Diseases of blood vessels

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Abstract

Cardiovascular disease is the number one worldwide killer of men and women. Atherosclerosis is characterized by deposition of lipids in arterial walls and is responsible for a wide spectrum of end-organ damage. Inflammation of the blood vessel wall (vasculitis) can occur as a secondary process in association with another disease or exposure, or as a primary idiopathic process. The primary vasculitides have individual patterns of vascular involvement and histopathological characteristics that influence their clinical features, severity, and management.

Keywords Aneurysm; atherosclerosis; vasculitis

Arterial disease in ageing populations

There are a number of disorders of arteries seen commonly in older individuals in Western society and with increasing frequency globally.

Arteriosclerosis

Arteriosclerosis, literally 'hardening of the arteries', can affect all arteries and arterioles. It is due to gradual replacement of vascular smooth muscle cells by collagen and accumulation of calcium salts throughout life. Arteriosclerosis lowers the compliance of the arterial tree. Arteriosclerosis differs from atherosclerosis in that there is no intimal lipid deposition or inflammation. Mönckeberg's sclerosis is medial calcification usually at the internal elastic lamina. It is common and occurs independently of atherosclerosis. It is more frequent in people over 50 years of age and in diabetic patients. In advanced cases of Mönckeberg's medial calcific sclerosis, vessels may become rigid and lose their distensibility. It can easily be seen as an opaque vessel on normal x-rays and purple material on histological slides. It is usually benign because it does not cause narrowing of the lumen (Figure 1).

Vascular calcification may also be seen in disorders of calcium metabolism, in chronic renal disease and in HIV-positive individuals. The calcification may be prominent radiologically and it is important that this is not taken as evidence of more serious vascular disease.

Atherosclerosis (atheroma)

Atherosclerosis is by far the most important arterial disease. It is the principal cause of death and disability in many Western countries. Together, ischaemic heart disease (IHD) and stroke cause almost one-third of deaths. Atherosclerosis is a focal intimal disease of medium to large arteries including the aorta, carotid, iliac, coronary and cerebral arteries. Some medium-sized arteries such as the internal mammary are spared, as are veins. In the absence of pulmonary hypertension the pulmonary arteries are also spared.

In atherosclerosis each focal discrete lesion is called a plaque. Within each plaque there are combinations of extracellular lipid, intracellular lipid within foam cells (predominantly of macrophage origin) and collagen with other connective tissue matrix components produced by smooth muscle cells. Plaques can be considered as an inflammatory—repair response to lipid within the intima. Many plaques undergo calcification.

Smooth muscle proliferation is one component of plaques, but is also a ubiquitous response of the vessel wall to any injury. Disease processes which solely consist of smooth muscle proliferation should not be called atherosclerosis. For this reason post-angioplasty stenosis, intimal thickening following experimental endothelial damage, hypertensive changes and age-related intimal thickening should not be called atherosclerosis.

Atherosclerosis is a biphasic disease. Virtually all individuals in the countries of the developed world will have some plaques, but only a minority will at some point in their life enter the second phase and develop clinical symptoms.

Pathology of atheroma: examination of the intimal surface of the human aorta opened longitudinally at autopsy shows plaques with considerable variation in their macroscopic appearances. The earliest lesion which is visible by naked eye examination is the fatty streak. This is a flat yellow dot or streak on the intima. Fatty streaks are the only lesions found in children up to 10 years of age. Although it seems likely that not all fatty streaks progress, they are considered the starting point in sequential plaque development. Low density lipoprotein (LDL) from the plasma freely moves in and out of the intima. Within the intima a small proportion of the LDL undergoes minor modification and then oxidative change. The oxidized LDL acts as an inflammatory stimulus and invokes monocyte migration and cytokine production. Once oxidized, the LDL is taken up by the macrophage scavenger receptors and lipid uptake continues until the cytoplasm is packed with lipid to form the foam cell. These foam cells eventually die and release the lipid.

The next stage of plaque evolution is elevation above the intimal surface as smooth oval humps. Foamy cell death releases extracellular lipid which causes chronic inflammation, smooth muscle proliferation and fibrosis in the vessel wall forming a palpable plaque, the raised fibrolipid or advanced plaque. Histologically at this stage the plaque has a central core of acellular lipid-containing cholesterol crystals. This core is surrounded by lipid-filled foam cells and contained within a capsule of collagen which is known as the plaque cap. The external colour of the raised fibrolipid plaque is basically yellow due to the carotenoid pigment in the lipid core, but if the plaque cap is thick the external colour is white. These occur in arteries down to 2 mm in diameter. The later stages of plaque evolution comprise complications such as calcification (Figure 2) and thrombosis which is usually symptomatic.

Thrombosis develops over plaques because of two different processes. The first is superficial intimal injury in which there are

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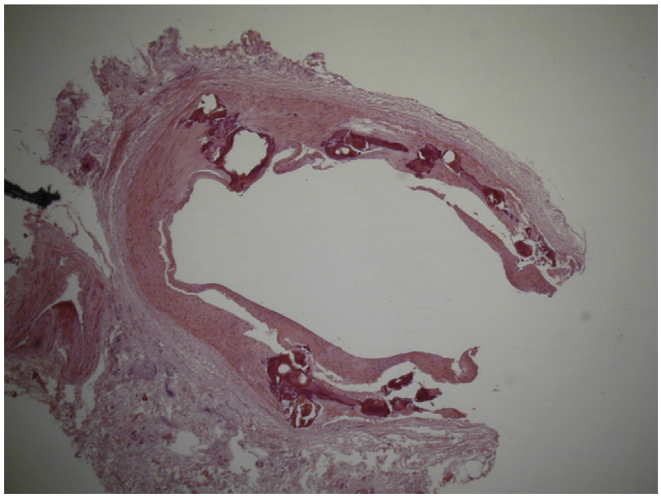

Figure 1 Section of internal mammary artery which shows calcification in the media which is typical of Monckeberg's calcification. Note that it is localized around the internal elastic lamina also.

large areas of endothelial loss and surface intimal erosion (acute ulceration) over a plaque. A thrombus forms, which is entirely superimposed onto the luminal surface of the plaque. While many of the coronary thrombi due to endothelial erosion over a plaque are small, a minority are larger and can lead to significant mural thrombi or even complete occlusion. These lesions are more common in elderly females.

In established plaques with a large lipid core, acute inflammation predisposes to plaque rupture and resultant occlusive thrombosis. The fibrous cap tears and the interior of the lipid core is exposed to blood and contains tissue factor that is intensely thrombogenic, and thrombus forms within the core due to activation of both platelets and the generation of thrombin. The thrombus within the plaque may then extend into the vascular lumen. Plaque disruption has a wide spectrum of severity. Small tears may have only an intraplaque component of thrombus. At the other extreme the cap may be lost over several millimetres and the whole bed of the core exposed with extrusion of the lipid contents. In the aorta or carotid arteries where both the plaques and the vascular lumen are much larger, chronic ulcers filled with thrombus develop as the result of disruption. In these large arteries confluent plaques may calcify, and ulceration leads to surface thrombus which will usually be asymptomatic. Sometimes thrombosis will narrow or occlude a major branch and cause mesenteric, cerebral or renal ischaemia. Thrombi and fatty debris from ulcerated plaques embolize into the cerebral circulation, legs and abdominal organs. This athero-embolism is also usually subclinical, but showers of microemboli, often released by an arteriography catheter or by anticoagulation may cause transient ischaemic attacks, renal failure, malignant hypertension, and may even mimic vasculitis.

In medium-sized arteries such as the coronary arteries, plaques tend to form at branching points and bifurcations. Plaque rupture is common in the proximal vessels and occlusive or semi occlusive thrombus on these disrupted or ulcerated plaques cause focal or transmural infarction. Thrombi and fatty debris from ulcerated plaques can embolize into the intramural vessels causing microinfarcts (Figure 3).

The circulations affected vary; atherosclerosis targets the aorta, leg, coronary, cerebral, gut and renal arteries. In diabetic patients and in smokers, the aorta and leg arteries are often diffusely and severely affected, causing peripheral vascular disease. In others, the cerebral and/or coronary arteries are sites of predilection. In young adults coronary arteries are most often targeted while severe cerebral atheroma mainly affects the elderly.

Atherosclerotic aneurysms typically affect hypertensive male smokers older than 60. They may be fusiform or saccular and occur in the lower abdominal aorta and often extend into the iliac arteries. Large atherosclerotic aneurysms may rupture, causing massive retroperitoneal haemorrhage. The larger the aneurysm, the greater the risk of rupture, and the risk is higher with fusiform than with saccular aneurysms. Aneurysms more than 5 cm in diameter rupture at a rate of 5% per year. Occasionally, due to chronic inflammation and fibrosis, the wall of the aneurysm may

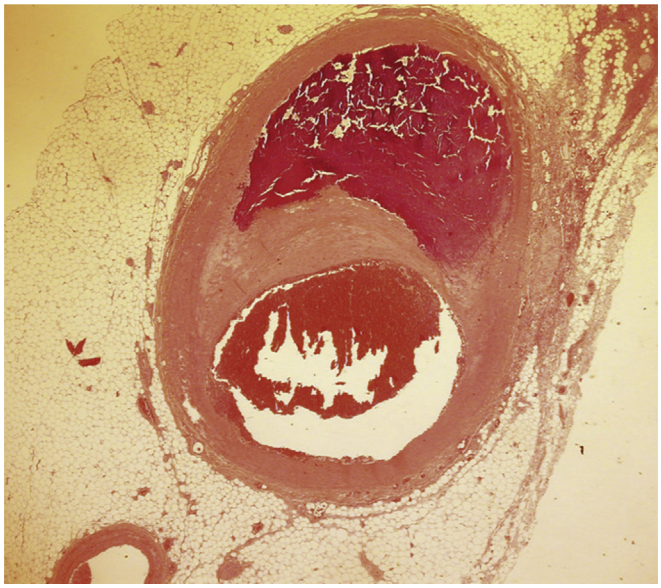

Figure 2 Coronary artery atheroma with extensive calcification in the plaque (lower part of picture, vascular lumen is above).

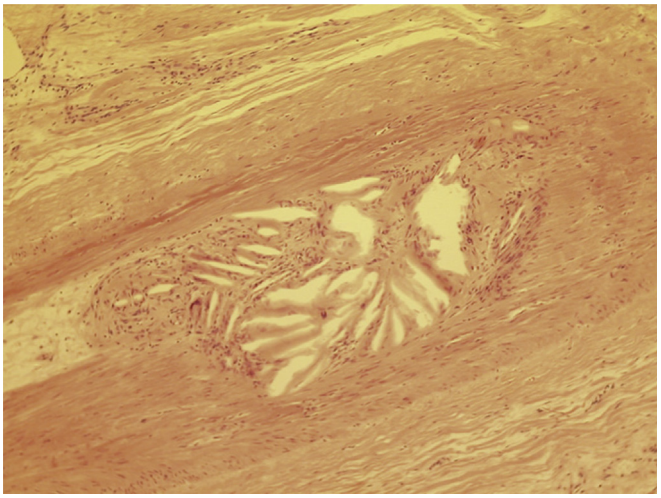

Figure 3 Cholesterol embolus (pale spaces within an intramural coronary artery) causing micro infarction.

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