Pathology of atherosclerosis

Dr: Salah Ahmed

Structure of the vascular wall:

Intima:

- consists of single layer of endothelial cells
- separated from media by internal elastic lamina

Media:

- consists of smooth muscle cells
- outer portion of media is separated from adventitia by external elastic lamina.

Adventitia :

- lies external to media
- consists of connective tissue with nerve fibers and vasa vasorum.

Atherosclerosis:

- Is characterized by formation of intimal lesions called atheromas (atheromatous, atherosclerotic plaques) that protrude into vascular lumen.
- Is a disease of large and medium sized blood vessels
- Responsible for:
1. Ischemic heart disease
- Myocardial infarction
- Angina pectoris
2. Cerebral infarction (stroke)
3. Gangrene of lower extremities, bowel

Risk factors of atherosclerosis:

- **Major**:

1- increasing age: Male >45, female >55 years
2- male sex
3- family history: family H of MI, stroke increases risk of AS
4- hyperlipidemia: formation of reactive O2 species
i- LDL (bad cholesterol):
- transports cholesterol in blood
- has a role in delivering cholesterol to the tissues
- increased levels associated with increased risk of AS
ii- HDL (good cholesterol):

- mobilize cholesterol from tissues (atheroma)
- increased levels associated with low risk of AS

5-hypertension:

- Induces mechanical injury to vessel wall

6- cigarette smoking:

- enhances atherosclerosis by damaging endothelial cells

7- diabetes mellitus:

- induces hypercholesterolemia, enhancing AS.

1- associated with increased risk of MI
2- associated with increased risk of stroke
3- associated with increased risk of gangrene of lower extremity

- Minor :

1- obesity
2- physical inactivity
3- stress
4- postmenopausal oestrogen deficiency
5- high carbohydrate intake
6- fat intake

Pathogenesis:

Response-to- injury hypothesis:

1- endothelial cell injury, caused by:

1- hyperlipidemia: increasing the production of reactive oxygen species

2- hemodynamic disturbances: disturbed flow: turbulence

3- cigarette smoke: accumulates CO with formation of carboxyhemoglobin that causes hypoxia and injury

4- hypertension: mechanical injury

5- toxins

6- infectious agents

7- homocysteine

2- EC injury causes endothelial dysfunction:

- increasing permeability
- expression of leucocytes adhesion molecules

3- Blood monocytes and platelets adhesion to damaged EC:

- monocytes adhere to damaged EC, migrate into intima and transform into macrophages
- platelets adhere to damaged EC, activated
- lipoproteins (LDL) accumulate into vessel wall at area of EC injury.
- activated platelets, macrophages, release growth

factors (e.g. PDGF) that cause migration of smooth muscle cells (SMC) to intima.
- macrophages accumulate lipid and become foam cells

4- SMCs and macrophages engulf lipid:
- the lipids accumulate within the cells and extracellularly

- development of fatty streak: accumulation of lipid-containing macrophages

5- development of atheroma
- SMC proliferate in intima and produce extracellular matrix (collagen and proteoglycans)
- Lipid deposition extracellularly and so formation of plaque, has two parts:
1- fibrous cap: (collagen, SMCs)
2- necrotic core: (lipid, debris, fibrin, foam cells)

6- advanced plaque formation
- macrophages release cytokines, oxygen radicals, growth factors cause lesion progression increase in size and subsequent development of complications

Morphology:
1- Fatty streaks:

- are flat or slightly raised yellow intimal lesions
- are composed of lipid-laden macrophages
- begin as multiple small spots that fuse into elongated one
- present at ostia of branch vessels
- do not cause any disturbance in blood flow
- may progress to atheroma but not all streaks do so
- present in all ages including newborn

2- Fibrofatty plaques (atheroma):

- raised on lumen white to yellow intimal lesions
- atheroma composed of: (3 components)

1- cells: SMCs, macrophages, T-cells

2- ECM: collagen, proteoglycan, elastic fibers

3- intracellular and extracellular lipid

- common in abdominal aorta, coronary arteries, popliteal artery internal carotid artery and arteries of circle of Willis
- it continues to change and enlarge (debris, ECM, thrombi)

Consequences of atheroma:

1- rupture, ulceration … thrombi formation
2- atheroembolism: ruptured plaques
3- aneurysm: ischemic atrophy, loss of elastic fibers and weakening of wall
4- hemorrhage into plaque: rupture of cap or newly formed vessels with hematoma formation
5- calcification
6- protrusion into lumen, narrowing lumen and obstructing flow: ischemic infarction

atherosclerosis in the aorta: **A:** Mild atherosclerosis (*arrow*)
B: Severe disease with diffuse and complicated lesions

Hemorrhage (ruptured atherosclerotic aneurysm)

Bowel gangrene
Lower limb gangrene
Thank you