CARDIOVASCULAR SYSTEM

MUSEUM CATALOGUE

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INTRODUCTION

Cardiovascular disease is an extremely common and important cause of morbidity and mortality in the western world. It is the leading underlying cause of death accounting for around 40% of all deaths in Australia. Overall approximately half of those deaths are due to ischaemic heart disease with cerebrovascular disease (mainly infarction and haemorrhage - both causing stroke) being the second greatest single killer and the leading cause of long-term disability in adults.

The normal heart weight in the adult varies with body weight. However, it averages approximately 250-300g (fixed weight) for females and 300 to 350 (fixed weight) for males.

HOW TO USE THIS CATALOGUE

This catalogue can be used as a tool to develop your knowledge, as well as provide an opportunity for revision.

It is divided into:

- Introduction and approach to specimens (pages 2-4).
- Index (pages 5-9). Examples of specific diagnoses can be found via the index.
- Core and classic disease processes (pages 10-38). This gives examples and discussion of core and/or classic diseases of the cardiovascular system. These are the specimens that students should focus on being able to identify initially. However, it depends to some extent on what you have covered in lectures and practical classes or resource sessions as to what you should know. Some of the specimens and discussion are directed more towards clinical medical students.
- Main catalogue (pages 39-83). This section covers the specimens in numerical order. Questions and/or comments accompany some of the specimens to help you expand your knowledge. In order to fit more specimens in the museum, not all of the pots are in numerical order on the shelves, and large specimens are often found on the bottom shelves.

You might find it useful to work quietly with a few friends and to have a few textbooks handy (e.g. pathology, medical, anatomy). As well as learning pathology, you will also find that you can learn and revise some anatomy and clinicopathological correlation from the specimens and information given.

You do not have to examine every specimen in the museum. However, just as in clinical practice, you will not become proficient in diagnosing something if you have only seen one case. Exposure to a variety of cases (specific diagnoses can be found via the index) to experience the variability in morphology will help your learning greatly. In general the red and blue dots on the pots indicate basic and straightforward pathology, whereas yellow dots tend to indicate less readily diagnosable conditions. This is not a hard and fast rule, and you will find yellow dot specimens turning up in resource sessions/practical classes and even exams, if they represent classic pathology.

As some of these specimens are very old (some up to 80 years), some of the investigations and treatments mentioned may be out of date.

In general

- read the clinical information given
- look at the entire specimen, not just the front
- identify and orientate the organ or tissue
- from your knowledge of pathology (which will come with time) look for relevant features to help you make the diagnosis. Of course to appreciate the abnormal you first need to have an appreciation of normal anatomy to be able to recognise and orientate the organ/tissue and the abnormalities
- make a diagnosis or differential diagnosis using any clinical information given to you – it is often relevant – sometimes the diagnosis is only made with a knowledge of the clinical features. Even when you know the diagnosis, attempt to identify relevant features in the specimen and understand why this is the diagnosis.
- attempt to correlate the pathological features with the clinical features (clinico-pathological correlation) i.e. explain how the pathological features have caused the patients symptoms and signs (when relevant)
- try to answer any questions presented yourself before reading the answers.

You may prefer to look at the specimen 'blind', without reading the clinical information given first.

In relation to pathology pot specimens in examinations, you may be asked

- for a diagnosis
- for a description
- about the predisposing factors and/or causes of the disease
- about the pathogenesis of the disease
- about the potential complications of the disease and how they arise
- to explain a patient's clinical symptoms and signs or investigation results in light of the pathological abnormalities present
- to describe the expected histological abnormalities in the abnormal areas

or other searching questions that we can concoct.

APPROACH TO CARDIOVASCULAR PATHOLOGY SPECIMENS

Students are expected to be able to give a brief succinct description of relevant macroscopic features of a specimen using appropriate terminology, as well as to arrive at a diagnosis or differential diagnosis. Even if not asked for a description, identification of relevant features is helpful in the diagnostic process. Your descriptive skills will improve with practice.

In any aspect of medicine, one needs to approach things in a systematic manner, otherwise important points may be omitted.

- Read the clinical history, it will often provide relevant information
- Look at the front of the pot first (i.e. the one with the number and the dot), but always make sure to look at the back and sides as well.
- Identify and orientate the specimen and identify and describe the abnormality.

Heart

The heart specimens are mainly either cross sections through the ventricles or pretty much the complete heart opened through a ventricle or atrium. The specimen is not necessarily orientated so that its front is at the front of the pot. You should thus be able to orientate the specimen – distinguish right ventricle from left ventricle, front from back, left atrium from aorta, and identify the valves (mitral and tricuspid with chordae tendineae and papillary muscles) etc. Remember that a knowledge of normal anatomy (and histology) is vital.

The left ventricle (LV) has a circular chamber and a wall of approx. 1-1.5cm in thickness in cross section. The interventricular septum is morphologically part of the LV. The right ventricle (RV) partly surrounds the LV in a crescentic shape, and its wall is thinner, approx. 0.5cm in thickness.

On the cross sections, medical students should be able to distinguish the front from the back of the specimen. The anterior surface of the heart tends to be more curved than the posterior (or inferior surface which sits on the diaphragm) and there is usually more adipose tissue in the epicardium anteriorly than posteriorly. You should also be able to recognise which areas are supplied by which arteries.

- the left anterior descending (LAD) coronary artery supplies the anterior LV, the apex, the anterior 2/3 of the interventricular (IV) septum (approx. 50% of LV mass) and the anterior RV
- the left circumflex coronary artery supplies the lateral LV (and posterior LV in approx. 20% of people) and the left atrium (LA)
- the right coronary artery supplies the posterior/inferior LV, the posterior 1/3 of the IV septum (30-40% of LV mass), the right atrium (RA), the atrioventricular (AV) node and the bundle of His

The 3 main coronary arteries are functionally end arteries with little overlap between their territories. Whichever coronary artery gives rise to the posterior descending (interventricular) branch is known as dominant (right in approx. 80%, left (circumflex) in approx. 20%).

When assessing the heart, consider whether the chamber on view (usually the LV) is dilated or the wall thickened. However, remember that macroscopic appearances are not entirely accurate (only offering a guide) when assessing hypertrophy. An apparently thickened LV may not be hypertrophied (depends on during which part of the cardiac cycle the patient dies) and a LV with a wall of normal thickness may be. Pressure loads (e.g. aortic stenosis, systemic or pulmonary hypertension) initially cause concentric ventricular hypertrophy where the ventricular myocytes and wall become thickened but the lumen of the ventricle is normal or reduced in size. In eccentric hypertrophy, the wall is generally not thickened, but the myocytes are enlarged lengthwise, caused by progressive dilation of the ventricle with volume loads. Looking at the thickness of the left ventricular wall is thus not a completely reliable indicator of hypertrophy. Weighing the heart is much more reliable.

Assess the myocardium. Is there a lesion? If so, it will usually be an infarct. Approximately how old is it, in what arterial territory is it, has it ruptured, is there overlying mural thrombus?
Examine the endocardium: is it fibrotic or focally covered by thrombus?
Examine the epicardium: is there a fibrinous exudate?
Also examine the valves: are the correct number of cusps present, are the cusps fused and/or fibrotic, are there vegetations, are there any holes in the cusps?
And examine the chordae: are they thickened or ruptured?
Is the cardiac anatomy normal? Some of the specimens demonstrate congenital abnormalities.

Once you have decided on the abnormality and diagnosis, see if you can correlate the clinical information given with the pathological abnormalities.

Vessels

You should certainly be able to identify the aorta but smaller vessels may be harder to identify. Nonetheless you should normally be able to distinguish arteries from veins (the former have thicker walls, are much less likely to be collapsed and are often atherosclerotic).

Remember that vessels normally have a smooth uniform intimal lining. Most of the aortic specimens show atherosclerosis and its complications, however, several demonstrate dissections or aneurysms of the ascending aorta (generally not atherosclerotic in origin) or congenital abnormalities. To help in orientation, at autopsy the aorta is longitudinally sectioned from behind (posteriorly).

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CORE AND CLASSIC DISEASE PROCESSES

ARTERIES: ATHEROSCLEROTIC AORTA

CASE 50069/83

Describe the specimen
The specimen consists of a short segment of aorta showing severe atherosclerosis with raised and ulcerated plaques.

What is the diagnosis?
Atherosclerotic aorta

What is seen microscopically in an atherosclerotic plaque?
Microscopically there is a variable combination of fibroblasts, smooth muscle cells, 'foam' cells (macrophages that have phagocytosed lipid), chronic inflammatory cells (mainly lymphocytes and macrophages), collagen and other extracellular components of connective tissue, lipid, cholesterol clefts and often calcification and small blood vessels.

By what general mechanisms does atherosclerosis cause complications?
- Narrowing of the vessel lumen -> ischaemia. This may be
    - chronic or
    - acute at times of increased oxygen demand e.g. in the heart or leg muscles on exertion
- Acute plaque event (ulceration, fissuring, rupture, haemorrhage into plaque) -> formation of overlying occlusive or non-occlusive thrombus which may cause infarction or acute ischemia or it may embolise
- Atrophy of media -> aneurysm formation ->
    - Thrombus formation -> embolism
    - Rupture
- Embolism: thrombus or plaque itself may embolise (thrombo-embolus, athero-embolus) -> ischaemia or infarction downstream

ARTERIES: THROMBOSED ATHEROSCLEROTIC ARTERY

CASE 10759

Clinical information

The patient was a man aged 73 who died of complications following a myocardial infarction. He had suffered from generalised atherosclerosis and for several days before his death the right foot had been pale and cold. At post-mortem the aorta was moderately atherosclerotic and the right femoral artery was completely occluded.

Describe the specimen

The specimen consists of several cross-sections of a medium sized artery as it branches (in this case the right femoral artery as it gives off its profunda femoris branch). All portions show luminal narrowing from atherosclerosis. There is also dark occluding thrombus in the artery. Haemorrhage is noted within the plaque (top right), which may have precipitated the overlying thrombus formation.

What is the diagnosis?

Thrombosed atherosclerotic artery

What is a thrombus?

A thrombus is a mass of clotted blood that forms in the un-ruptured cardiovascular system during life.

Why does a thrombus form when the vascular endothelium is damaged?

Intact endothelium is important in inhibiting coagulation. Traumatized cell membranes release a complex of factors called tissue thromboplastin that activates the extrinsic coagulation pathway, ultimately resulting in the activation of fibrinogen. Exposure of blood to intimal collagen and trauma to blood itself that may arise from turbulence in the area of damaged endothelium, result in platelet activation and also in the activation of factor XII, the latter being the first step in the intrinsic coagulation pathway.

What complications may thrombosis occurring in an artery cause in general?

- Complete occlusion of the artery -> acute ischaemia or infarction
- Acute partial narrowing of the artery -> acute ischaemia
- Embolism -> occlusion of a vessel downstream

How do thromboses heal?

Thromboses heal by organization i.e. the thrombus is gradually removed by macrophages and infiltrated by granulation tissue which forms scar tissue. In some cases small vessels form through the scar tissue within the lumen of the vessel (recanalisation).

What other fates may thrombi have?

- Fibrinolysis/dissolution
- Infection (rare)
- Persistence e.g. thrombi in aortic aneurysms

ARTERIES: ATHEROSCLEROTIC ABDOMINAL AORTIC ANEURYSM

CASE 24884

Clinical information

The patient was a man aged 83 who presented with a 7-hour history of sharp abdominal pain accompanied by anorexia and nausea. A large palpable mass could be felt in the mid-line of the abdomen and plain x-ray showed an aortic aneurysm. He died on the 3rd day after admission. At post-mortem there was a very large retroperitoneal haematoma surrounding both kidneys and adrenal glands and extending into the root of the mesentery.

Describe the specimen

The specimen is the aorta and iliac arteries opened from behind to show the large fusiform aneurysm measuring 10 x 12cm above the aortic bifurcation. A thick layer of antemortem thrombus adheres to the inner wall of the aneurysm and haemorrhage is present externally. The iliac arteries are somewhat dilated. There is gross calcific and ulcerative atherosclerosis of the aorta above the aneurysm.

What is the diagnosis?

Ruptured atherosclerotic abdominal aortic aneurysm

Comment

While a specific rupture site is not obvious in the specimen, the haemorrhage around the outside of the aorta indicates that this aneurysm has ruptured.

As the aorta is such a large vessel, atherosclerosis does not normally cause significant narrowing. However, it can give rise to athero or thrombo-emboli and aneurysms. Aneurysms arise as the atherosclerosis in the intima can eventually extend into and put pressure on the media leading to medial atrophy with weakening and dilation of the wall.

Atherosclerotic aneurysms may develop at other sites, but the abdominal aorta is the commonest. Aneurysms are not only caused by atherosclerosis, however, by far the majority of abdominal aortic aneurysms are atherosclerotic in origin.

Aneurysms arise due to weakening of the vessel wall. Other causes include:

- Infection in an artery wall (mycotic aneurysm)
- Inflammation: vasculitis
- Genetic connective tissue diseases e.g. Marfan's syndrome -> 'cystic medionecrosis' and fusiform aneurysm of the ascending aorta
- Congenital weakness in the wall - probable cause of berry aneurysms around the circle of Willis
- Systemic hypertension -> microaneurysms in cerebral arterioles from arteriolar damage
- Traumatic arterial injury

In general there are 2 main architectural types of aneurysm: fusiform (dilation of the full circumference of the wall) and saccular (focal dilation of one area of wall).

Clinical question

Ruptured abdominal aortic aneurysms, and sometimes the aneurysm itself, cause pain felt in the back. Why?

ARTERIES: ANEURYSM OF THE ASCENDING AORTA

CASE 24651

Clinical information
The patient was a man aged 80 who was admitted with a resolving pneumonia that had been present for 2 weeks. He was known to be hypertensive and on examination was breathless, wasted and slightly demented. The BP was 150/70 and systolic murmurs were audible in the mitral and aortic areas. Chest x-ray showed an enlarged heart, aneurysmal dilatation of the ascending aorta and evidence of resolving pneumonia. He slowly deteriorated until his death after 3 weeks in hospital. Serological tests were positive for syphilis.

Describe the specimen
The specimen consists of the heart and the greater portion of the aorta. There is marked dilatation of the ascending aorta and arch, including the origins of the great vessels. The aneurysm measures about 10 x 10cm and its wall shows gross calcific and ulcerative atherosclerosis that extends proximally and distally also. The aortic valve cusps are a little thickened and the aortic ring a little dilated. The left ventricular myocardium appears normal.

What is the diagnosis?
Aneurysm of the ascending aorta

What are the causes of aneurysms of the ascending aorta?
Many years ago, the most common cause of ascending aortic aneurysm was tertiary syphilis. This causes a vasculitis of the vasa vasorum of the proximal aorta that leads to ischaemia and scarring in the media with consequent weakening and dilation.

Now, most aneurysms of the ascending aorta would arise in patients with genetic connective tissue diseases such as Marfan's syndrome where histologically the typical finding is 'cystic medionecrosis' (fragmentation of the elastic lamellae with pools of connective tissue ground substance in the aortic media) – a misnomer as there is no necrosis or true cyst formation. Aortitis, as may occur for example in giant cell arteritis (or syphilis), is another cause.

Aneurysms of the ascending aorta are rarely due to atherosclerosis. Atherosclerotic aneurysms arise in the descending and abdominal aortas. Aneurysms of the ascending aorta are uncommon.

The atherosclerosis in this specimen may well have arisen secondarily to the underlying abnormality.

How and why do such aneurysms present clinically?
Such aneurysms often present with symptoms and signs related to aortic incompetence from dilation of the aortic valve ring. However, the underlying abnormality also predisposes them to dissection, so some present with back pain and shock etc.

Clinical question
What are the symptoms and signs of aortic incompetence?

ARTERIES: ACUTE AORTIC DISSECTION

CASE 13353

Clinical information

The patient was a man aged 55 who, while driving his car, experienced sudden severe central chest pain passing through to the back between the shoulders. There was also sudden loss of power in the legs and he had to be driven home in a taxi, but recovered the use of his limbs 5 hours later. Next day he became breathless and was admitted to hospital. He was cyanosed, and the BP in the right arm was 150/100 and in the left arm 130/90. The right carotid pulse was reduced. There were basal systolic and diastolic murmurs in the heart. He became increasingly distressed with evidence of cardiac failure and died on the 16th day after the onset of the illness.

Describe the specimen

The specimen is of the base of the heart, the arch of the aorta with the origins of the great vessels and the descending thoracic aorta. There is a transverse intimal tear about 4cm in length on the posterior wall of the aorta, 5cm above the aortic valve. From this point a dissection has tracked down the aorta and around the origin of the innominate artery. Blood can be seen within the dissection track running in the media, well demonstrated in the descending aorta. The dissection extends proximally towards the aortic valve and also distally beyond the end of the specimen.

What is the diagnosis?

Recent aortic dissection

What is an aortic dissection?

Aortic dissection refers to the phenomena of blood entering the vessel wall, generally from a tear in the intima, and dissecting along the wall in the media (usually at the junction of the inner 2/3 and outer 1/3).

Those arising in the ascending aorta have an especially high mortality rate due a variety of potentially life threatening complications. Name them.

- Aortic rupture -> hypovolaemic shock
- Retrograde rupture into the pericardium -> haemopericardium and cardiac tamponade
- Weakening of the aortic valve ring leading to acute incompetence of the valve and acute cardiac failure
- Continuation of the dissection around branches of the aorta e.g. coronary arteries (-> myocardial ischaemia or infarction), cerebral arteries (-> cerebral ischaemia or infarction)

What other problems may an acute aortic dissection cause?

Weakening of the aortic wall eventually leading to aneurysm formation

What are the risk factors for aortic dissection?

The main risk factor for this condition is systemic hypertension. Certain hereditary diseases of connective tissue also pose a risk (the main one being Marfan's syndrome - aortic dissection is the major cause of morbidity and mortality in patients with this syndrome). Other less common risk factors include bicuspid aortic valve, aortic coarctation, aortitis of any cause (e.g. giant cell arteritis) and in the 3rd trimester of pregnancy. Atherosclerosis is relatively less important though may be present incidentally.

Comment

At autopsy, this dissection was found to extend down to the left common iliac artery where there was a re-entry rupture. It was also said to extend around the origins of the coronary arteries and there was evidence

of sub-endocardial infarction from external blood putting pressure on and narrowing the coronary arteries. This or aortic incompetence would have been the cause of the heart failure.

Clinical questions

Why can the blood pressure differ between the right and left arms following an aortic dissection?
Why is pain typically felt in the back as well as the chest following a dissection?
How are aortic dissections classified clinically?
How are aortic dissections diagnosed?

ARTERIES: OLD AORTIC DISSECTION

CASE 16437

Clinical information

The patient was a man aged 44 who had been perfectly well until 11 months previously, when he developed quite suddenly a severe pain in the lower central chest while at work, accompanied by paraesthesiae in the left arm and by profuse sweating and vomiting. The pain lasted 45 minutes and was relieved by morphia. ECG and serum enzyme levels were normal. The next day there was a fever of 39.5^{0} C with a non-productive cough and bilateral basal crepitations. Chest x-ray showed patchy consolidation. He was treated with tetracycline and discharged home 11 days later. Nine days thereafter he began to experience breathlessness on exercise and when lying flat. Simultaneously there was a stabbing pain in the left costal margin, worse on deep breathing. These symptoms became progressively worse and then night sweats began. He felt generally tired, weak and lethargic. He began to lose weight and to sleep on 4 pillows. He was admitted to the RAH. On examination the BP was 150/40, pulse 120 regular and collapsing, temp. 40^{0} C. There were visible neck pulses, capillary pulsation and systolic murmurs over the femoral arteries. The apex beat was in the 6th left interspace 14cm from the midline. There was an apical triple rhythm, an aortic systolic murmur and thrill and a long aortic diastolic murmur. There was an added high-pitched systolic sound in the aortic region. The liver and spleen were palpable. The ESR was 45mm. He was treated with digoxin, diuretics and antibiotics and the fever gradually settled, the heart slowed and congestive failure was relieved.

By the time of discharge his exercise tolerance was greatly improved and orthopnea had almost disappeared. The spleen was no longer palpable. Although blood cultures were repeatedly negative a diagnosis of subacute endocarditis was made. On his final admission congestive failure had occurred and there were signs in the chest. Orthopnea increased with a poor response to diuretics and he died with a rising blood urea and oliguria 2 weeks after his final admission.

Describe the specimen

The specimen consists of the heart, the aorta with its major branches, and the kidneys. There is dilatation but not obvious thickening of the left ventricle. The mitral valve appears normal but the aortic ring appears stretched and the valve mildly thickened. The intima has been torn transversely over a wide area of the ascending aorta just above the aortic valve. A broad fold of intima hangs down over the aortic valve cusps. The proximal and distal margins of the split gape widely, being about 3cm apart. The underlying exposed media is irregular and has become re-endothelialised. From this primary rupture, a dilated dissection track (from which the blood has been removed proximally) extends along the posterior wall of the ascending aorta, around the arch and down the posterior descending aorta. This track has not been opened for most of its length but can be seen as a bulge in the wall protruding into the aortic lumen. The origins of the intercostal arteries are surrounded by the dissection track in the thoracic portion of the vessel and can be seen at the summit of a long smooth ridge, pushed forward by the blood in the dissection track behind. The track extends down to the left common iliac artery where it terminates in a re-entrant rupture 1cm from the origin of the vessel, on its posterior wall. There is a further re-entrant rupture at the level of the renal arteries and the intramural haematoma can be seen within this opening. The dissection also extends into the innominate and then right subclavian arteries where it extends for about 8cm before terminating in a third re-entrant rupture, and also for about 5cm along the right common carotid artery. The dissection does not involve the origins of the coronary arteries. The kidneys macroscopically appear essentially normal. Note how little aortic atherosclerosis there is.

What is the diagnosis?

Old re-entrant aortic dissection

Comment

Patients may survive for many years with such re-entrant dissections. The dissection track usually ultimately becomes dilated. Ongoing cardiac failure in this case (from which the patient ultimately died) may well have been caused by aortic regurgitation secondary to dilation of the aortic valve ring related to the tear in the vessel and/or extension of the dissection proximally. There is slight scarring of the aortic valve, especially of the free edge, which can arise as a result of regurgitation in this scenario. There is no current evidence of infective endocarditis.

Clinical questions

What features in the clinical history suggest infective endocarditis?
Why were the liver and spleen enlarged?
What does a collapsing pulse indicate?

VEINS: DEEP VENOUS THROMBOSIS

CASE 25211

Clinical information

The patient was a woman aged 83 known to be hypertensive for 10 years (BP 240/120). She was admitted in congestive cardiac failure uncontrolled by digitalis and diuretics. She died on the 5th day. At post-mortem an adenocarcinoma was found in the tail of the pancreas with metastases in the liver. There was a blood stained left pleural effusion and there were recent haemorrhagic infarcts in the lower lobes of both lungs. Both innominate veins were occluded by thrombus that extended to the left jugular vein. The right femoral and right long saphenous veins also contained antemortem thrombus.

Describe the specimen

The specimen is of a large vein measuring 33cm in length with 17cm of adjacent artery (in this case the right femoral vein and artery). The femoral vein and its saphenous tributary are occluded by recent antemortem thrombus. Pale laminae of fibrin and platelets stand out against darker areas where red cells predominate. The head of the thrombus is pointed and lies free in the lumen of the vein. The artery is mildly dilated and shows some intimal atherosclerosis.

What is the diagnosis?

Deep venous thrombosis

What risk factors did this patient have for deep venous thrombosis (DVT)?

This patient had a number of risk factors for this condition: pancreatic adenocarcinoma, congestive cardiac failure and quite possibly limited mobility related to severe cardiac failure.

What are the risk factors for deep venous thrombosis in general?

The main risk factors for deep venous thrombosis are slowing of blood flow in the legs and hypercoagulability. Endothelial damage may contribute in a small proportion of cases.

- Slowing of blood flow
    - Restricted mobility e.g. elderly, post surgical, unconscious, long plane flights
    - Cardiac failure
    - Hyperviscosity e.g. polycythaemia
- Hypercoagulability of blood
    - Post-operative state
    - Certain genetic abnormalities
    - Certain malignancies, probably via the release of procoagulant substances
    - High oestrogens: peri-partum, some oral contraceptives

What are the risk factors for thrombosis in general (not just venous)?

The risk factors for thrombosis fall into 3 main areas (Virchow's triad)

- Changes in blood flow: slowing or turbulence
  - Turbulence:
    - In aneurysms
    - Over atherosclerotic plaques
    - Around abnormal cardiac valves
    - Atrial fibrillation
  - Slowing
    - Restricted mobility e.g. elderly, post surgical, unconscious, long plane flights
    - Cardiac failure
    - Hyperviscosity e.g. polycythaemia
- Hypercoagulability of blood
  - Post-operative state
  - Certain genetic abnormalities
  - Certain malignancies, probably via the release of procoagulant substances
  - High oestrogens: peri-partum, some oral contraceptives
- Changes to endothelium or endocardium
  - Direct trauma
  - Immunologic or infective inflammation of endothelium or endocardium e.g. bacterial endocarditis, vasculitis
  - Atherosclerosis
  - Endocardial damage in myocardial infarction

Comment

As deep venous thrombosis is such a common and clinically significant condition, you should know all about its risk factors and how they lead to thrombus formation, and its complications that include chronic venous insufficiency in the legs and a variety of outcomes from pulmonary embolism.

It is also important for you to have a clear understanding of the difference between pulmonary emboli, which usually start in the deep veins of the leg and travel through the venous system to the right side of the heart and pulmonary arteries to lodge in the lungs, and arterial emboli which result from detachment of mural thrombi, atheromatous plaques etc and which travel via the systemic (arterial) circulation to lodge in sites such as the brain or kidney. The pathogenesis of each is also different. Venous thrombi tend to arise as a result of sluggish blood flow +/- hypercoagulability, whilst arterial (and cardiac) thrombi tend to arise as a result of endothelial damage and turbulent blood flow.

HEART: RECENT MYOCARDIAL INFARCTION

CASE 25559

Clinical information

The patient was a woman aged 70 with a history of angina pectoris and hypertension. On her final admission there was severe chest pain radiating down both arms, accompanied by nausea and vomiting. The BP was 220/80, the pulse 80 and regular, and ECG showed recent left bundle branch block. Enzyme changes were consistent with myocardial infarction. A week later she suffered a cardiac arrest and died. At post-mortem the heart weighed 670gm.

Describe the specimen

The specimen consists of a horizontal slice through the heart. The posterior and lateral walls of the left ventricle and posterior one third of the interventricular septum show transmural mottled pallor and haemorrhage in keeping with recent infarction. The left ventricular wall and septum appear mildly thickened, but the right ventricle is of normal size.

What is the diagnosis?

Recent myocardial infarction

Which coronary artery is likely to have been occluded to cause this infarction?

The right coronary artery

What is the main cause of transmural regional myocardial infarction?

The vast majority of such regional and often transmural infarcts are due to acute occlusion of the coronary artery supplying the area resulting from an acute event (fissuring, ulceration) in an atherosclerotic plaque in the artery leading to thrombus formation.

Approximately how old is the infarct?

The appearances in the specimen are in keeping with an infarct of anywhere between a couple of days - several weeks of age. The dead tissue is paler than the normal myocardium. The surrounding dark discolouration is from haemorrhage and congestion (blood often looks dark brown or black in the pots) from leaky blood vessels, inflammation +/- granulation tissue that is very vascular. There is little white fibrous tissue visible yet.

Describe how the microscopic appearances of a myocardial infarct change with time.

As with infarction in any organ, the macroscopic and microscopic features are not usually seen until 6-12 hours after the event. Healing by organization then takes place following a period of acute inflammation initiated by tissue necrosis.

- 0-8 hr: no change
- 8-24 hr: early coagulative necrosis with increasing eosinophilia of myocytes, karyolysis, patchy haemorrhage, beginning neutrophil infiltrate, oedema
- 1-3 days: as above but more prominent
- 3-5 days: beginning disintegration of neutrophils, early phagocytosis, vascular granulation tissue begins to form
- 5 days-weeks: progressive removal of dead myocytes and collagen formation by granulation tissue which becomes progressively more fibrous
- Months-years: old scar

What type of necrosis is demonstrated in a myocardial (and also for example renal) infarct? What changes occur in this type of necrosis?

Coagulative necrosis occurs in myocardial and renal infarcts. Proteins coagulate following death of the tissue from prolonged ischaemia. This is seen histologically as an increase in eosinophilia in H&E sections with retention of tissue architecture and cellular outlines but fading and eventual disappearance of nuclei (karyolysis).

What is a cardiac arrest?

Cardiac arrest refers to the abrupt cessation of cardiac pump function that may be reversible by a prompt intervention but will lead to death in its absence.

What causes most cases of cardiac arrest?

Most cases of cardiac arrest are caused by a potentially fatal arrhythmia (e.g. ventricular fibrillation) arising in an acutely ischaemic or infarcted left ventricle.

What else may cause a cardiac arrest?

- Other causes of acute myocardial ischaemia e.g. significant left ventricular hypertrophy (e.g. secondary to systemic hypertension, aortic stenosis or in hypertrophic cardiomyopathy), anomalous coronary artery anatomy, coronary vasculitis
- Myocarditis -> myocyte irritability and fatal arrhythmia
- Myocardial scarring -> myocyte irritability and fatal arrhythmia
- Drugs, toxins, cocaine
- Electrolyte imbalances

At what time following an ischaemic myocardial event are cardiac arrests most likely to occur?

They usually occur within the first 24 hours.

What is ventricular fibrillation and how does it cause death?

Abnormal electrical discharges can arise from irritable myocytes. Ischaemia/infarction, myocardial inflammation, scarring and electrocution can cause myocyte irritability. These abnormal impulses can spread throughout the myocardium and restimulate different parts of the muscle in an uncoordinated way, resulting in no coordinated contraction and no or minimal cardiac output. This will of course lead to lack of blood flow to the brain and loss of consciousness within seconds and ultimately irreversible neuronal damage beginning within minutes if the patient is not resuscitated.

HEART: OLD MYOCARDIAL INFARCTION

CASE 50242/82

Clinical information
The patient was a man aged 73 who had had a myocardial infarction 4 years prior to his death and had angina following that episode. He died from a ruptured aneurysm of the abdominal aorta.

Describe the specimen
The specimen consists of a slice of heart through both ventricles. There is marked fibrotic thinning and endocardial fibrosis of the anterior and lateral walls of the left ventricle with patchy fibrosis in the posterior wall also. These appearances are consistent with old myocardial infarcts.

What is the diagnosis?
Old myocardial infarction

Describe how the macroscopic appearances of a myocardial infarct change with time.
As with infarction in any organ, the macroscopic and microscopic features are not usually seen until 6-12 hours after the event. Healing by organization then takes place following a period of acute inflammation initiated by tissue necrosis.

- 0-8 hr: no change
- 8-24 hr: indistinct mottling
- 1-3 days: mottling with pale centre
- 3-14 days: obvious pale/yellow area with patchy surrounding haemorrhage and congestion, fibrinous pericarditis
- 2wks-months: progressive scarring (grey-white) with thinning of the wall
- Months-years: scar with thinning of wall

HEART: MYOCARDIAL INFARCTION: COMPLICATIONS

CASE 22620

Clinical information
The patient was a man aged 62 who was admitted with acute severe chest pain. ECG suggested recent myocardial infarction, which was confirmed by a rise in serum enzyme levels. He developed congestive cardiac failure with many ventricular extrasystoles and died suddenly on the 14th day. At post-mortem there was a haemopericardium from rupture of the infarct.

Describe the specimen
The specimen consists of the heart showing pericardial congestion and whispy fibrinous exudate. The left ventricle reveals focal thinning, stretching and patchy pallor of the wall in the apical region with overlying mural thrombus. The infarct has ruptured through to the exterior anteriorly (seen through left side of pot).

What is the diagnosis?
Recent myocardial infarction with early aneurysmal bulging/infarct expansion, mural thrombus, pericarditis and rupture

Which coronary artery is likely to have been occluded to cause this infarct?
The left anterior descending coronary artery.

At what time following a myocardial infarction is cardiac rupture most likely to occur and why?
Rupture is most likely to occur between about 1-10 days following an infarct. This is because the muscle is maximally necrotic at this time but after 5 days or so, collagen is beginning to be laid down which strengthens the wall.

What may rupture following a myocardial infarction and what will the consequences be?
- LV free wall (most common) -> haemopericardium -> tamponade and rapid death (other example specimens: 20815, 23060)
- Interventricular septum -> L->R shunt -> acute cardiac failure (example specimens: 21451, 22385, 22504, 24132)
- Papillary muscle -> acute mitral incompetence -> acute cardiac failure (example specimens: 7493, 23348, 24229)

Why does the fibrinous pericardial exudate develop and what is its clinical significance?
An inflammatory response develops around the infarcted tissue, as around any necrotic tissue. Some of this infarcted tissue is adjacent to the pericardium that also becomes inflamed. Being a serosal surface, much of the exudate is fibrin. The pericarditis may cause chest pain that has to be distinguished from a new episode of ischaemic cardiac pain. Hearing a pericardial friction rub on auscultation may help in the diagnosis.

Outline the different consequences of myocardial infarction and the times they are most likely to develop.

Within hours:

- Arrhythmias e.g. ventricular fibrillation (VF), asystole, heart block, atrial fibrillation
- Cardiac failure, especially acute left ventricular failure +/- acute pulmonary oedema, cardiogenic shock

Days–weeks:

- Congestive cardiac failure
- Rupture:
    - Free wall -> haemopericardium and tamponade
    - Interventricular septum -> L->R shunt
    - Papillary muscle -> mitral incompetence
- Thrombo-embolic complications from mural thrombus
- Papillary muscle dysfunction if involved in the infarct area
- Infarct expansion
- Fibrinous pericarditis
- Dressler syndrome

Months-years

- Congestive cardiac failure
- Thrombo-embolic complications from mural thrombus
- LV aneurysm +/- thrombosis -> thrombo-embolic complications
- Papillary muscle dysfunction

Complications depend on the infarct size, site and type (i.e. transmural or subendocardial).

Infarction of which area of the myocardium is most likely to be associated with heart block? Why?

Inferior/posterior infarction as this is usually due to right coronary occlusion. This artery also supplies the AV node and bundle of His, ischaemia/infarction of which can cause heart block.

Infarction of which area of the myocardium most commonly causes severe acute cardiac failure? Why?

Anterior infarction from occlusion of the left anterior descending coronary (or left main) artery, as this artery supplies a greater volume of the left ventricular muscle than the circumflex or right coronary arteries.

Comment

Death following a myocardial infarction may result from a variety of the complications above. Different complications occur at different stages after the infarct. You should know about the complications (what they are, their pathogenesis, clinical implications etc) of myocardial infarction in detail because it is so common.

HEART: MYOCARDIAL INFARCTION: COMPLICATIONS

CASE 21232

Clinical information

The patient was a man aged 57 who had suffered an anterior septal infarction 3 months previously. Thereafter he became progressively weaker and disorientated. A month after the onset the left ventricle was considered to be only slightly enlarged but 2 months later, in the week before his last admission, he became severely breathless and confused and there was slight jaundice. Chest x-ray showed a large heart and pneumonic changes at both lung bases. Myocardial failure persisted and he died after 4 days in hospital.

Describe the specimen

The specimen is the heart and thoracic aorta. There is a very large apical aneurysm in the left ventricle measuring 7cm across the neck and 10cm in its greatest diameter. The sac is largely filled with old laminated antemortem thrombus. The wall of the aneurysm is thin and fibrous and is about 2mm thick.

What is the diagnosis?

Old myocardial infarction with apical left ventricular aneurysm and mural thrombus

Explain how an aneurysm develops following a myocardial infarction.

Infarct expansion can occur in the first few days-weeks following an infarct as the dead muscle stretches secondary to the pressure in the left ventricle. The infarct is replaced by scar tissue which does not contract and the region can expand further -> aneurysm of the left ventricle – a dilation in the region of the now healed thinned scarred wall.

Why does thrombus form in a left ventricular aneurysm?

The aneurysm often fills with thrombus due to turbulent blood flow within the aneurysm +/- endocardial damage.

What clinical problems may a patient with a left ventricular aneurysm have?

These hearts often fail as there are large areas of non-functioning muscle and patients may experience thrombo-embolic complications, such as a cerebral infarction. Left ventricular aneurysms rarely, if ever, rupture.

HEART: CONCENTRIC HYPERTROPHY OF THE LEFT VENTRICLE

CASE 14390

Clinical information
The patient was a man aged 53 who had been in good health. Two hours before death there was sudden vomiting associated with cyanosis, stertorous breathing and loss of consciousness. His BP was noted to be greater than 260/160. He died of a cerebellar haemorrhage that had extended into the 4th ventricle.

Describe the specimen
The specimen is of the heart that is enlarged. There is marked thickening of the wall of the left ventricle, without dilatation. The right ventricular wall is also thickened. What can be seen of the valves appears normal.

What is the diagnosis?
Concentric hypertrophy of the left ventricle due to systemic hypertension

What is concentric hypertrophy of left ventricle and what are its main causes?
Concentric hypertrophy is when the ventricular wall thickens but the chamber is normal or even reduced in size. The normal thickness of the LV wall is about 1-1.5cm. The main causes of concentric hypertrophy of the LV are aortic stenosis and systemic hypertension i.e. pressure loads. When the LV has to pump against a greater resistance, the cardiac myocytes enlarge, mainly in width. The wall thus becomes thickened but the lumen of the ventricle is normal or reduced in size.

What are the potential complications of concentric left ventricular hypertrophy? Explain their pathogenesis.
- LV failure and CCF: concentric left ventricular hypertrophy predisposes to myocardial ischaemia (subendocardial myocytes are especially susceptible) as the thickened myocardium has an increased demand for oxygen and oxygen supply is impaired as the elevated LV diastolic pressure (from impaired relaxation) reduces the perfusion pressure gradient between the aorta and the myocardium. Also, the thickened wall is stiffer, impairing diastolic filling. This and the ischaemia can then lead to left ventricular and subsequently right ventricular failure.
- Angina and myocardial infarction: Angina can arise from the ischaemia that will be worse on exertion as the heart needs more oxygen. Subendocardial ischaemia may be so severe as to lead to subendocardial infarction.
- Increased risk of sudden cardiac death: Irritable ischaemic myocytes can also give rise to fatal arrhythmias such as ventricular fibrillation, leading to sudden death.
- Atrial fibrillation: As left ventricular diastolic filling is impaired, left atrial hypertrophy develops to aid filling. Atrial hypertrophy predisposes to atrial fibrillation.

What are the other potential complications of systemic hypertension?
- Complications of atherosclerosis (for which hypertension is a risk factor): ischaemic heart disease, cerebral infarction and transient ischaemic attacks, abdominal aortic aneurysms, peripheral vascular disease etc
- Aortic dissection
- Chronic renal failure (from hyaline arteriolosclerosis -> chronic glomerular and tubular ischaemia -> tiny foci of atrophy of tubules and glomeruli, interstitial fibrosis -> ‘benign nephrosclerosis’ and occasionally chronic renal failure)
- Intracerebral haemorrhage (from hyaline arteriolosclerosis and Charcot-Bouchard microaneurysm formation -> rupture)

- Cerebral lacunar infarction
- ?promotion of rupture of berry aneurysms -> subarachnoid haemorrhage
- Visual disturbance and blindness related to hyaline arteriolosclerosis in retina -> arteriolar narrowing, arteriovenous nipping, silver and copper wiring, exudates, haemorrhages, microinfarcts

Other complications can occur in malignant or accelerated hypertension:

- Acute renal failure: hyperplastic arteriolosclerosis ("onion skin" endarteritis), fibrinoid necrosis, thrombosis of small arteries and arterioles -> acute glomerular ischaemia and necrosis
- Hypertensive encephalopathy with papilloedema
- Acute damage to retinal vessels

Comment

Assessment of left ventricular wall thickness is not a reliable method of assessing hypertrophy. In some situations, the left ventricle is hypertrophied but the wall is of normal thickness.
Weighing a heart (most of the weight of which is left ventricle and which varies depending on body weight) and comparing it to body weight is a more reliable method.

HEART: ECCENTRIC HYPERTROPHY OF THE LEFT VENTRICLE

CASE 50473/82

Clinical information

The patient was a man aged 76 who died after prolonged congestive cardiac failure with shortness of breath on exertion, raised JVP and bilateral ankle oedema. He terminally developed deep venous thrombosis with multiple pulmonary emboli. At autopsy, all the coronary arteries were grossly narrowed by advanced atherosclerosis.

Describe the specimen

The specimen shows a pale liver with a recognisable nutmeg pattern. The left ventricle is dilated but the wall is of normal thickness. There are patchy small areas of subendocardial fibrosis in the left ventricular wall in keeping with chronic ischaemia.

What is the diagnosis?

Dilated left ventricle with subendocardial scarring and congested ('nutmeg') liver in keeping with congestive cardiac failure

Explain the likely relationship between the coronary atherosclerosis, subendocardial fibrosis, dilated left ventricle, nutmeg liver, clinical symptoms and signs, deep venous thrombosis and pulmonary embolism.

This patient had severe coronary atherosclerosis that caused chronic myocardial ischaemia and subsequent subendocardial (area most susceptible to ischaemia) fibrosis from patchy myocyte death. The left ventricle dilated as a result of the chronically ischaemic myocardium not being able to pump out enough blood causing persistently raised end systolic and subsequently end diastolic volumes. Slight stretching/dilatation of the left ventricular myocardium initially improves contractility and stroke volume, but subsequent overstretching impairs myocardial contractility. When the left ventricle fails, the pressure in the left atrium and subsequently the pulmonary veins and capillaries increase with subsequent development of interstitial pulmonary oedema. Initially compensatory mechanisms prevent significant pulmonary oedema and symptoms at rest but dyspnoea develops on exertion as the requirements for an increased cardiac output on exertion result in tachycardia and subsequently a reduction in ventricular filling time resulting in further increase in the left atrial and pulmonary venous pressures -> oedema. Shortness of breath then develops from reduced lung compliance (from increased fluid) requiring the respiratory muscles to work harder to inflate the lungs. However the delivery of oxygen to these muscles is reduced as a consequence of the reduced cardiac output. This contributes to fatigue of the respiratory muscles and the sensation of shortness of breath. Activation of receptors in the lungs contributes to the rapid, shallow breathing. Ventilation is prevented in oedematous alveoli, and reflex pulmonary arteriolar constriction occurs to shunt blood away from under ventilated areas. Subsequent pulmonary hypertension increases the afterload on the right ventricle, ultimately leading to right heart failure also. Right heart failure leads to build-up of blood proximally, with subsequent congestion of liver (leading to a 'nutmeg' pattern as blood first builds up in the hepatic vein radicles) and spleen, raised JVP (as blood doesn't drain so readily from the neck veins) and ultimately peripheral oedema. The latter arises as a result of increased hydrostatic pressure in gravity dependent areas of the body (ankles in ambulatory persons) that can force fluid out of, and also impairs its return into capillaries and venules. Heart failure and pulmonary and peripheral oedema are contributed to by impaired renal perfusion with subsequent salt and water retention and increased body fluid volume as a consequence of the left heart failure.

Congestive cardiac failure is a risk factor for deep vein thrombosis as a result of impaired venous return to the heart and subsequently sluggish blood flow in the legs. His mobility may also have been impaired due to severe congestive cardiac failure, resulting in reduced pumping of venous blood by the calf muscles.

Thrombi from the deep leg veins can detach (-> thrombo-emboli) and travel to the lungs via the IVC, right heart and pulmonary artery.

Comment

This is an example of eccentric hypertrophy. Eccentric hypertrophy results from chronic volume loads. The chamber dilates as the end diastolic volume increases and the cardiac myocytes enlarge predominantly lengthwise. There is thus hypertrophy but the wall is not thickened. Assessment of left ventricular wall thickness is thus not a reliable method of assessing hypertrophy. Weighing a heart (most of the weight of which is left ventricle and which varies depending on body weight) and comparing it to body weight is a more reliable method.

Cardiac failure is a clinical syndrome, not a diagnosis, and the cause should always be sought and treated if possible. Whatever the cause, a failing left ventricle often becomes dilated (-> displacement of apex beat to left, enlarged heart on chest x-ray) as it is not pumping out sufficient blood -> increased end diastolic volume.

Heart failure may be classified as low output (most common) or high output.
Causes of low output heart failure (related to abnormalities of the heart)

- Increase in afterload e.g. aortic stenosis, systemic hypertension.
- Decrease in preload (from impaired filling) e.g. mitral stenosis, tamponade.
- Increase in preload (volume load) e.g. aortic incompetence, L-> R shunts.
- Intrinsic muscle disease e.g. myocardial infarction, chronic myocardial ischaemia, myocarditis, cardiomyopathies.
- Arrhythmias

Some cases will be multifactorial.
Causes of high output failure (heart itself is normal but is overloaded from excessive venous return) include: anaemia, pregnancy, hyperthyroidism

HEART: ACUTE RHEUMATIC FEVER

CASE 3824

Describe the specimen
This specimen is the heart opened to display the mitral valve. The line of closure of the valve is covered by a continuous row of small brown thrombotic vegetations. The cavity of the ventricle is not dilated and the myocardium is macroscopically normal.

What is the diagnosis?
Rheumatic vegetations on the mitral valve

Are organisms present in these vegetations?
Organisms are not present in rheumatic vegetations

Name 3 other diseases or situations in which vegetations can develop on cardiac valves. What is the pathogenesis of each?
- Infective endocarditis. Infection of the endocardium can develop at sites of turbulence and endocardial damage where microthrombi have formed. Infection then promotes further thrombus formation.
- Non-bacterial thrombotic or marantic endocarditis. In severely debilitated patients e.g. with widespread malignancy, coagulability is altered (probably from release of various procoagulant cytokines) and thrombus can develop on the valves.
- Libman-Sacks endocarditis in systemic lupus erythematosis. Thrombi develop on the valves as a result of underlying inflammation.

Comment
Such tiny fibrin and platelet vegetations along the line of closure of the valve are typical of those seen in acute rheumatic fever, a multi-system inflammatory disease that sometimes follows Group A, beta haemolytic Streptococcal pharyngitis. Vegetations seen in infective endocarditis are generally much larger.

In the heart, a pancarditis involving endocardium, myocardium and pericardium arises in 40-60% of affected patients. There are no organisms in the lesions; the inflammation is caused by immunological mechanisms. Histologically, characteristic Aschoff nodules/bodies are seen in the heart, particularly in the myocardium. The nodules are foci of fibrinoid necrosis surrounded by lymphocytes, macrophages, and specialised activated macrophages called ‘Anitschkow cells’ that have an elongated wavy nucleus. Small multinucleate cells are also present. Acute rheumatic vegetations form over tiny areas of inflammation in the valves. The carditis of acute rheumatic fever may cause heart failure. Inflammation in the conduction system can cause arrhythmias. A mitral regurgitant murmur may be heard due to dilation of the mitral valve ring. However, the most significant cardiac complications result from ongoing inflammation and scarring in the valves (mainly mitral, +/- aortic) over many years (chronic rheumatic valve disease), particularly when there is recurrent Streptococcal infection, often resulting in valve stenosis and/or incompetence and predisposing to infective endocarditis.

HEART: CHRONIC RHEUMATIC VALVE DISEASE

CASE 17394

Clinical information
This heart was removed from a 33 year old woman who had disseminated gastric cancer but died from sepsis following rupture of the ileum secondary to the effects of abdominal radiotherapy. There was no history of previous acute rheumatic fever and no cardiac murmurs had been detected.

Specimen description
The specimen is the heart opened to show the left atrium and left ventricle. The mitral valve and chordae tendineae show fibrotic thickening and the chordae are shortened. The muscle coat of the left atrium is mildly thickened. The left ventricle appears normal.

Diagnosis
Fibrotic mitral valve

What is the most likely pathogenesis of this abnormality?
The appearances are in keeping with the effects of chronic rheumatic valve disease. Ongoing chronic inflammation in the valve following acute rheumatic fever over many years leads to fibrosis and thickening of the valve and chordae tendineae.

Which valves does chronic rheumatic valve disease usually affect?
It most commonly affects the mitral valve. The aortic valve may also be affected but is less commonly involved alone.

When severe, scarred valves, whether mitral or aortic, can become stenotic and/or incompetent. What is the commonest cause of mitral stenosis?
By far the commonest cause of mitral stenosis is chronic rheumatic valve disease.

What are the causes of mitral incompetence?
- Cusp disease
    - Rupture in infective endocarditis
    - Post inflammatory scarring (chronic rheumatic valve disease or infective endocarditis)
    - Mitral valve prolapse ('floppy' mitral valve)
- Papillary muscle or chordae dysfunction
    - Rupture (papillary muscle) in myocardial infarction
    - Scarring (papillary muscle) post myocardial infarction
    - Rupture (chordae) in infective endocarditis
    - Rupture (chordae) with floppy mitral valve
- Mitral ring dilation: from LV dilation

HEART: INFECTIVE ENDOCARDITIS

CASE 3965

Clinical information
The patient was a woman aged 26 who had a high swinging fever. Red cells were found in the urine.

Specimen description
The specimen consists of the heart and portions of spleen and kidney. The mitral valve is covered by large friable vegetations that extend down the chordae tendineae. The underlying valve and chordae do not appear thickened to suggest old rheumatic valvulitis. The left ventricle is not dilated or thickened. The spleen shows a wedge-shaped area of pallor on one side and the kidney also shows a smaller wedge-shaped area of pallor with a congested border near one pole.

Diagnosis
Infective endocarditis with infarcts of spleen and kidney

How is the pathology in the spleen and kidney explained in light of the pathology in the heart?
Vegetations from the heart have embolised to the spleen and kidney, lodging in branches of the splenic and renal arteries causing occlusion and infarction.

Why has this patient got haematuria?
Probably from the renal infarct, but it can also be caused by endocarditis related glomerulonephritis (not diagnosed macroscopically).

What are the complications of infective endocarditis?
Complications include:
Fever, malaise
Cardiac

- Cusp perforation or chordal rupture -> incompetence and acute cardiac failure
- Organisation of vegetations -> valve stenosis/incompetence -> cardiac failure
- Paravalve abscess
- Ischaemic heart disease from coronary emboli

Embolism ->

- Infarction at distant sites
- Abscess formation at distant sites
- Mycotic aneurysm which can rupture

Immunological

- Glomerulonephritis (from circulating immune complexes) -> proteinuria, haematuria, impaired renal function
- Splinter haemorrhages, skin rashes

Splenomegaly, anaemia (in subacute infective endocarditis)

HEART: CHRONIC RHEUMATIC VALVE DISEASE AND INFECTIVE ENDOCARDITIS

CASE 3236

Clinical information
The patient was a man aged 59 who had congestive cardiac failure.

Describe the specimen
The specimen is a heart showing a dilated left ventricle with a thickened wall. There is marked fibrotic thickening of the aortic valve with fusion of the cusps. The under surfaces of the cusps show friable necrotising vegetations.

What is the diagnosis?
Aortic valve scarring and cusp fusion with left ventricular concentric hypertrophy and dilation and infective endocarditis

Explain the likely pathogenesis of the aortic valve fibrosis, left ventricular wall thickening and dilation and infective endocarditis.
The scarring and fusion of the aortic valve cusps is probably related to chronic rheumatic valve disease. This has developed following Streptococcal (Group A beta haemolytic) throat infection in childhood initiating an immunological response in the endocardium that persisted over many years -> chronic inflammation and scarring with cusp fusion. As a result the valve has become stenotic causing secondary left ventricular concentric hypertrophy (thickening). It is probably also incompetent causing some dilation of the ventricle from the volume load. The abnormal valve has also predisposed it to the development of infective endocarditis, following the formation of tiny thrombi in areas of turbulence and endocardial damage related to the valve abnormality, in which bacteria in the blood stream (e.g. from dental procedures, skin infections, poor oral hygiene, IV lines) can settle and proliferate.

What are the causes of aortic stenosis?
- The commonest cause of aortic stenosis in industrialised countries is age related degenerative calcification and scarring in an otherwise normal tricuspid valve. In these cases, aortic stenosis tends to develop in the seventh decade or later.
- Such degenerative calcification and scarring occur earlier in congenitally bicuspid valves, an abnormality present in 1-2% of the general population. Most congenitally bicuspid valves function normally at birth and remain asymptomatic, but some may be incompetent or develop calcification and cause stenosis in adulthood.
- Other congenital valve deformities (rare) cause stenosis from birth.
- Post inflammatory scarring i.e. in chronic rheumatic valve disease or post infective endocarditis
- Other rare causes, including autoimmune connective tissue diseases and mucopolysaccharidoses

What are the potential complications of aortic stenosis? Explain their pathogenesis.
- LV failure and CCF: Increased afterload -> concentric left ventricular hypertrophy which predisposes to myocardial ischaemia (subendocardial myocytes are especially susceptible) as the thickened myocardium has an increased demand for oxygen and oxygen supply is impaired as the elevated LV diastolic pressure (from impaired relaxation) reduces the perfusion pressure gradient between the aorta and the myocardium. Also, the thickened wall is stiffer, impairing diastolic filling. This and the ischaemia can then lead to left ventricular and subsequently right ventricular failure.
- Angina and myocardial infarction: Angina can arise from the ischaemia that will be worse on exertion as the heart needs more oxygen. Subendocardial ischaemia may be so severe as to lead to subendocardial infarction.

- Increased risk of sudden cardiac death: Irritable ischaemic myocytes can also give rise to fatal arrhythmias such as ventricular fibrillation, leading to sudden death.
- Patients may experience exertional syncope as the fixed stenotic valve orifice prevents the necessary increase in LV output on exertion. Peripheral vasodilatation in exercising muscles contributes to decreased cerebral perfusion
- Increased risk of infective endocarditis from turbulence and microthrombus formation around abnormal valve

Comment

Infective endocarditis can cause scarring and stenosis or incompetence of the valve as it heals, but in this case, these, and the left ventricular hypertrophy, have probably antedated the endocarditis.

HEART: INFECTIVE ENDOCARDITIS CAUSING AORTIC INCOMPETENCE

CASE 7261

Clinical information

The patient was a man aged 28 with no significant past medical history. The illness began a month before admission with shivering, sweating and malaise. On admission there were signs of aortic regurgitation and a mitral diastolic murmur. The temperature was 38.5 degrees C, the spleen was enlarged and blood cultures grew Streptococcus viridans. He was treated with penicillin with good result, but after 5 weeks he suddenly developed acute heart failure and died. There was no history of rheumatic fever. At post-mortem there was marked cardiac enlargement, pulmonary oedema, pleural effusions and ascites, together with an infarct in the left kidney. The spleen was slightly enlarged (weight 275gm).

Specimen description

The specimen consists of the heart opened to show the greatly dilated left ventricle. The aortic valve is bicuspid and the cusps show mild fibrous thickening. The ventricular surface of one cusp is covered by pale friable vegetation and the vegetations have spread to the adjacent cusp. The principally affected cusp has ruptured and shows a large tear measuring about 2 x1cm. The mitral valve and chordae tendineae are not thickened. The ascending aorta and coronary orifices appear essentially normal.

Diagnosis

Ruptured bicuspid aortic valve with infective endocarditis, dilated left ventricle

What is the most likely pathogenesis of these abnormalities? Give time scales.

The bicuspid aortic valve is a congenital abnormality. This has predisposed the patient to infection of the valve (structural cardiac abnormalities cause turbulent blood flow and often endocardial damage, promoting thrombus formation in which organisms may settle and proliferate) that developed a month before admission, explaining the shivering, sweating and malaise. The clinical history and organism suggest that this is a subacute case. The sudden development of acute heart failure before death was probably precipitated by perforation of the aortic valve (from necrosis related to infection and acute inflammation) causing aortic incompetence. However acute aortic incompetence does not usually cause dilation of the left ventricle straight away, so there has probably been a degree of underlying incompetence of the valve (in keeping with the reported signs on admission and causing a volume load and thus eccentric hypertrophy) for longer.

From what has this patient died?

This patient probably died from cardiogenic shock caused by acute aortic incompetence.

What are the causes of aortic incompetence?

- Cusp disease
  - Congenitally malformed valve (usually bicuspid)
  - Post inflammatory scarring (chronic rheumatic valve disease or infective endocarditis)
  - Rupture in infective endocarditis
- Lack of cusp support: aortic dissection
- Aortic ring dilation
  - Non-inflammatory medial changes e.g. Marfan's syndrome
  - Inflammatory medial changes (aortitis) e.g. syphilis, giant cell arteritis

Comments

In understanding disease, clinicopathological correlation (i.e. explaining the clinical information in light of the underlying pathology or vice versa) is very important, and one should have an understanding of the time course of various pathologies and diseases.

The aortic valve is normally tricuspid. Congenitally bicuspid valves are, however, not uncommon, affecting approx. 1% of the population. Most are asymptomatic and don't cause problems, however, some can be incompetent and others can become stenotic in adulthood due to premature calcification and thickening related to wear and tear.

Clinical question

What are the symptoms and signs of aortic incompetence?

HEART: FIBRINOUS PERICARDITIS

CASE 15547

Clinical information
The patient was a man aged 59. At the age of 46 he had a total cystectomy with uretero-colic transplantation for a bladder carcinoma. Six years later there was a severe attack of acute right-sided pyelonephritis. At his last admission he was lethargic, thirsty and had lost weight. There was dyspnoea on exertion and swelling of the ankles. The urine specific gravity was 1008 with 4+ albumen. The serum creatinine was elevated. Congestive cardiac failure became worse in spite of treatment. He died on the 10th day. At post-mortem the left kidney was small and both showed gross scars of chronic pyelonephritis. Recent bilateral acute pyelonephritis was also present.

Specimen description
The specimen consists of an enlarged heart. Both the visceral and parietal surfaces of the pericardium are covered by dense fibrinous exudate.

Diagnosis
Fibrinous pericarditis

Why has this patient developed lethargy, thirst, loss of weight, congestive cardiac failure and fibrinous pericarditis?
These are all manifestations of chronic renal failure.

What is the cause of this man's chronic renal failure and what is its likely pathogenesis?
The man's chronic renal failure has been caused by chronic pyelonephritis. This has probably been caused by repeated episodes of acute pyelonephritis, related to reflux and infections following the uretero-colic implantation.

What are the causes of fibrinous pericarditis?
There are a variety of causes of fibrinous pericarditis including chronic renal failure, acute rheumatic fever, SLE, malignant infiltration of the pericardium, certain viral infections, post myocardial infarction and post surgical.

Comments
Fibrinous pericarditis is not a very common pathology but it is a classic one that you should be able to recognise. It is classically described as a bread and butter pericarditis, being likened to the buttery surface of two slices of bread that have been buttered, placed together and then pulled apart. Typically a loud pericardial friction rub is heard on auscultation.
A similar picture is seen on the pleura overlying, for example, lobar pneumonia and pulmonary infarcts.