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