Vascular Disease

I. Arteriosclerosis – “Hardening of the Arteries”
Four types of arteriosclerosis:
A. Atherosclerosis
B. Monckeberg’s Medical Calcific Sclerosis
C. Fibromuscular intimal hyperplasia
D. Arteriolosclerosis – Hypertension Induced

II. Atherosclerosis
A. Involves
   1. Elastic Arteries
      i. Aorta (abdominal >> thoracic)
      ii. Carotid
         iii. Iliac, popliteal
   2. Muscular Arteries
      i. Coronary
      ii. Circle of Willis
      ii. Mesenteric/Renal arteries involved at ostia
B. Risk Factors/Pathogenesis– full discussion refer to Dr. Kahn’s lecture “Atherosclerosis, Hyperlipidemia”

C. Morphology of Atheroma:
   Atheromas consist of
   1. Fibrous cap
      i. Composed of smooth muscle cells, dense connective tissue
   2. Cellular area beside cap
      i. Composed of macrophages, smooth muscle cells, T-lymphocytes
   3. Necrotic Core
      i. Contains lipid, cholesterol clefts, cellular debris, lipid laden foam cells, plasma proteins, fibrin.
   4. Periphery of lesion
      -Has foci of neovascularization (new blood vessel formation)

E. Fatty Streak
   1. May be a precursor of atheromatous plaque
   2. Fatty streaks are yellow, flat lesions composed of lipid laden foam cells, T-lymphocytes, extracellular debris
   3. They are present in some infants <1 year old, founds in all persons >10 years old

F. Advanced atherosclerotic plaques may develop
   1. Rupture/ulceration/erosion
2. Emboli (cholesterol emboli or atheroemboli) – reminder we introduced this topic during block 1 Disorders of Circulation lecture

3. Hemorrhage
4. Thrombosis
5. Weakening of media and aneurysmal dilatation
6. Calcification, progressive growth, luminal occlusion

G. Complications of atherosclerosis include

1. Myocardial ischemia
   i. Angina, infarcts, sudden death
2. Cerebral ischemia
   i. TIA, stroke
3. Peripheral vascular disease
   i. Claudication, gangrene
4. Aneurysms
   i. Rupture

III. Monckeberg’s Medial Calcific Sclerosis
   A. Finding: Calcific deposits centered in internal elastic lamina and media of medium sized muscular arteries (the intima is not involved)
   B. The lesions are nonobstructive – does not obstruct blood flow.
   C. If the calcification is extensive, the arteries affected may be palpated or seen on plain radiographs

IV. Fibromuscular Intimal Hyperplasia
   A. Develops in muscular arteries larger than arterioles
   B. Characterized by smooth muscle cell and extracellular-matrix rich lesions resulting in intimal thickening
   C. Driven by inflammation or mechanical injury
      a. Inflammation – transplant-associated arteriopathy, healed arteritis (ie giant cell arteritis)
      b. Mechanical injury - associated with stents, balloon angioplasty
   D. Result of substantial stenosis of vessel by the intimal thickening leading to

V. Hypertension Induced Arteriolosclerosis
   Affects small arteries and arterioles
   2 forms – hyaline arteriolosclerosis and hyperplastic arteriolosclerosis
   A. Hyaline Arteriolosclerosis
      1. Seen in patients with hypertension, diabetes (can also be seen in normotensive elderly individuals)
      2. Findings: Homogeneous pink hyaline thickening of arterioles and luminal narrowing resulting from plasma protein leakage across injured endothelial cells and increased smooth muscle cell matrix in response to hemodynamic stress.
“hyaline” – general definition: appearing glassy pink on H&E stain
3. The luminal narrowing ultimately impairs blood supply to affected organs ie kidney (benign nephrosclerosis), brain

B. Hyperplastic Arteriolosclerosis
1. Seen in severe hypertension
3. The process results in lumenal narrowing and potentially end organ ischemia
4. With Malignant Hypertension (rapidly rising blood pressures – usually systolic >200, diastolic >120), in addition to hyperplastic changes, see development of necrosis
   - “necrotizing arteriolitis” or “fibrinoid necrosis”
   
   Fibrinoid necrosis refers to plasma proteins that leaking into the wall of damaged vessels producing a bright pink, amorphous appearance on H&E stained sections called fibrinoid (fibrinlike) by pathologists

VI. Aneurysms
A. Definition of “aneurysm”– localized abnormal dilatation of blood vessel
B. Pathogenesis
1. Abnormal connective tissue synthesis
2. Excessive tissue degradation (increased matrix metalloproteinase activity)
3. Loss of smooth muscle cells
C. Etiology
1. Two most important disorders predisposing to aortic aneurysms are atherosclerosis and hypertension.
2. Other conditions predisposing to the development of aneurysms– Marfan syndrome, Ehlers-Danlos syndrome, vitamin C deficiency, infections, trauma, congenital (ie berry aneurysms)

VII. Abdominal Aortic Aneurysm
A. Etiology
1. Most common etiology is atherosclerosis

B. Pathogenesis
1. Matrix metalloproteinase (MMP) production by inflammatory cell infiltrates involved in the pathogenesis of atherosclerosis plays a key role
2. Also, atheromas compress the aortic media, compromise nutrient and waste diffusion from the vascular lumen into the arterial wall.
3. As a result of both factors above, the media undergoes degeneration and necrosis leading to overall arterial wall weakness and thinning.

C. Pathology
1. Most often located infrarenal and above aortic bifurcation
2. May be saccular (spherical outpouching, involves only a portion of the vessel wall) or fusiform (diffuse circumferential dilation of a long vascular segment)

C. Clinico-pathologic correlation
- On physical exam may be noted as a pulsatile abdominal mass
- May impinge on adjacent structures (ie. ureter, vertebra)
- May have downstream embolism of atheroma or mural thrombus
  
Rupture
- Related to size: 4-5cm risk of rupture 1%/year; 5-6 cm risk of rupture 11%/year; >6cm risk of rupture 25%/year

VIII. Aortic Dissection
A. Pathology
1. Aortic dissection refers to an intimal tear of the aorta
2. Blood then enters media of aorta
3. A blood filled channel (“false lumen”) is created within the aortic media (usually between middle and outer thirds)

B. Classification
1. Type A (DeBakey type I and II)
   i. Proximal lesions involving ascending aorta only or ascending and descending aorta
1. Type B (DeBakey type III)
   i. Distal - do not involve ascending aorta (usually begin distal to the subclavian artery)

C. Etiology
1. Hypertension (>90% of cases)
   Contributing factors: Pressure related mechanical or ischemic injury; Medial hypertrophy of the vasovasorum; Degenerative changes of the media, loss of smooth muscle cells
2. Systemic or localized connective tissue abnormality ie medial degeneration (seen in Marfan’s syndrome)

D. Clinico-pathologic correlation
1. Classic clinical presentation – sudden onset of ripping chest pain radiating to the back
   (chest x-ray shows mediastinal widening)
2. Complications
   i. Rupture
   ii. Retrograde extension toward aorta
   iii. Distal extension
3. Treatment
   
i. Aggressive blood pressure control
   
   \[\beta\]-Blockers are the preferred initial antihypertensive agent because they reduce both blood pressure and heart rate
   
   Why? anti-impulse therapy in the form of blood pressure lowering and decreasing the velocity of left ventricular contraction decreases aortic shear stress and minimizes the tendency for the dissection to propagate
   
   ii. Surgical intervention for acute proximal dissection and selected cases of distal dissection

Self-Study

IX. Select Vascular Neoplasms
   
   A. Angiosarcoma
      
      a. Highly malignant neoplasm of endothelial cell origin
      
      b. Can develop anywhere – most commonly skin, soft tissue, breast, liver
         
         i. Hepatic angiosarcoma – associated with carcinogen exposure: arsenic, thorotrast, vinyl chloride
         
         ii. Angiosarcoma associated with lymphedema – most common scenario is development in upper extremity post mastectomy/lymph node dissection for breast cancer
      
      c. Histologically characterized by atypical endothelial cells forming vascular channels
      
      d. Endothelial origin of cells can be demonstrated by immunohistochemical staining for CD 31 and von Willebrand factor
         
         i. Particularly useful with poorly differentiated (anaplastic) tumors
   
   B. Hemangiomas
      
      a. Benign
      
      b. Composed of vessels filled with blood, lined by endothelial cells
      
      c. Common benign neoplasm of infancy, childhood (some regress as child grows)
      
      d. Multiple sub-types
Practice Questions

1. A 57-year old man with hyperlipidemia, HTN and diabetes mellitus type 2 presents with crushing substernal chest pain. He undergoes urgent coronary angiography which shows an atherosclerotic left circumflex coronary artery with an occluded lumen. The cardiologist suspects acute plaque rupture. The material that has occluded the vessel is likely composed of which of the following cellular components?

   A. Activate endothelial cells
   B. Lipid-laden (foamy) macrophages
   C. Multinucleated giant cells
   D. Platelets and red blood cells
   E. Segmented neutrophils

2. A 35-year old woman develops the “worst headache of my life” and then loses consciousness. A CT scan of the brain reveals subarachnoid hemorrhage. The etiology of the hemorrhage is a ruptured berry aneurysm. The pathogenesis of this vascular abnormality is most closely linked to which of the following conditions?

   A. Atherosclerosis
   B. Congenital defect of the arterial wall
   C. Cystic medial necrosis
   D. Endarteritis of the vasa vasorum
   E. Fibrinoid necrosis

Answers

1-D; 2-B