is said to have ARF if there is the presence of two major manifestations or one major and two minor manifestations AND supporting evidence of an antecedent GAS infection. It should be noted that these are classification criteria, not diagnostic criteria, so clinical judgement is paramount.

1. The major manifestations of the Jones criteria can be remembered by using the mnemonic JONES = J-O-N-E-S and imagining a heart shape in place of the O!

J = migratory polyarthritis (J stands for joints!)
O = carditis (O shaped like a heart!)
N = subcutaneous nodules (N stands for Nodules!)
E = erythema marginatum (rash) (E stands for Erythema!)
S = Sydenham chorea (S stands for Sydenham!)

2. The minor manifestations of the Jones criteria include fever, arthralgia, elevated acute phase reactants (ESR/CRP), and a prolonged PR interval on ECG.

3. Supporting evidence of an antecedent GAS infection can be obtained with elevated streptococcal antibody titres (anti-streptolysin O or anti-deoxyribonuclease B) or a positive throat swab.

4. Joint (arthritis or arthralgias) and cardiac (carditis or prolonged PR interval) manifestations can only be counted once as either a major or minor criterion but not both.

Epidemiology and Etiology

As mentioned previously, ARF is predominantly a childhood disease. It typically occurs in children between the ages of 6-15 years at a 1:1 ratio between males and females. Children in developing countries have the highest incidence, while children in Western Europe and North America have seen a decline in incidence as a result of less crowding in homes/schools and increasing access to healthcare. Interestingly, a higher incidence of ARF is not just based on geographic location. Despite residing within high-income countries, communities with lower socioeconomic status, like certain First Nations communities, have a higher incidence of ARF. These communities face much of the similar issues as developing countries do (i.e. higher rates of overcrowding, poverty, and lack of medical access). ARF is most common in countries with a tropical climate and tends to have a seasonal incidence during the spring months, following the winter

peak season of GAS pharyngitis. Ethnically, ARF is more common among African American and Hispanic children than Caucasian children.
ARF is a complication of tonsillopharyngitis caused only by the GAS bacterial pathogen. It is caused by molecular mimicry. Antibodies against GAS cross-react with antigens on the organs (e.g. heart) of susceptible hosts. Only 2% of individuals with GAS pharyngitis develop ARF based on a combination of factors that include a susceptible host, a virulent strain of GAS, and the site of infection. ARF can usually be prevented with appropriate identification and treatment of tonsillopharyngitis within 10 days after onset of symptoms (i.e. sore throat).

Clinical Presentation and Differential Diagnosis

Now that we have established the criteria for the diagnosis of ARF, let's review how ARF would typically present in an outpatient setting. The onset of ARF occurs 2-3 weeks following an initial tonsillopharyngeal infection with GAS. After an asymptomatic interim period, the onset of ARF is often accompanied by minor manifestations of the disease including fever, arthralgias, elevated acute phase reactants, and a prolonged PR interval on ECG. These are non-specific and can be found in multiple other conditions. The severity and duration of the manifestations vary from one individual to another.

Arthritis is the most common of the major manifestations, occurring in 70% of patients with ARF. The arthritis primarily affects large joints, such as the knees and ankles, and is different from the arthritis in most other rheumatologic diseases in that it is migratory in nature. It often comes and goes and will involve different joints over time. The arthritis of ARF responds well to treatment with ASA or other NSAIDs.

Carditis is the next most common major manifestation and occurs in approximately half of the children with ARF. Classically, the carditis of ARF presents with concomitant arthritis and is inflammation that involves all three heart layers (i.e. pancarditis). Recent evidence points to endocarditis and valvulitis as being predominantly responsible for progression of ARF into rheumatic heart disease (RHD), a major cause of morbidity and mortality. The valves most commonly involved in RHD are the mitral and aortic valves. Mitral insufficiency is characterized by a holosystolic ejection murmur that can be best heard in the left lateral decubitus position over the apex of the heart, with radiation to the left axilla. Aortic regurgitation is a diastolic murmur that is best heard over the third left intercostal space with the patient leaning forward in end expiration. Valvular insufficiency leads to valvular stenosis from scarring during the chronic stages of rheumatic heart disease and can result in acute heart failure in 5% of children. Thus, carditis is aggressively treated with high dose aspirin for at least 4-8 weeks depending on clinical response. Other NSAIDs are not yet recommended by experts for treatment of carditis. In cases of severe carditis with congestive heart failure, oral prednisone monotherapy for 2 weeks (with tapering over the following 2-3 weeks) is the preferred treatment option. To prevent rebound of symptoms upon the withdrawal of steroids, aspirin therapy is commenced one week prior to the termination of prednisone.

Sydenham chorea is an extrapyramidal movement disorder that results from CNS inflammation of the basal ganglia and caudate nucleus. It is characterized by dance-like involuntary jerky movements involving the distal extremities, as well as the tongue and face, which are usually symmetric. While frustrating for the patient, these symptoms are usually self-limiting and spontaneously resolve in a few weeks.

Erythema marginatum is one of the cutaneous manifestations that a patient with ARF may present with to the clinic. The lesions are small in diameter and present on the trunk and inner aspects of limbs. This macular rash is characterized by an erythematous border in a snake-like or 'serpiginous' distribution. This rarely occur in patients with ARF and can be accentuated by warmth.

Subcutaneous nodules are the final major manifestation of ARF and are extremely rare. A patient with ARF may present with multiple firm, painless, small nodules over the extensor surfaces of joints, like the elbows and knees.

Other clinical manifestations of ARF may include abdominal pain, chest pain, tachycardia, and general malaise. It is always important to keep in mind a list of potential differential diagnoses. In the case of ARF, it must be distinguished from other diagnoses, specifically rheumatologic diseases that can be misdiagnosed as ARF. The arthritis in ARF can often be confused with that of systemic JIA, post-streptococcal reactive arthritis (PSRA), lupus, Kawasaki disease, serum sickness, and infectious arthritis. Some of the cardiac findings may be present in other conditions like pericarditis or bacterial endocarditis, which may present in the setting of lupus or another systemic disease. The chorea of ARF also needs to be distinguished from other neurological disorders like PANDAS or OCD. Careful evaluation of the signs and symptoms with which a patient presents, as well as their unique characteristics and response to treatment can help distinguish ARF from a number of other diagnoses.

Investigations

Laboratory findings may be mostly unremarkable. The CBC may show a normocytic anemia indicative of chronic disease or leukocytosis. Acute phase reactants (CRP and ESR) may be markedly elevated in severe disease. A positive throat culture is required to confirm a preceding infection with GAS. If this is not possible to obtain because of the latency period, a significantly elevated increase in ASO antibody titres would provide adequate evidence for an antecedent streptococcal infection. ECG findings may include a prolonged PR interval. Echocardiogram evidence of mitral or aortic regurgitation along with auscultatory findings help to make the diagnosis of valvulitis and cardiac involvement in ARF. If there is an absence of auscultatory findings, echocardiogram and Doppler studies can still be used to diagnose subclinical carditis. Neuroimaging is often normal in individuals with Sydenham chorea, but a T2-weighted MRI may indicate increased intensity in the basal ganglia in a small percentage of patients.

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Primary and Secondary Treatment

The treatment approach for ARF involves a combination of primary prevention, secondary prevention, and symptom management. Primary prevention of the acute disease involves eradication of the streptococcal disease and consists of treatment with a single dose of Penicillin G IM or a 10-day course of oral penicillin. In patients with penicillin allergies, clindamycin, azithromycin, or clarithromycin may be substituted. Secondary prevention is aimed at the prevention of recurrences of rheumatic fever. ARF often recurs within the first 5 years and so treatment duration is often indicated for at least 5 years or until the child turns 21 years old (whichever is longer) in patients with no cardiac involvement. If cardiac tissue is involved, prophylactic antimicrobial treatment is recommended for longer, sometimes for life. Treatment consists of Penicillin G IM once a month or Penicillin V orally BID. As discussed beforehand, treatment of arthritis consists of NSAIDs, that of carditis includes ASA or high dose steroids, and treatment of chorea, rashes, and nodules is often supportive care as they are self-limited in nature.

Clinical Pearls

1. ARF is a multi-system condition following tonsillopharyngeal infection by GAS.
2. ARF is more common in developing countries where there is overcrowding and decreased access to healthcare but also prevalent in lower socioeconomic status communities within high-income countries, such as certain First Nations communities.
3. ARF is typically diagnosed based on the fulfillment of the Jones criteria which includes two major manifestations, or one major and two minor manifestations with supportive evidence of an antecedent GAS infection.
4. It is important to rule out other potential differential diagnoses, especially rheumatologic ones that often share similar clinical presentations.
5. Management of ARF consists of primary prevention, secondary prevention, and anti-inflammatory and supportive management for the various organ manifestations.
6.

Thank you for listening to this podcast on ARF! We hoped that you enjoyed it and that you will stay tuned for more podcasts to come!

References

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http://www.uptodate.com/contents/acute-rheumatic-fever-clinical-manifestations-and-diagnosis.

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