CARDIOVASCULAR DISORDERS:

ARTERIOSLLEROSIS:

- It is the general term for thickening & loss of Arterial wall elasticity.

→ It affect small arteries & Arterioles. - narrowing of lumen.

two types

Hyaline Atherosclerosis | hyperplastic

def: It is primarily a progressive disease of intima involving large-Medium sized elastic & Muscular Arteries.
It is characterized by focal lipid Rich intimal lesion called Atheromas.

→ Coronary Artery is an imp manifestation of Atherosclerosis

RISK FACTORS:

- High cholesterol level
- hypertension
- diabetes.
- smoking
- Receptor gene mutations.

Risk May be classified into modifable, non modifable, Additional

Modifable Major Risk factors

→ Hyperlipidemia → ↑LDL level (HDL help to mobilize cholesterol from the peripheral tissue to liver)
→ Hypertension
→ Cigratte → Strong dose linked Relationship b/w cigratte smoking & ischemic HD
→ Diabetes.

B) Non modifiable Risk factors

→ Inherited causes → familial hypercholesterolemia

→ Family history

→ Age → plaque is slow one.

→ Male gender → Premenopausal women have a lower Risk.

Other

→ Inflammation is observed during all stages of Atherogenesis & clearly Associated with the formation & Rupture of Atherosclerotic plaques

→ C Reactive Proteins → predict the Risk of Atherosclerosis-Related diseases

→ Herpes viruses, Cytomegaloviruses / Chlamydia pneumoniae have been found in Atheromatous plaques.

→ Hyperhomocysteinemia → Rare Autosomal Recessive Inborn error.

→ Stressful lifestyle

→ Alcohol consumption

PATHOGENESIS OF ATHEROSCLEROSIS

Several theories:

→ Imbibation hypothesis → focal Accumulation of lipid in a vessel wall is due to imbibition (transport) of plasma lipoproteins across intact endothelium

→ Encrustation hypothesis → small mural thrombi are formed at the site of endothelial damage.

↓ They organise to form plaques

→ Monoclonal hypothesis - single clone of smooth muscle migrates from the underlying media into the intima & then proliferates.

→ Response to injury hypothesis

ATHEROSCLEROTIC INJURY HYPOTHESIS:

1) Endothelial Injury: Etiological culprits → Endothelium injury → Endothelium is Activated → ↑ expression of Adhesion molecule, VCAM-1 → ↑ permeability to endothelium → Lipoprotein accumulate within intima.

Chemic endothelial Injury → Hypercholesterolemia, smoking, Hypertension, Virus, Immune Reaction, Toxin

→ Det vascular permeability → Platelet Adhesion And thrombus

⇒ Movement of low density lipoproteins

2) Migration of leukocytes: Monocytes & Lymphocyte cross endothelial barrier → Accumulate in subendothelial intimal space → Monocytes Become macrophages (when migrate to intima)

Activated macrophage form oxygen free Radicals → Cause oxidation of LDL → oxidized LDL ingested by Macrophage → form foam cells. → As their cytoplasm become foamy

3) Smooth muscle cell migration & proliferation:

Inflammatory cells in subendothelial intimal space

↓

Secrete cytokines (PDGF, TGF α, FGF)

↓

Migration of smooth muscle cells from Media to subendothelial intimal space

↓

Proliferation of smooth muscle cell in intima.

↓

Smooth muscle cell also ingest lipid.

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4.) Maturation of Plaque:

Smooth Muscle cells.

synthesize collagen in intima

↓

Mature fibrofatty Atheroma.

Cholesterol in the plaque is due to An imbalance b/w influx of efflux

MORPHOLOGY:

Fatty streaks → They may be the earliest appearing lesion of Atherosclerosis.

Gross → Multiple small flat yellow lesion in the intima.

may coalesce to form long streaks 1cm or more.

Microscopy → lipid filled foamy Macrophages.

ATHEROSCLEROTIC PLAQUE:

It protrude into the lumen.

Gross

site: Major vessels → Lower Ab Aorta, coronary, popliteal, ICA, circle of willis

color of nature → They r white to pale yellow. & are Raised Above the surrounding smooth intima.

If Any ulcerated plaque → Reel-brown.

Size & shape → 0.3 to 1.5 cm in diameter

irregular in shape with well defined Borders.

Distribution → patchy (focal) involve only a portion of involved Arterial wall.

Composition → soft, yellow, grumous core of lipid covered by white fibrous cap.

MICROSCOPY:

cell → include variable number of smooth muscle cells, Tcells, macrophages

ECM → include collagen, elastic fibre, proteoglycans.

lipid → both intra & extracellular.

1) superficial fibrous cap → composed of smooth muscle cells & collagen.

2) Necrotic core → deeply fibrous capsule

The extracellular cholesterol usually form crystalline aggregates that r washed out during routine tissue processing → This is seen as empty needle-shaped cleft like space → cholesterol

3) Shoulder → peripheral region beneath to the ends of cap. Cells.

3) foam cells

4) Necrotic debris

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CLINICOPATHOLOGICAL MANIFESTATIONS:

- Atherosclerotic stenosis:

→ They Reduce the size of the lumen of vessel lead to tissue ischemia — critical stenosis.

Consequences → effect → Arterial supply
Metabolic demand
lead to ischemic.
mesenteric occlusion
sudden cardiac death.
diminished perfusion of the extremities.

Acute Plaque change

① Rupture, ulceration or erosion of luminal surface of Atheromatous plaques.

② Hemorrhage into a plaque. →

③ Atheo embolism → microemboli

Vulnerable plaques → They have → necrotic centre
→ foam cell of extracellular lipid
→ thin fibrous caps
→ clusters of inflammatory cells.

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