Rheumatic fever, a rare disease in industrial countries, occurs several weeks after an infection with group A *Streptococci*. The severity of the disease depends on the manifestation of endocarditis.

**Definition**

Rheumatic fever is an inflammatory connective tissue disease caused by bacterial toxins after an infection with group A *Streptococci* (GAS). It is a nonsuppurative sequela of the infection.

**Epidemiology**

As streptococci infections of the oropharyngeal tract are usually treated with antibiotics (i.e. penicillin) and prevented with timely vaccines, rheumatic fever is rare in industrial countries.

Contrary to this, in developing countries, where there are high rates of poverty, poor housing and ventilation, and lack of antibiotics, bacterial infections with GAS are common, leading to many cases of rheumatic fever. Rheumatic fever occurs primarily in children, especially between the ages of 5 to 15.
Etiology

**Tonsillitis** or **pharyngitis** due to group A beta-hemolytic *Streptococci* may lead to an infection-induced autoimmune reaction, which in turn can cause rheumatic fever.

Increased prevalence has also been reported in persons with HLA-DR class II alleles (D8/17).

Pathophysiology of Rheumatic Fever

Two main pathogenic mechanisms have been postulated:

1. **Cytotoxic theory** where Group A *Streptococci* produce cytotoxic streptolysin O and streptolysin S. These antibodies at elevated levels are used in detecting disease through antistreptolysin O (ASO) titers.

2. **The immunologic theory** explains the occurrence of the disease days after the infection. There is molecular mimicry between the M protein on the protosin membrane of GAS with the tropomyosin and myosin of the heart muscles.

Both pathways lead to an antibody-antigen reaction with mediators such as TNF-α, IFN-γ, and IL-10 being predominant with a reduction in the inflammatory regulatory cytokine IL-4. The disease leads to pancarditis that can cause stenosis of the valves 2-10 years after the initial rheumatic fever episode.
Clinical Presentation

Typically, rheumatic fever occurs 2 to 3 weeks after infection. It presents general symptoms like **fever, headaches, and sweating**. Also, **migrating polyarthritis** with swelling and reddening occurs. The heart can also be affected by rheumatic fever. Depending on which structure is affected, the disease can expand to a pancarditis. **Subcutaneous rheumatic nodules** can be found on the skin.

A late sequela is **Sydenham chorea** (chorea minor), which can occur months after the infection with the *Streptococci*.

**Diagnosis**

The clinical examination shows a **friction rub on auscultation** and signs of pericardial effusion or heart insufficiency. Other signs include tachycardia, cardiac dysrhythmia, and audible cardiac murmurs if cardiac valves are affected.

Laboratory tests may reveal increased inflammatory parameters. Also, *Streptococci* can be detected in the **throat swab**. Antibodies like antistreptolysin O or antideoxyribonuclease B can be determined. If the cardiac valves are affected, this can be detected in **echocardiography**. The **ECG** can demonstrate unspecific changes.
Pathology

Histologically, so-called **Aschoff bodies** (image on the right) can be found, which consists of fibrinoid necroses around which rotund and giant cells have accumulated. Also, **Anitschkow cells**, which are histiocytes with owl-like nucleoli, are typical of rheumatic fever.

**Differential Diagnosis**

**Rheumatoid arthritis** has to be distinguished from rheumatic fever.
Therapy of Rheumatic Fever

The 3 main treatment goals are:

1. Eradication of GAS: Both penicillin V and amoxicillin are suitable for treatment. If allergic to penicillin, switch to macrolides.
2. Symptom relief: For the treatment of inflammation, nonsteroidal anti-inflammatory drugs (NSAIDs) are used.
3. Prophylaxis for rheumatic fever recurrence requires using penicillin or a macrolide depending on the severity as follows:
   1. In those with rheumatic fever without carditis for 5 years or up to 21 years, whichever is longer
   2. In those with rheumatic fever and carditis with no residue dysfunction for 10 years or up to 25 years, whichever is longer
   3. In those with residual heart dysfunction for life or up to 40 years

References


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