Pathology of atherosclerosis

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 **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