Primary Cast Episode 2 - Cardiovascular Pathology

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1. Abdominal Aortic Aneurysm

What is an aneurysm?
Abnormal dilatation in an artery due to weakness on the vessel wall

What are the risk factors for abdominal aortic aneurysm?
Most significant are HTN and atherosclerosis. Others include being male, smoking, age > 60s, FHx, Connective tissue disease i.e. Marfans, Ehlers-Danlos, vasculitis, diabetes, trauma, congenital abnormalities of the aorta, infection and inflammation.

What are the most common causes of AAA?
- Atherosclerosis
- Congenital disease
- Mycotic
- Immunological
- Syphilis
- Trauma
- Salmonella

What are the morphological features of an abdominal aortic aneurysm?
- Localised dilatation of the abdominal aorta
- Usually between the renal arteries and the bifurcation of the aorta into iliac arteries
- Aneurysm often contains atheromatous ulcers covered with mural thrombi, with associated thinning and destruction of the media

Describe the pathogenesis of an aneurysm
- Aneurysms occur when the structure or function of the connective tissue within the vascular wall is compromised.
- Atherosclerotic plaque in the intima, compresses the media, causing degradation.
- This leads to cystic medial degeneration.
- There is local inflammation, proteolytic enzymes degrade the collagen, there is involvement of matrix metalloproteinases
- This results in loss of vascular smooth muscle cells, and
- Inappropriate synthesis of non-elastic extracellular matrix

What are the clinical consequences of an aneurysm?
- Painless mass
- Rupture - risk is increased with a diameter >5cm - haemorrhage can be retroperitoneal or intraperitoneal
- Obstruction - of branches such as mesenteric, vertebral or renal arteries

- Embolism of plaque or thrombus
- Impingement or compression of adjacent structures
- Infection or mycotic aneurysm.

What is the risk of rupture of an AAA?

It is related to size

- <4cm negligible
- 4-5cm 1% per year
- 5-6cm 11% per year
- >6cm 35% per year

2. Aortic dissection

What are the risk factors for aortic dissection?

- Male sex
- Age 40-60
- Hypertension
- Connective tissue disorders i.e. Marfan's
- Iatrogenic: complication of arterial cannulation, coronary artery bypass
- Trauma

Describe the pathogenesis of an aortic dissection.

- Hypertension with medial hypertrophy of vasa vasorum and degeneration of the media
- and/or connective tissue disease (inherited or acquired)
- These cause weakness in the media
- Dissection begins with an intimal tear and blood dissects into a tear in the media either distally or proximally within the media

How are dissections classified?

By the site of involvement

- Stanford - Type A is proximal, type B distal
  OR
- Debakey I - ascending and descending, II ascending only, III descending only

What are the potential consequences of aortic dissection?

- Rupture back into the intima or out through the adventitia
- Rupture out or into the pericardial, pleural or peritoneal cavities
- Cardiac tamponade, aortic insufficiency via involvement of the aortic valve, MI, distal or spinal cord ischaemia via dissection into renal, mesenteric, femoral or spinal vessels
- Death

3. **Aortic Stenosis**

What are the pathological consequences of aortic stenosis?

- Concentric left ventricular hypertrophy
- LV outflow obstruction
- Angina/Myocardial ischaemia in the absence of CAD
- Syncope
- Aortic dissection
- Heart Failure
- Endocarditis (uncommon)

What are the causes of aortic stenosis?

- Calcific/degenerative
- Bicuspid valve
- Rheumatic heart disease

What clinical signs may differentiate calcific aortic stenosis from rheumatic aortic stenosis?

- Rheumatic disease typically involves more than one valve
- So the absence of MS/MR and the absence of aortic regurgitation are more suggestive of calcific aortic stenosis

What are the predisposing factors for calcific aortic stenosis?

- Age - over 70 for normal valve
- Wear and tear, chronic injury to the valve
- Bicuspid valve or other congenital abnormality
- Hyperlipidaemia
- Hypertension
- Inflammation

What are the potential complications of a congenital bicuspid aortic valve?

- Major: Calcification and stenosis
- Others: regurgitation, infective endocarditis, aortic dilatation, dissection

4. **Atherosclerosis**

What are the systemic and local factors that lead to atherosclerosis?

Systemic

- Hypertension
- Hyperlipidaemia
- Smoking
- Hyperhomocysteinemia
- Infection
- Inflammation and inflammatory cytokines

Local

- Haemodynamic disturbances i.e. turbulence at branch points
- Endothelial dysfunction

Which arteries are most often affected by atherosclerosis?

- Lower abdominal aorta
- Coronary arteries
- Popliteal arteries
- Internal carotids
- Vessels of the Circle of Willis

Outline the steps involved in the pathogenesis of atherosclerosis

- Endothelial injury and dysfunction
- LDL accumulation and oxidation in the vessel wall
- Monocyte adhesion and migration into the intima and transformation into foam cells & macrophages
- Platelet adhesion
- Smooth muscle cell migration from media to intima
- Smooth muscle cell proliferation in the intima
- Enhanced lipid accumulation within the intimal cells

Describe the difference between a stable and unstable plaque

- Stable: Dense collagen, thick fibrous cap, minimal inflammation, small atheromatous core.
- Unstable: Thin fibrous cap, increased inflammation, large lipid core

How does an atherosclerotic plaque suddenly cause symptoms?

- **Rupture, ulceration or erosion** of the intimal surface of the plaque
  Exposes the blood to underlying thrombogenic substance and triggers **thrombosis**
  The thrombus can partially or completely occlude the lumen and lead to downstream ischaemia
- **Haemorrhage** into plaque via rupture of the fibrous cap can cause intra-plaque expanding volume haemorrhage which occludes the vessel
- **Atheroembolism** - plaque rupture can discharge atherosclerotic debris into the bloodstream producing microemboli
- **Aneurysm formation -** via atherosclerosis induced pressure atrophy of underlying media, causing weakness of vessel wall, dilatation and potentially rupture of the vessel.

5. Cardiomyopathy

What is the definition of cardiomyopathy?

- Heterogenous group of diseases of the myocardium
- Associated with mechanical and/or electrical dysfunction
- Usually inappropriate ventricular hypertrophy or dilatation
- Divided into primary (congenital or acquired) or secondary (where myocardium is affected as a component of systemic, multisystem disorder)

What are the types of cardiomyopathy and some causes of each type?

- **Hypertrophic** - 75% is genetic, autosomal dominant
- **Dilated -** alcohol, myocarditis (infective, autoimmune), ischaemic, drugs (chemotherapy), idiopathic, peripartum, genetic,
- **Restrictive -** Infiltrative i.e. amyloidosis, sarcoidosis; non-infiltrative i.e. idiopathic, scleroderma

How do dilated and hypertrophic cardiomyopathy differ?

- Dilated - cardiac dilatation, poor LVEF (<40%) systolic dysfunction/impaired contractility
- Hypertrophic - Myocardial hypertrophy, normal of high LVEF, impared compliance (diastolic dysfunction)

What are some of the pathological consequences of dilated cardiomyopathy?

- Valve dysfunction (mitral and tricuspid most common)
- Mural thrombi with embolisation
- Arrhythmia
- Atrial fibrillation
- Death from progressive failure

What are the pathological features of hypertrophic cardiomyopathy?

- Macroscopic: Hypertrophy without dilatation, asymmetrical hypertrophy, LV outflow obstruction
- Microscopic: Myocyte hypertrophy, disarray of myocytes and interstitial fibrosis

What are the complications of HOCM?

- AF, CCF, sudden cardiac death

6. Cor Pulmonale

What is cor pulmonale?

- Right sided heart failure that is not due to left sided heart failure
- Acute - massive PE
- Chronic - Chronic lung disease

What are the common causes of cor pulmonale

- Anything that causes pulmonary hypertension
- Disease of pulmonary parenchyma - COPD, fibrosis, bronchiectasis
- Disease of pulmonary vessels - Pulmonary HTN, recurrent PE, pulmonary arteritis
- Disorders of chest movement - marked obesity, kyphoscoliosis, neuromuscular disorders
- Disorders causing pulmonary artery constriction - hypoxaemia, metabolic acidosis, chronic sleep apnoea, altitude sickness

What are the major morphological features of pulmonary hypertension?

- Pulmonary congestion is minimal but systemic and portal systems may be engorged
- Heart - RV hypertrophy and dilatation, leftward bulging of septum
- Liver/portal system - hepatomegaly, centrilobular necrosis, congestive splenomegaly
- Effusions and ascites within pleural, pericardial and peritoneal spaces
- Subcutaneous oedema in peripheries and dependent portions of the body

7. Infective Endocarditis

What factors predispose to infective endocarditis?

Host Factors

- Bacteraemia - recent dental work, loss of skin integrity
- IVDU
- Immunodeficiency
- Drug induced immunosuppression
- Malignancy
- Neutropaenia
- Diabetes
- Alcohol excess

Cardiac Factors

- Degenerative MV prolapse
- Calcific aortic stenosis
- Bicuspid aortic valve
- Prosthetic valves
- Congenital valve defects
- Rheumatic heart disease

Which organisms commonly cause endocarditis?

- Strep viridans
- Staph aureus
- Staph Epidermidis

- Enterococci
- Gram negative bacilli
- HACEK organisms (Haemophilis, Actinobacillus, Cardiobacterium, Eikinella, Kingella)
- Fungal

What are the complications of endocarditis?

Local

- Erosion/destruction of tissue/valve
- Abscess formation (ring abscess)

Systemic

- Septic infarcts to brain, lung, kidneys
- Mycotic aneurysm
- Embolic phenomena - janeway lesions, roth spots (retina)
- Immune mediated glomerulonephritis

8. Heart Failure

What is heart failure?

When the cardiac function is impaired and/or the heart is unable to maintain a cardiac output sufficient to meet the body's metabolic needs.

Please classify the types of heart failure

By type of pump failure

- **Systolic dysfunction (Inability to contract)**
  - Myocardial ischaemia
  - Acute MI
  - Pressure or volume overload (hypertension)
  - Dilated cardiomyopathy
- **Diastolic dysfunction (Inadequate filling)**
  - LV hypertrophy
  - Myocardial fibrosis
  - Amyloidosis
  - Pericarditis
- **Others**
  - Arrhythmias
  - Valvular disease
  - Outflow obstruction i.e. AS
  - Regurgitant flow
  - HOCM

What are the clinical features of heart failure?

- Respiratory - dyspnoea, orthopnoea, PND, APO, Pleural effusions
- Cardiac - 3rd HS or gallop rhythm, displaced apex beat, AF, murmur, JVP elevation
- Renal - activation of the RAAS resulting in fluid retention, peripheral oedema and AKI
- CNS - Confusion secondary to hypoxia
- Hepatic - engorgement, ascites, cirrhosis (late)

What are the pathological changes seen in the liver caused by heart failure?

- Nutmeg liver
- Centrilobular necrosis (from central hypoxia)
- Centrilobular fibrosis
- Cirrhosis

9. Hypertension

How is hypertension classified?

- Primary (or essential)
- Secondary

What factors are thought to contribute to primary or essential HTN?

- Multiple genetic polymorphisms and interacting environmental factors
- Genetic - Familial, multiple gene-foci, genetic disorders altering Na handling
- Vasoconstrictive influence - structural changes cause increased peripheral vascular resistance which leads to HTN
- Environmental factors - tress, obesity, smoking, lack of physical activity and high salt intake

What are the long term consequences of essential HTN?

- HTN is a major risk factor for atherosclerosis
- CAD
- Cerebrovascular disease
- Aortic dissection
- Renal failure
- Cardiac hypertrophy + failure
- Multi-infarct dementia
- Retinal changes

What are some causes of secondary HTN?

- Renal
    - Acute GN
    - CKD
    - PCKD
    - Renal artery stenosis

    - Renal vasculitis
    - Renin-producing tumours
- Endocrine
    - Adrenocortical hyperfunction - cushings, hyperaldosteronism, CAH, Conn Syndrome
    - Exogenous hormones - glucocorticoids, oestrogens, MAOis, sympathomimetics
    - Pheochromocytoma
    - Acromegaly
    - Hypo or Hyperthyroidism
    - Pregnancy induced HTN
- Cardiovascular
    - Aortic coarctation
    - Increased intravascular volume
    - High cardiac output
- Neurological
    - OSA
    - Raised ICP
- Psychogenic
    - Acute stress
    - Surgery
    - Pain

What are the clinical features of malignant HTN?
Severe HTN systolic >200 diastolic >120 plus features of end organ dysfunction, such as:

- Renal failure
- Encephalopathy
- CVS abnormalities
- Retinal haemorrhages / papilloedema
- Often superimposed on previous benign HTN
- Rapidly rising BP

What morphological changes are seen in hypertensive heart disease?

- Thickened LV wall
- No dilation
- Left atrial enlargement
- Increased weight of the heart

What are the pathological consequences of hypertensive heart disease

- Stiff ventricle
- Impared diastolic filling
- Atrial dilatation and atrial fibrillation

- Heart failure
- Sudden cardiac death

10. Acute coronary syndrome

What is acute coronary syndrome?

ACS is a clinical manifestation of ischaemic heart disease and can present as unstable angina, NSTEMI, STEMI or sudden cardiac death

Describe the pathogenesis of myocardial infarction due to atherosclerosis

- Acute plaque change
  - rupture/fissuring/erosion/ulceration or haemorrhage into the atheroma
- Thrombus formation
  - Platelet adhesion, aggregation and microthrombi formation
  - Platelet release of mediators causing vasospasm
  - Activation of coagulation cascade leading to thrombus
- Vasoconstriction, stimulated by:
  - Circulating adrenergic agonists
  - Locally released platelet contents
  - Endothelial dysfunction causing reduced NO
  - Perivascular inflammatory mediators
- Vessel occlusion, leading to
  - Decreased myocardial blood flow
  - Myocyte necrosis

Following an acute MI, what complications might a patient have?

- Contractile dysfunction causing hypotension and shock
- Arrhythmias i.e. sinus bradycardia, AF, heart block, tachycardia, VT, VF
- Myocardial rupture: ventricular free wall, septum, papillary muscles
- Ventricular aneurysm
- Pericarditis or Dresler's syndrome
- Infarct expansion
- Papillary muscle dysfunction
- Progressive heart failure

Describe the time course of myocardial injury after acute coronary occlusion
Reversible

- Cessation of aerobic metabolism (immediately)
- Loss of contractility (2 mins)
- Decreased ATP production (down to 50% in 10 mins, 10% in 40 mins)
- Lactic acid production
- Structural changes - cell and mitochondrial swelling, myofibrillar relaxation

Irreversible (20-40 mins)

- Myocyte injury, sarcolemma disruption, cell membrane rupture (>30 mins)
- Initially subendocardial and then transmural myocyte death
- Microvascular injury (1 hour)
- Coagulation necrosis (>2 hours)

11. Pericarditis

Describe the clinical feature of pericarditis

- Chest pain - typically positional, pleuritic
- Fever
- Congestive cardiac failure
- Pericardial friction rub
- Constrictive pericarditis - muffled heart sounds, raised JVP

What are the causes of pericarditis

- Infectious - viral, pyogenic bacteria, TB, fungal
- Immune mediated: Rheumatic fever, SLE, Scleroderma, post cardiotomy, Dressler's syndrome post MI, drug hypersensitivity
- Others: MI, uraemia, neoplastic, neoplastic, trauma, radiation

What types of pericardial fluid exudate occur?

- Serous - non infectious inflammation i.e. SLE. Also viral, uraemia, tumours
- Fibrinous - post MI, trauma, post surgery but also sometimes infectious
- Purulent/Suppurative - bacterial invasion from local infection, lymphatic or blood seeding, surgical
- Haemorrhagic - rupture, dissection,
- Caseous - TB