ACUTE RHEUMATIC FEVER

MBchB IV

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RHEUMATIC FEVER

Definition ; RHF is an inflammatory ds which occurs as a delayed sequel to pharyngeal throat infection by $\mathcal{B}$-hemolytic strep of Lancefield gp A after latency period of about 3- 4 weeks.

- The pharyngitis is often purulent.
- M Serotypes 3,5,18,19,24 have been frequently associated with RHF.
- Not all strains in these serotypes are rheumatogenic

RHEUMATIC FEVER

- Rheumatic process is an inflammatory reaction involving multiple organs- Joints, skin, brain and the heart.

- The usual manifestations in the acute form are ;
  Migratory polyarthritis, fever and carditis.

- Other manifestations are ;

Sydenham's Chorea, subcutaneous nodules and erythema marginatum.

RHEUMATIC FEVER

- Joints, skin and brain involvement is normally self limited.

- Cardiac involvement can lead to severe and life threatening acute inflammation or to a chronic disease that results in permanent cardiac scarring and dysfunction.

EPIDEMIOLOGY

- Untreated group A streptococcal pharyngitis precipitates an attack of RF in 2-3 % of individuals who've not had previous attack of RF. These individuals have genetic predisposition.

- Some studies have emphasized relationship between occurrence of Rheumatic fever and severity of clinical manifestations of antecedent streptococcal pharyngitis.

EPIDEMIOLOGY

- However 1/3 of all cases of acute RF follow mild or almost asymptomatic phargngitis. Some patients with Rheumatic heart disease have no history of pharyngitis.

- Initial attacks of Rheumatic Fever are encountered between ages 6 and 15 years in developed world. In developing countries it seen at younger ages – up to 4 yrs.

EPIDEMIOLOGY

- Increased incidences of RF has been seen in young adults who're at risk of strep pharyngitis e.g. military recruits and parents of school age children.

- No sexual preference

EPIDEMIOLOGY

- Racial and ethnic differences in incidence of RF have been described ;
- e.g. in New Zealand there's higher incidence among the Maori population.

- In the U.S. it is more common among African and Hispanic American than in caucasians.

EPIDEMIOLOGY

- Incidence of RF higher in developing countries. In developed world incidence was 0.5 -3.1/100,000 at the turn of the century.
- In developing countries mortality from RHD is 10x higher than in the developed world.

- Some of the factors which influence this are:
  Crowding in homes and schools
  Availability of health care
  Health seeking behavior.

Host susceptibility

- Only 2-3% of individuals who've suffered strep pharyngitis develope RF. However in patients who've had RF previously, incidence is 50%

- Genetic susceptibility is mediated by single recessive gene. Examination of human lymphocytes has revealed presence of a specific B cell alloantigen in 99 % of patients with RF and only 14 % in controls.

Host susceptibility

- There is high incidence of class II human leucocyte (HLA) in patients with RF.

PATHOGENESIS

Mechanism of Tissue injury

- Thought to result from immune reaction
- Kaplan et al showed that common antigenic determinants were shared between group A streptococci and myocardial tissue

Antigenic mimicry

- Antibodies produced against strep cross react with host tissue leading to tissue damage.
- Strep M protein and myocardial sarcolemma have immunologic cross-reactivity.

Antigenic mimicry

- Similar cross reactivity has been seen between a protoplast membrane antigen and sarcolemmal membrane of myocardium.
- Other immunologic cross reactions:

Streptococcal glycoprotein → *valvular glycoprotein*

Strep protoplast membrane → *Neuronal tissue of subthalamic and caudate nuclei.*

Hyaluronate of capsule → *articular cartilage*

PATHOLOGY

- Inflamatory reaction in RhF involves connective or collagen tissue. Most tissues of body maybe involved but clinically important manifestations primarily involve joints, heart and brain.

SKIN

- Skin rash reflects presence of vasculitis mainly involving small vessels. Vessels show proliferation of endothelial cells.
- Subcutaneous nodules rarely seen in acute Rh fever.

PATHOLOGY

Subcutaneous Nodules

- Seen more in chronic valvular heart DS e.g. mitral stenosis.

- Subcutaneous nodules consists of central fibrinoid recrosis surrounded by epithelial & mononuclear cells.
- Lession similar to that described for Aschoff body (pathologic hallmark of Rheumatic Carditis)

PATHOLOGY

CARDIAC INVOLVEMENT

In acute Rh fever, process often involves endocardium and myocardium. Pericardium may get involved in severe myocarditis.

PATHOLOGY

PANCARDITIS

- Histological findings not specific. Degree of histological change doesn't correlate with severity of clinical findings.
- In early stages when cardiac dilation is a prominent feature, histological changes maybe minimal though cardiac function maybe so severely impaired as to be fatal.
- As inflamatory rxn progresses, exudative and proliferative reaction becomes more apparent.

PANCARDITIS

- Oedematous changes occur in the tissues followed by a cellular infiltrate consisting of lymphocytes and plasma cells. Lymphocytes are predorminatly CD4 type.

- Fibrinoid (eosinophilic granular substance) is seen scattered in the tissue, includes collagen fibres plus granular material derived from degenerating collagen in a mixture of fibrin, globulin and other substances.

PANCARDITIS

- Other tissues affected by disease process e.g. joint tissue may show fibrinoid necrosis.
- Aschoff cell (Aschoff body) formation follows the above stage.
- Lession consists of a perivascular infiltrate of large cells with polymorphous nuclei and basophilic cytoplasm arranged in a rossette around the centre of fibrinoid.
- It is pathognomonic of Rheumatic carditis. Commonly found at IVS, LV wall and LA appendage.

PATHOLOGY

- Aschoff body not found in acute Rheumatic carditis but rather in patients with chronic disease.

ENDOCARDITIS

Affects valvular tissue and mitral endocardium. Mitral valve involvement is commonest. Aortic involvement is 2nd and much less frequent and pulmonary valve is rarely involved.

CLINICAL FEATURES

- Acute Rheumatic Carditis is manifested by appearance of heart murmurs.
- In severe cases signs and symptoms of pericarditis and CCF will be eveident.
- Death from heart failure may occur in the acute phase of ds.
- Permanent valvular damage may occur.
- Carditis may range from a fulminating fatal course to a low grade subclinical inflammation.

CARDITIS

- Hence in pts whose RhF is manifested only as mild carditis, ds is often missed until later in life when they are found to have RHD ds.In such pts no definite hx of RhF can be established.
- Pts with acute carditis may manifest with tachycardia, cardiomegaly, hepatomegaly, changing heart murmurs

Clinical features

ARTHRITIS

- The **classic** attack of RhF appears as acute migratory polyarthritis anf fever.
- Large joints of upper and lower limbs are most frequently affected in a migratory manner.
- Sometimes several joints are involved at the same time.
- This is usually associated with high ESR.

CLINICAL FEATURES

Subcutaneous Nodules

- Small pea-sizes painless swellings over bony prominences.
- Often not noticed.
- Usually appear on extensor tendons of hands and feet, elbows,margins of patellae, scalp, scapulae, vertebrae etc.

CLINICAL FEATURES

- Erythema Marginatum
- Erythematous rash with clear centres and round or serpiginous margins.
- They occur on trunk and proximal part of extremeties and **never** on the face.
- Rash is transient and migratory.
- It is non-pruritic and not indurated.

CLINICAL FEATURES

Chorea

- Sydenham's chorea, St Vitus' dance.
- Disorder of the CNS ; Sudden aimless irregular movements often associated with muscle weakness and emotional instability.
- Often a late manifestation which appears long after other features of acute RhF have subsided.
- Onset gradual. Symptoms subside during sleep.

GUIDELINES FOR DX RHF
MODIFIED JONES CRITERIA (1992)

MAJOR MANIFESTATIONS	MINOR
Carditis	**Clinical**
Polyarthiritis	Fever and arthralgia
Sydenham's chorea	**Lab**
Erythema Marginatum	↑Acute phase reactants
Subcutaneous nodules	ESR, CRP
	Prolonged P-R interral

GUIDELINES FOR DX RHF
MODIFIED JONES CRITERIA (1992)

SUPPORTING EVIDENCE OF ANTECEDENT Gp A STREP INFECTION	
➢Increased or rising strep ab titre (s) ➢+ve throat culture or rapid strepcoccal ag test	

GUIDELINES FOR DX RF MODIFIED JONES CRITERIA (1992)

- 2 major or

- 1 major +2 minor manifestations indicates high probability of acute rheumatic fever. If supported by evidence of preceding group A throat infection.

Treatment

CARDITIS

Mild to moderate

- Salicylates 90-100 mg/kg/day

- Maintain serum levels 25-30 mg / dl
  Treat for 4-6 weeks

- With improvement treatment is withdrawn gradually over 2 weeks

Severe carditis

- Prednisone 2mg/kg/day. Given in acute period and gradually withdrawn over 2-3 wks.
- One wk prior to withdrawal of steroids patient should be started on therapeutic dose of salicylates.

Digitalis

- Used in pts with severe carditis and heart failure. Digitalize (0-02-0.03 mg/kg) (TDD)
- Then maintenance ¼ TDD given in 2 doses daily

Severe carditis

- Additional cardiac drugs maybe considered if response is not adequate.
- May use Lasix, aldactone.
- Bed rest: Recommended for acute carditis with slow resumption of normal activity.

ARTHRITIS

- Salicylates (ASA) 50-70/kg/day for 2 months then gradually withdraw over 2-3 wks
- Decline in ESR parallels clinical response

SYDENHAM'S CHOREA

Mild:

- Bed rest and avoidance of stress.

Severe:

Anticonvulsants phenobarb or haloperidol.

- Phenobarbitone 3-8 mg/kg/day
- Haloperidol: 0.5 mg/kg/ day 8 hourly: may increase to 2 mg 8 hourly
- Sodium valproate 15-20/kg/day

PROPHYLAXIS

PRIMARY PREVENTION

Eradication of steptococci

- Benzathine pen 600,000–1.2 m.u.
- Pen V 250 mg TDS x10/7
- Erthromycin 20–40 g/kg/dx10/

Others:

Cefpodoxime 10 mg/kg /24 hr x5/7 –od

- Azitromycin 12 mg/Kg / day x12/7 –od

PROPHYLAXIS

Secondary prevention

- 3 to 4 weekly Benzathine pen G
  600,000 IU for < 27 kg.
  1.2 m.u. > 27 kg

- Others: Pen V, sulfadiazine, erythromycin

PROPHYLAXIS

Health education of parents/ caretakers and child.

END

Thank you