DEPARTMENT OF PATHOLOGY AND MICROBIOLOGY

CARDIOVASCULAR SYSTEM

Ischemic heart disease / IHD

a group of related syndromes resulting from myocardial ischemia-an imbalance between cardiac blood supply (perfusion) and myocardial oxygen demand.

- There are four basic clinical syndromes of IHD:
- Angina pectoris
- Acute myocardial infarction
- Chronic IHD
- Sudden cardiac death

Angina pectoris

- uncomfortable sensation in the chest or neighboring anatomic structures produced by myocardial ischemia
- the ischemia causes pain but is insufficient to lead to death of myocardium.
- angina may be stable (occurring reliably after certain levels of exertion),
- may be due to vessel spasm (variant angina or Prinzmetal angina),
- or may be unstable (occurring with progressively less exertion or even at rest)
    - Stable = 75% vessel block, transient (<15 minutes), aggravated by exertion, relived by rest & Nitroglycerin (VD)
    - Prinzmetal = coronary spasm, episodic, Typical ECG change – ST elevation, Relived by VD but not rest
    - Unstable = 90% vessel block or Acute plaque change (superimposed thrombus), prolonged (>15 min.), not relived by rest, VD, Pre-infarction Angina

Signs & Symptoms accompany Angina

- Dyspnoea, nausea, diaphoresis resolve quickly after cessation of angina.
- Angina is a diffuse sensation rather than discrete.
- Myocardial infarction (MI) or acute myocardial infarction (AMI)/ heart attack is the interruption of blood supply to part of the heart, causing some heart cells to die
- Results from acute thrombus at side of coronary atherosclerotic stenosis
- May be first clinical manifestation of ischemic heart disease or history of Angina Pectoris
- Sex = Male > Female
- Risk factors
    - Major modifiable- DM, HTN, Smoking, Hypercholesterolemia
    - Postmenopausal females – will not protect the heart

Pathogenesis

- most MIs are caused by acute coronary artery thrombosis.

- In most cases, disruption of an atherosclerotic plaque results in the formation of thrombus.
- Vasospasm and/or platelet aggregation can contribute
- Coronary artery obstruction blocks the myocardial blood supply, leading to profound functional, biochemical, and morphologic consequences.
- Within seconds of vascular obstruction, cardiac myocyte aerobic glycolysis ceases, leading to inadequate production of ATP and accumulation of potentially noxious breakdown products (e.g., lactic acid).
- **functional consequence**

is a striking loss of contractility, occurring within a minute or so of the onset of ischemia.

- **Ultrastructural changes**

myofibrillar relaxation, glycogen depletion, and cell and mitochondrial swelling also become rapidly apparent, these early changes are reversible, and myocardial cell death is not immediate .

- Only severe ischemia lasting at least 20 to 40 minutes causes irreversible injury and myocyte death; the predominant pattern is coagulation necrosis .
- Irreversible injury of ischemic myocytes first occurs in the subendocardial zone .
- With more prolonged ischemia, a wavefront of cell death moves through the myocardium to involve progressively more of the transmural thickness of the ischemic zone, so that an infarct usually reaches its full size within 3 to 6 hours.
- MIs can be located in the anterior, septal, lateral, posterior, or inferior walls of the left ventricle.

MI – Types

Transmural

- Full thickness
- Superimposed thrombus in atherosclerosis
- Focal damage

Sub-endocardial

- Inner 1/3 to half of ventricular wall
- Decreased circulating blood volume(shock, Hypotension, Lysed thrombus) circumferential

SYMPTOMS

- Circadian variability: occurring most commonly in morning hours, soon after awakening
- Symptoms usually begin while at rest, and only occasionally are brought on by physical exertion
- Some patients have less pronounced symptoms: generalized weakness, dyspnoea, and indigestion.

MI –Morphology

- light microscopy
  - First 12 hrs. after MI – no change
  - Up to 3 days = Coagulative necrosis, neutrophils

- 1-2 weeks = Granulation tissue
- ≥ 3 weeks = fine scar
- ≥ 2 months = dense scar

- EM – membrane disruption and Mitochondrial densities
- Most common and nonspecific change in ischemia = sub-endocardial myocyte vacuolization

MI – Complications

- Poor prognosis in = elderly, females, DM, old case of MI, Anterior wall infarct – worst, posterior –worse, Inferior wall – best
  - 1. Arrhythmia = Ventr. Fibrillation – arrhythmia lead to sudden death in MI patients, before they reach hospital
  - 2. pump failure – LVF, cardiogenic shock, if >LV wall infarcts, lead to death (70% of hospitalized MI pts)
  - 3.Ventricular rupture = Free or lateral LV wall, later cause false aneurysm,
  - 4.True aneurysm = rupture is very rare
  - 5.Pericarditis (Late complication)
  - 6.Recurrence

DIAGNOSIS

- Electrocardiogram:
  hallmark of acute myocardial injury is the presence of ST segment elevations. horizontal or downsloping ST segments or T wave inversions which normalize after pain resolution
- ST elevation suggest severe transmural ischemia or coronary artery spasm which is less often

Serum Markers of Infarction

- Certain proteins are released into circulation during an MI
- Creatine kinase CK rises in plasma within 4 to 8 hours, peaks at 24 hours, returns to normal by 48 hours to 72 hours
- Troponin I and T are sensitive and highly specific markers of acute MI
- Levels begin to rise within 3 hours after onset of infarction and remain elevated for several days
- Higher Troponin I levels or early (+) of Troponin T assay correlate with greater short-term mortality
- CK-MB isoenzyme is more specific for diagnosis of AMI
- CK-MB rises and peaks slightly earlier than total CK and returns to normal within 36 – 72 hours
- Myoglobin is released into circulation very early after myocardial injury and detected within 2 hours of infarction
- LDH- Rises within 24 to 48 hours of MI
- Peaks at 3 – 5 days and returns to baseline by 7-10 days
- Usefulness in patients who are admitted to hospital 2 – 3 days after onset of symptoms

- Level of LDH-1 greater than LDH-2 = myocardial necrosis

SUDDEN CARDIAC DEATH (SCD

can result from a lethal arrhythmia following myocardial ischemia.

- unexpected death in one hour due to cardiac causes with or without clinical symptoms
- Cause – Atherosclerosis (90%), others (10%)
    - Romano- Ward syndrome – Long Q-T syndrome (K+, Na+ channel defects)
- Mechanism- Most likely due to arrhythmias (VF)
- Patients – young athletes, with Pul. HTN, IHD
- Morphology
    - Prominent finding – increased heart mass
    - Vacuolations in Sub – endocardial myocardium

CHRONIC IHD

- refers to progressive cardiac decompensation (heart failure) following MI.
- also called ischemic cardiomyopathy
- Patients = post heart transplant receipts, previous MI
- Cause =compromised ventricular function
- Morphology =vacuoles, Myocyte Hypertrophy

INFECTIVE ENDOCARDITIS

- an infection of the heart's endocardial surface
- Classified into four groups:
    - Native Valve IE
    - Prosthetic Valve IE
    - Intravenous drug abuse (IVDA) IE
    - Nosocomial IE

Pathophysiology

1. Turbulent blood flow disrupts the endocardium making it "sticky"
2. Bacteremia delivers the organisms to the endocardial surface
3. Adherence of the organisms to the endocardial surface
4. Eventual invasion of the valvular leaflets

Infecting Organisms

- Common bacteria
    - S. aureus Streptococci Enterococci
- Not so common bacteria
    - Fungi Pseudomonas

Symptoms

- Acute
    - High grade fever and chills, Arthralgias/ myalgias , Abdominal pain, Pleuritic chest pain Back pain

- Subacute
  - Low grade fever Anorexia Weight loss Fatigue Arthralgias/ myalgias
  - Abdominal pain N/V
- Signs: Fever Heart murmur
- Nonspecific signs – petechiae, subungal or "splinter" hemorrhages, clubbing, splenomegaly, neurologic changes
- More specific signs - Osler's Nodes, Janeway lesions, and Roth Spots

VALVULAR HEART DISEASE

- Abnormal Valve Function
- Valve Stenosis
  - Obstruction to valve flow during that phase of the cardiac cycle when the valve is normally open.
  - Hemodynamic hallmark -"pressure gradient"
- Valve Regurgitation, Insufficiency, Incompetence
  - Inadequate valve closure---→ back leakage

Mitral Valve Disease: Etiology

- **Mitral Stenosis**

Rheumatic - 99.9% Congenital Prosthetic valve stenosis Mitral Annular Calcification

Left Atrial Myxoma

Acute Mitral Regurgitation: Infective endocarditis Ischemic Heart disease Papillary ms rupture

Mitral valve prolapse Chordal rupture Chest trauma

Mitral Regurgitation-Pathophysiology

- MR: Leakage of blood into LA during systole Increased LA pressure
- Pulmonary HTN Dyspnea Atrial arrhythmias Low output state

Mitral Stenosis –Pathophysiology

- Restriction of blood flow from LA→LV during diastole.
  - Normal MVA 4-6$cm^{2.}$ Mild MS 2-4$cm^{2.}$ Severe MS < 1.0$cm^{2.}$
- MV Pressure gradient – As HR increases, diastole shortens disproportionately and MV gradient increases.

Aortic Valve Disease: Etiology

- Aortic Stenosis
  - Degenerative calcific (senile) Congenital – Uni or bicuspid
  - Rheumatic Prosthetic
- Acute Aortic Insufficiency

Infective endocarditis

Acute Aortic Dissection- Marfan's Syndrome, Chest trauma

Aortic Regurgitation

- Pathophysiology:

- LV receives both blood from LA & AO →volume overload →LV dilation → pulmonary edema →relative MI,MS; - Diastolic pressure↓,pulse pressure↑

- Clinical Manifestations:

- Symptom: palpitation, angina - Sign: apical impulse→ left, inferior cardiac dullness →left, inferior Boot-shaped shadow—cardiac waist↓ DM in AV2 area →apex S1↓,

Aortic Stenosis – Pathophysiology

- Normal AVA 2.5-3.0cm^2 Severe AS <1.0cm^2 Critical AS <0.7cm^2; <0.5cm^2/m^2
- Hemodynamic Hallmark
  - Systolic pressure gradient AV grad ~ AV flow//AVA AV flow = CO/SEP (systolic ejection period)
  - 50-100mmHg gradients are common in severe A

c/f: Asymptomatic for many years

- Symptoms develop when valve is critically narrowed and LV function deteriorates
  - Bicuspid AV 5^{th} - 6^{th} decade Senile AS 7^{th}-8^{th} decades
- Classic Symptom Triad
  - Angina pectoris – 5 years CHF 1-2 years Syncope 2-3 years
  - Sudden Death

CHD

Noncyanotic CHD (L →R)

- ☐ Atrial septal defects (ASD)
- ☐ Ventricular septal defects (VSD)
- ☐ Patent ductus arteriosus (PDA)
- ☐ Obstruction to blood flow
  - ◘ Pulmonic stenosis (PS) Aortic stenosis (AS)
  - ◘ Aortic coarctation
- ☐ ASD: Most commonly asymptomatic
- ☐ Essentials of diagnosis:
  - ◘ Right ventricular heave S_2 widely split and usually fixed
  - ◘ Grade I-III/VI systolic murmur at the pulmonary area
  - ◘ Widely radiating systolic murmur mimicking PPS in infancy

Cardiac enlargement on CXR

- ☐ Three major types
  - ◘ Ostium secundum
    most commonIn the middle of the septum in the region of the foramen ovale
  - ◘ Ostium primum
    Low positionForm of AV septal defect
  - ◘ Sinus venosus
    - ■ Least common Positioed high in the atrial septum

Ventricular Septal Defect

- Single most common congenital heart malformation, 30% of all CHD
- Defects can occur in both the membranous portion of the septum (most common) and the muscular portion

Patent Ductus Arteriosus

- Persistence of normal fetal vessel joining the pulmonary artery to the aorta
- Closes spontaneously in normal term infants at 3-5 days of age.
- Accounts for about 10% of all cases of CHD
- Higher incidence of PDA in infants born at high altitudes (over 10,000 feet)
- More common in females

Cyanotic CHD (R $\rightarrow$L)

- Tetralogy of Fallot (TOF)
- Tricuspid atresia (TA)
- Total anomalous pulmonary venous return (TAPVR)
- Truncus arteriosus
- Transposition of the great vessels
- Hypoplastic left heart syndrome (HLH)
- Pulmonary atresia (PA) / critical PS
- Double outlet right ventricle (DORV)

Tetralogy of Fallot

- This malformation consists of a true anatomopathologic type represented by the tetralogy:
- (1) Stenosis of the pulmonary artery;
- (2) Interventricular communication;
- (3) Deviation of the origin of the aorta to the right; and
- (4) Hypertrophy, almost always concentric in type, of the right ventricle.
- Failure of obliteration of the foramen ovale seen occasionally.
- Tet spells most commonly start around 4 to 6 months of age and are charcterized by
    - Sudden onset or deepening of cyanosis Sudden onset of dyspnoea
    - Alterations of consciousness Decrease in intensity of systolic murmur

CARDIAC TUMOURS

- Primary rare -
- Secondary tumors of the heart - are typically either metastatic from another part of the body, or infiltrate the heart via direct extension from the surrounding tissues.
    - Myxoma: always single and are most commonly located at the atrial septum.
    - <1 cm to ≤10 cm
    - sessile or pedunculated masses
    - globular hard masses to soft, translucent, villous lesions with a gelatinous appearance.

PERICARDITIS is an inflammation of the pericardium. A characteristic chest pain is often present.
causes viral infections of pericardium,
idiopathic causes, uremic pericarditis ,
bacterial infections of the pericardium (TB) post-infarct pericarditis