Acute Rheumatic Fever and Rheumatic Heart Disease: Narrative Literature Review

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ARTICLE INFO

Keywords:
Children
Pathophysiology
Rheumatic fever
Rheumatic heart disease

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.59345/sjped.v1i1.15

1. Introduction

Rheumatic fever is a systemic inflammatory disease caused by an immune and inflammatory response to infection by group A beta-hemolytic streptococci in individuals with a genetic predisposition. In its acute form, rheumatic fever is a febrile illness that occurs about 2 to 3 weeks after infection and is characterized by inflammation of the joints, skin, nervous system, and heart. If left untreated, rheumatic fever can lead to scarring and structural deformities of the heart resulting in rheumatic heart disease (RHD).¹⁻³

The incidence of acute rheumatic fever declined in the United States during the 1960s, 1970s, and early 1980s because of medical and socioeconomic improvements and changes in group A streptococcal virulence. It occurs most frequently in children between 5 and 15 years of age. Appropriate antibiotic therapy given within the first 9 days of infection usually prevents rheumatic fever. Individuals who have experienced one attack of acute rheumatic fever are more susceptible to repeated attacks.⁴⁻⁷ This literature review aimed to describe acute rheumatic fever and rheumatic heart disease in children.

Pathophysiology

Acute rheumatic fever can develop only as a sequel to pharyngeal infection by group A beta-hemolytic streptococci. Streptococcal skin infections do not develop into acute rheumatic fever because the strains of microorganisms that infect the skin do not have the
same antigenic molecules in their cell membranes as those that cause pharyngitis and therefore do not elicit this type of response same immunity. Acute rheumatic fever is the result of an abnormal humoral and cellular immune response to the M protein in microorganisms that cross-react with normal tissues (Figure 1).

Antibodies to streptococcal bacterial antigens show cross-reactivity to laminin, a protein present in the extracellular tissue around heart cells and in valves. Cardiac myosin and vimentin are other target antigens.8,9

Autoimmunity and associated intense inflammation produce diffuse, proliferative, and exudative lesions in connective tissue, especially in the heart, joints, and skin. Repeated bouts of acute rheumatic fever lead to chronic proliferative changes with resulting scarring, granulomas, and thrombosis. About 10% of cases of rheumatic fever develop RHD. RHD begins as carditis or inflammation of the heart. Although rheumatic fever can cause carditis in all three layers of the heart wall (endocardium, myocardium, pericardium), the primary lesion usually involves the endocardium, which includes the heart valves. Inflammation of the endocardium causes swelling of the valve leaflets, with secondary erosion along the leaflet contact lines. Small bead-like clumps of vegetation containing platelets and fibrin were deposited on the eroded valve tissue and on the chordae tendineae (Figure 2). The valve loses its elasticity, and the leaflets can stick together. Scar tissue and shortening of the structures involved occur over time.10,11
If the inflammation penetrates the myocardium, local fibrin deposits develop, which are surrounded by areas of necrosis. These necrotic fibrinoid deposits are called Aschoff’s bodies. Pericardial inflammation is usually characterized by a serofibrinous effusion within the pericardial cavity. Cardiomegaly and left heart failure may occur during untreated episodes of acute or recurrent rheumatic fever. Conduction defects and atrial fibrillation are frequently associated with rheumatic heart disease.

Clinical manifestations

Common symptoms of acute rheumatic fever are fever, lymphadenopathy, arthralgia, nausea, vomiting, epistaxis (nosebleeds), abdominal pain, and tachycardia. The main clinical manifestations of acute rheumatic fever (carditis, acute migratory polyarthritis, subcutaneous nodules, chorea, and erythema marginatum) usually occur alone or in combination 1 to 5 weeks after streptococcal infection of the pharynx.12-17

Carditis

Carditis occurs several weeks after the initial infection in approximately 50% of patients with acute rheumatic fever, with the mitral valve being the most affected structure. Cardiac manifestations of acute rheumatic fever may include previously undetected murmurs caused by mitral or aortic valve dysfunction, chest pain, and pericardial friction caused by pericardial inflammation or cardiomegaly unexplained by heart failure.

Polyarthritis

Acute migratory asymmetric polyarthritis (inflammation of more than one joint) occurs in the majority of individuals with rheumatic fever, although severe monoarthritis is also an emerging feature in high-risk populations. Although any synovial joint may be involved, the large limb joints are most commonly involved. Two or more joints are usually involved simultaneously or successively, with each joint being symptomatic for approximately 2 to 3 days, while polyarthritis as a whole persists for up to 3 weeks. Exudative synovitis causes heat, redness, swelling, intense pain, and tenderness but does not cause permanent disability.

Subcutaneous nodules

Palpable subcutaneous nodules occur in less than 5% of cases of acute rheumatic fever. They develop over bony prominences and along the extensor tendons of the elbows, wrists, knees, and ankles. They do not interfere with joint function and often go unnoticed.

Chorea

Sydenham chorea, or St. Vitus, is a CNS disorder characterized by sudden, aimless, disorganized, and involuntary movements. It affects up to 15% of people
with rheumatic fever and is the most common acquired chorea in children. Korea is self-limiting, although severe cases may require the use of dopamine receptor blockers and antiepileptic drugs. It resolves in 1 to 6 months and has no permanent neurological sequelae.

**Marginal erythema**

Erythema marginata is a rare manifestation and presents as a characteristic rash that often accompanies acute rheumatic fever. It consists of annular erythema with a nonpruritic appearance and pink, erythematous macules radiating outward. The rash is temporary and can change within minutes or hours.

**Evaluation and treatment**

The original Jones criteria for the diagnosis of rheumatic fever have been updated by the American Heart Association (Table 1). Supportive evidence for group A beta-hemolytic streptococci includes positive throat cultures and measurement of serum antibodies to hemolytic factor streptolysin O. However, cultures may be negative when a rheumatic attack begins. Several other antibody tests are sensitive prognosticators of streptococcal infection, including anti-deoxyribonuclease B (anti-DNase B), anti-hyaluronidase, and anti-streptozyme (ASTZ).

Measurements of elevated white blood cell count, erythrocyte sedimentation rate, and C-reactive protein suggest inflammation. All three usually increase when the heart or joint symptoms begin to appear.18-20

**Table 1. Major and minor diagnostic criteria for acute rheumatic fever according to the Jones criteria.**

<table>
<thead>
<tr>
<th>Major criteria in a low-risk population</th>
<th>Major criteria in a high-risk population</th>
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</thead>
<tbody>
<tr>
<td>Carditis (clinical and/or subclinical)</td>
<td>Carditis (clinical and/or subclinical)</td>
</tr>
<tr>
<td>Arthritis (polyarthritis only)</td>
<td>Arthritis (monoarthritis or polyarthritis; polyarthralgia)</td>
</tr>
<tr>
<td>Chorea</td>
<td>Chorea</td>
</tr>
<tr>
<td>Marginal erythema</td>
<td>Marginal erythema</td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td>Subcutaneous nodules</td>
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<tr>
<td></td>
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<tr>
<td>Minor criteria in a low-risk population</td>
<td>Minor criteria in moderate and high-risk populations</td>
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<tr>
<td></td>
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<tr>
<td>Polyarthralgia</td>
<td>Monoarthralgia</td>
</tr>
<tr>
<td>Fever (≥38°C; 100.4°F)</td>
<td>Fever (≥38°C; 100.4°F)</td>
</tr>
<tr>
<td>ESR ≥60 mm/hour and/or CRP&gt; 3.0 mg / dL</td>
<td>ESR ≥30 mm/hour and/or CRP&gt; 3.0 mg / dL</td>
</tr>
<tr>
<td>Prolonged PR interval</td>
<td>Prolonged PR interval</td>
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</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Therapy for acute rheumatic fever is aimed at eradicating streptococcal infection regimen 10 days of antibiotics. NSAIDs are used as agents of anti-inflammatory for rheumatic carditis and arthritis and help relieve symptoms but do not prevent complications. Serious carditis may require diuretics and vasodilators, and recovery may take up to 12 months. Damaged valve repair surgery may be necessary in cases of recurrent chronic rheumatic fever or carditis. Persistent chorea requires psychosocial support, protection against falls and injuries, and treatment with antiepileptic or neuroleptic drugs. NSAIDs or paracetamol can relieve symptoms of arthralgia. Because recurrent rheumatic fever occurs in more than half of affected children, continuous prophylactic antibiotic therapy may be required for up to 5 years.

**2. Conclusion**

Rheumatic fever is a systemic inflammatory disease caused by an immune and inflammatory response to infection by group A beta-hemolytic streptococci in individuals with a genetic predisposition. If left untreated, rheumatic fever can
lead to scarring and structural deformities of the heart resulting in rheumatic heart disease (RHD).

3. References