MORPHOLOGICAL CHANGES OF ISCHEMIC HEART DISEASE

DR. K.SARITHA
ASSISTANT PROFESSOR
PATHOLOGY DEPT
• Ischemic heart disease (IHD) is the leading cause of death worldwide for both men and women (7 million total per year).

• IHD is the generic designation for a group of pathophysiologically related syndromes resulting from myocardial ischemia—an imbalance between the supply (perfusion) and demand of the heart for oxygenated blood.

• Ischemia -1)insufficiency of oxygen
  2) reduces the availability of nutrients and the removal of metabolites
ETIOPATHOGENESIS

1) Coronary atherosclerosis- fixed obstruction - 90% cases

2) Super added changes in coronary atherosclerosis

3) Non atherosclerotic causes - 10%
ATHEROSCLEROSIS

- *athero* = porridge; *sclerosis* = scarring

- Atherosclerosis is a specific form of arteriosclerosis affecting primarily the intima of large and medium-sized muscular arteries and is characterised by fibrofatty plaques or atheromas.
1) Distribution-

- Anterior descending branch of LCA > RCA > circumflex branch of LCA
LOCATION

– 75% reduction cross sectional area coronary artery leads to MI

– Severest involvement -3 to 4 cms from coronary ostia near bifurcation of arteries-suggesting role of haemodynamic forces in atherogenesis
SUPER ADDED CHANGES IN CORONARYATHEROSCLEROSIS

• Lead to attacks of acute coronary syndromes

1) Acute changes in chronic atheromatous plaque
• Plaque haemorrhage, fissuring, ulceration
• Due to spasm, tachycardia, hypercholesteremia

2) Coronary artery thrombosis-
• Initiation of thrombosis due to surface ulceration of fixed chronic atheromatous plaque-----luminal obstruction
• Lipid core is thrombogenic --- embolise to terminal coronary branches---microinfarcts of myocardium
NONATHEROSCLEROTIC CAUSES

- Vasospasm
- Stenosis of coronary ostia-syphilitic aortitis
- Arteritis-vasculitic disorders
- Embolism
- Thrombotic diseases-hypercoagulability
- Trauma
- Aneurysms-extension of dissecting aortic aneurysms into coronary artery
- Compression-primary or secondary tumor of heart

Local platelet aggregation -- coronary artery spasm--thromboxane A2
ATHERTOSCLEROSIS

- AFFECTS

Elastic arteries:
- Aorta, Carotid, Iliac

Medium sized muscular arteries:
- coronary & popliteal
Abdominal aortic aneurysm

Myocardial infarct

Cerebral infarct

Gangrene of extremities
# RISK FACTORS FOR ATHEROSCLEROSIS

<table>
<thead>
<tr>
<th>Major</th>
<th>Lesser, Uncertain, or Nonquantitated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonmodifiable</strong></td>
<td></td>
</tr>
<tr>
<td>Increasing age</td>
<td>Obesity</td>
</tr>
<tr>
<td>Male gender</td>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Family history</td>
<td>Stress (<em>type A</em> personality)</td>
</tr>
<tr>
<td>Genetic abnormalities</td>
<td>Homocysteine</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal estrogen deficiency</td>
</tr>
<tr>
<td></td>
<td>High carbohydrate intake</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
</tr>
<tr>
<td></td>
<td>Lipoprotein(a)</td>
</tr>
<tr>
<td></td>
<td>Hardened (trans) unsaturated fat intake</td>
</tr>
<tr>
<td><strong>Potentially Controllable</strong></td>
<td><em>Chlamydia pneumoniae</em></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
</tbody>
</table>
ROLE OF OXIDIZED LDL IN ATHEROGENESIS

1) Readily ingested by macrophages
2) Chemotactic for circulating monocytes
3) Increases monocyte adhesion
4) Inhibits motility of macrophages
5) Favours recruitment and retention of macrophages
6) Stimulates release of growth factors and cytokines
7) Cytotoxic to endothelial and smooth muscle cells
8) Immunogenic
ROLE OF MACROPHAGE INATHEROGENESIS

MACROPHAGE

IL-1, TNF, and MCP-1

Increases adhesion of leukocytes

Growth stimulators & inhibitors

Modulate the proliferation of SMCs
Deposition of ECM proteins

Toxic oxygen species

Oxidation of LDL
ROLE OF ENDOTHELIAL CELL IN ATHEROGENESIS

• Increase in the permeability of the wall to lipoproteins
• Acceleration of lipoprotein accumulation.
• Permit platelet interaction with the vessel wall
• Subsequent release of growth factors
• Allow the formation of thrombus on the surface
• Neovascularization in the shoulders of fibrous caps
PDGF                              NO
bFGF                              PGI2
IL-1                              IGF-1
TGF                               ox LDL

Endothelial cell

Antigens

PLASMA
Angiotensin
LDL

PDGF                      EGF
TGF
α
TGFβ
TxA2                       IGF-1
PLASMA

Antigens

SMOOTH MUSCLE CELL

IFNγ
TGFβ
TNFα
IL-1

T-LYMPHOCYTE

bFGF
IGF-1
IL-1
M-CSF
TGFβ
TNFα
PGE
HB-EGF
MCP-1
GM-CSF

Collagen
Elastic Fibers
Proteoglycans

Antigens

MACROPHAGE

Antigens

PDGF
bFGF
HB-EGF
TGFβ
TNFα
IL-1
PGE
oxLDL
ox LDL
MORPHOLOGY

• FATTY STREAK

• ATHEROMATOUS PLAQUE
  ➢ FIBROUS
  ➢ FIBROFATTY
  ➢ LIPID
  ➢ FIBROLIPID PLAQUES

• COMPLICATED PLAQUE
Fatty streak (collection of foamy macrophages in intima)
Components of intimal atheromatous plaque

**FIBROUS CAP**
- Smooth muscle cells
- Dense connective tissue
- Mixture of macrophages, smooth muscle cells, T lymphocytes

**NECROTIC CENTRE**
- Disorganised mass of lipid, cholesterol clefts, foam cells
- Thrombus

**MEDIA**
Gross-Atherosclerosis of aorta
<table>
<thead>
<tr>
<th>Nomenclature and main histology</th>
<th>Sequences in progression</th>
<th>Main growth mechanism</th>
<th>Earliest onset</th>
<th>Clinical correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I (initial) lesion</td>
<td>I</td>
<td>Growth mainly by lipid accumulation</td>
<td>From first decade</td>
<td>Clinically silent</td>
</tr>
<tr>
<td>Isolated macrophage foam cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type II (fatty streak) lesion</td>
<td>II</td>
<td></td>
<td>From third decade</td>
<td></td>
</tr>
<tr>
<td>Mainly intracellular lipid accumulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type III (intermediate) lesion</td>
<td>III</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type II changes and small extracellular lipid pools</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type IV (atheroma) lesion</td>
<td>IV</td>
<td></td>
<td>From fourth decade</td>
<td>Clinically silent or overt</td>
</tr>
<tr>
<td>Type II changes and core of extracellular lipid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type V (fibroatheroma) lesion</td>
<td>V</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid core and fibrotic layer, or multiple lipid cores and fibrotic layers, or mainly calcific, or mainly fibrotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type VI (complicated) lesion</td>
<td>VI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surface defect, hematoma-hemorrhage, thrombus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pathogenic events and complications of atherosclerosis

Pre-Clinical Phase
Usually young age

FATTY STREAK

NORMAL ARTERY

At lesion-prone areas, and accelerated by risk factors:
Endothelial dysfunction
Monocyte adhesion/emigration
SMC migration to intima
SMC proliferation
ECM elaboration
Lipid accumulation

FIBROFATTY PLAQUE

Cell death/degeneration
Inflammation
Plaque growth
Remodeling of plaque and wall ECM
Organization of thrombus
Calcification

ADVANCED/VULNERABLE PLAQUE

Clinical Phase
Usually middle age to elderly

Mural thrombosis
Embolization
Wall weakening

ANEURYSM AND RUPTURE

Plaque rupture
Plaque erosion
Plaque hemorrhage
Mural thrombosis
Embolization

OCCLUSION BY THROMBUS

Progressive plaque growth

CRITICAL STENOSIS
COMPLICATED ATHEROSCLEROSIS

• CALCIFICATION

• ULCERATION

• FOCAL RUPTURE (Atheroemboli)

• HEMORRHAGE

• SUPERIMPOSED THROMBOSIS

• ANEURYSMAL DILATATION
THROMBOEMBOLISM
AORTIC ANEURYSM
Effects of Myocardial Ischemia
Pathogenesis of acute coronary syndromes

NORMAL

Atherosclerosis

FIXED CORONARY OBSTRUCTION
(Typical angina)

Platelet aggregate

PLAQUE DISRUPTION

SEVERE FIXED CORONARY OBSTRUCTION
(Chronic ischemic heart disease)

Thrombus

MURAL THROMBUS WITH VARIABLE OBSTRUCTION / ? EMBOLI
(Unstable angina or acute subendocardial myocardial infarction or sudden death)

OCCLUSIVE THROMBUS
(Acute transmural myocardial infarction or sudden death)

ACUTE CORONARY SYNDROMES
Myocardial infarction
Also called as Heart Attack/ Myocardial Necrosis

- Death of cardiac muscle due to prolonged ischemia
  - Etiopathiogenesis
    1) Myocardial ischemia

  2) Role of platelets

  3) Tissue factor activates coagulation pathway-thrombus

  4) Non atherosclerotic causes

  5) Transmural vs Subendocardial infarcts
PATHOGENESIS OF MI

1. CORONARY ARTERY OCCLUSION
   Disruption of plaque-platelets exposed to subendothelial collagen, undergo adhesion, aggregation, activation, release of potent aggregators. Vasospasm stimulated.

2. VASOSPASM

3. EMBOLI --- atrial fibrillation, --- vegetative endocarditis, --- paroxysmal emboli

4. UNEXPLAINED
<table>
<thead>
<tr>
<th>Time</th>
<th>Gross Features</th>
<th>Light Microscope</th>
<th>Electron Microscope</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>REVERSIBLE INJURY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–½ hr</td>
<td>None</td>
<td>None</td>
<td>Relaxation of myofibrils; glycogen loss; mitochondrial swelling</td>
</tr>
<tr>
<td><strong>IRREVERSIBLE INJURY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>½–4 hr</td>
<td>None</td>
<td>Usually none; variable waviness of fibers at border</td>
<td>Sarcolemmal disruption; mitochondrial amorphous densities</td>
</tr>
<tr>
<td>4–12 hr</td>
<td>Dark mottling (occasional)</td>
<td>Early coagulation necrosis; edema; hemorrhage</td>
<td></td>
</tr>
<tr>
<td>12–24 hr</td>
<td>Dark mottling</td>
<td>Ongoing coagulation necrosis; pyknosis of nuclei; myocyte hypereosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate</td>
<td></td>
</tr>
<tr>
<td>1–3 days</td>
<td>Mottling with yellow-tan infarct center</td>
<td>Coagulation necrosis, with loss of nuclei and striations; brisk interstitial infiltrate of neutrophils</td>
<td></td>
</tr>
<tr>
<td>3–7 days</td>
<td>Hyperemic border; central yellow-tan softening</td>
<td>Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border</td>
<td></td>
</tr>
<tr>
<td>7–10 days</td>
<td>Maximally yellow-tan and soft, with depressed red-tan margins</td>
<td>Well-developed phagocytosis of dead cells; early formation of fibrovascular granulation tissue at margins</td>
<td></td>
</tr>
<tr>
<td>10–14 days</td>
<td>Red-gray depressed infarct borders</td>
<td>Well-established granulation tissue with new blood vessels and collagen deposition</td>
<td></td>
</tr>
<tr>
<td>2–8 wk</td>
<td>Gray-white scar, progressive from border toward core of infarct</td>
<td>Increased collagen deposition, with decreased cellularity</td>
<td></td>
</tr>
<tr>
<td>&gt;2 mo</td>
<td>Scarring complete</td>
<td>Dense collagenous scar</td>
<td></td>
</tr>
<tr>
<td>TIME</td>
<td>GROSS</td>
<td>MICRO</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------</td>
<td>--------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>12 Hrs</td>
<td>No changes</td>
<td>Coagulation necrosis: 12-18hrs</td>
<td></td>
</tr>
<tr>
<td>12-18Hrs</td>
<td>Slight Pallor -</td>
<td>Neutrophilic infilt</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contraction bands</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myocytolysis</td>
<td></td>
</tr>
<tr>
<td>4—5 DAYS</td>
<td>Pale, Firm, Well</td>
<td>Macrophages</td>
<td></td>
</tr>
<tr>
<td></td>
<td>defined</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 DAYS</td>
<td>yellow area</td>
<td>Granulation tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>red purple zone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 weeks</td>
<td></td>
<td>Collagen</td>
<td></td>
</tr>
<tr>
<td>8 weeks</td>
<td></td>
<td>Scar tissue</td>
<td></td>
</tr>
</tbody>
</table>
12-18 Hrs
12 to 18 hrs.
3--4 days
1 to 2 wks.
Light microscopic changes in MI

Changes during first 24 hrs

Changes during first 72 hrs

Changes by the end of first week
Coagulative necrosis with wavy fibres

Neutrophilic infiltrate 3-4days

Phagocytosis of necrotic myocytes 7-10days
Light microscopic changes in MI

Granulation tissue-loose collagen, abundant capillaries

Well healed infarct-dense collagenous scar
Old Myocardial infarct

Infarcted area shows ingrowth of inflammatory granulation tissue
MI healed-Grey white thinning at apex due to healed fibrous scarring
Changes in early infarcts

1) Electron microscopic changes
   - Evident in less than 30 min on onset of infarction
   - Disappearance of perinuclear glycogen granules within 5 min of ischemia
   - Swelling of mitochondria in 20-30 min
   - Disruption of sarcolemma
   - Nuclear alterations – peripheral nuclear clumping

2) Chemical and histochemical changes
   - Glycogen depletion
   - Increase in lactic acid
   - Loss of k+, increase in Na+
   - Influx of Ca++ into cells --- irreversible injury
Complications

1. **Arrhythmias** (most common)
2. **Congestive heart failure** ---40% deaths
3. **Cardiogenic shock** ---10% deaths
4. **Mural thrombosis and thromboembolism** ---12% deaths
5. **Rupture** ---5% deaths (ventricular wall, iv septum, papillary muscle)
6. **Acute Pericarditis** ---2nd day
7. **Postmyocardial infarction syndrome/Dresslers syndrome** ---1-6 weeks, autoimmune, fibrinous haemorrhagic pericarditis
8. **Infarct extension and expansion**
9. **Ventricular aneurysm** ---5% deaths (late complication)
10. **Progressive heart failure**
Complications

Anterior myocardial rupture

Rupture of ventricular septum
Complications

Complete rupture of necrotic papillary muscle  Fibrinous pericarditis
Complications

Antero apical infarct with wall thinning and mural thrombus

Large apical left ventricular aneurysm
Salvage in early infarcts and reperfusion injury

- Reversible -30 min
  1. Thrombolytic therapy-tPA-relieves only thrombus
  1. PTCA with stent-relieves thrombus+underlying plaque
  3. CABG-restores flow in blocked vessels

Complication-myonecrosis-Ca++,ROS

Gross-haemorragic infarct
Micro-contraction band necrosis
Consequences of myocardial ischemia following reperfusion

Contraction bands and haemorrhage
ENZYME CHANGES

• CK   Sensitive but not specific
  Rises in 2-4 Hrs
  Peaks in 24 Hrs
  Normal in 72 Hrs

• CK-MB More specific
  Rises in 4-8 Hrs
  Peaks in 18 Hrs
  Normal in 48-72 Hrs
• LDH & AST-useful only after 48 Hrs
• CARDIAC Troponin
  Troponin--I
  Troponin--T
Sensitivity similar to CK-MB

Elevated for 7-10 days

Marker for Unstable Angina

• SERUM MYOGLOBIN-preceedes CK-MB by 2-5 Hrs
  Increases in 2-6 Hrs
  Peaks in 8-12 Hrs
CHRONIC IHD

• Seen in ELDERLY
• Previous MI/ Bypass Surgery
• Severe obstructive coronary artery disease with or without acute or healed MI
Chronic ischemic heart disease/myocardial fibrosis/ischaemic cardiomyopathy

- Appears postinfarction due to functional decompensation of hypertrophied noninfarcted heart

Pathogenesis:

Healing of minute areas of focal myocytolysis

- loss of myofibrils but nuclei remain intact
- infiltrated by macrophages
- replaced by proliferation fibroblasts and collagen
Chronic ischemic heart disease-
MORPHOLOGY

- Gross-enlarged and heavy due to left ventricular hypertrophy and dilatation

- Discrete scars-healed infarcts

- Mural endocardium-patchy, fibrous thickening, mural thrombi

- Micro-Myocardial hypertrophy
  Diffuse subendocardial vacuolisation
  Fibrosis
Chronic ischemic heart disease-microscopy
SUDDEN CARDIAC DEATH

- Unexpected death from cardiac cause, either asymptomatic or early onset symptoms within 1 hr.
- Lethal arrhythmias
- Critical stenosis >75% lumen compromised
Lesions in Coronary artery in various forms of IHD

<table>
<thead>
<tr>
<th>Types of IHD</th>
<th>Coronary Lesion</th>
<th>Morphology</th>
<th>Clinical Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable angina</td>
<td>• Critical coronary narrowing (3/4th)</td>
<td>[Diagram A]</td>
<td>Nil</td>
</tr>
<tr>
<td>Chronic IHD</td>
<td>• Chronic progressive coronary atherosclerosis</td>
<td>[Diagram B]</td>
<td>Stable angina, CIHD</td>
</tr>
<tr>
<td>Unstable (pre-infarction) angina</td>
<td>• Plaque rupture, haemorrhage, ulceration</td>
<td>[Diagram C]</td>
<td>Plaque haemorrhage, unstable angina</td>
</tr>
<tr>
<td>Maocardial infarction</td>
<td>• Plaque haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fissuring and ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Complete mural thrombosisis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden ischaemic death</td>
<td>• Severe multivessel disease</td>
<td></td>
<td>Acute coronary syndromes</td>
</tr>
<tr>
<td></td>
<td>• Acute changes in plaque</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thrombosis with thromboembolism</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NON ATHEROMATOUS CORONARY ARTERY DISEASE

1) Congenital anomalies

2) Spontaneous dissection of coronary arteries

3) Arterial bridging

4) Coronary aneurysms
Spontaneous dissection of coronary arteries

Coronary aneurysms
THANK YOU