Neuropathology of cerebrovascular diseases

Aditya G Shivane

Abstract

Cerebrovascular diseases cause significant global economic burden to the healthcare systems, stroke being the third leading cause of death in the developed world. With the advent of newer imaging techniques, the majority of common cerebrovascular diseases are accurately diagnosed in life, but in some cases the precise aetiology of stroke is only determined after post-mortem examination. This review discusses the basic cerebrovascular anatomy, pathology of cerebral ischaemia/infarction and haemorrhage, various causes for cerebrovascular disease and lastly, an approach to post-mortem examination in a cerebrovascular death.

Keywords amyloid angiopathy; CADASIL; haemorrhage; infarction; ischaemia; post-mortem; small vessel disease

Introduction

The term 'stroke' or cerebrovascular event refers to abrupt onset of focal or global neurological deficit lasting more than 24 hours caused by either ischaemia or haemorrhage.[1] Stroke is the third leading cause of death in developed countries, after heart disease and cancer, and causes a considerable global economic burden to the healthcare systems. Most cases are accurately diagnosed on clinical grounds, but the precise type of stroke is determined by brain imaging and/or by post-mortem examination. The incidence of stroke is low in children and high in the ageing population with crude incidence rates of 112–223 per 100,000 person years in high-income countries. In western countries, approximately 60–80% of first-time strokes are due to cerebral infarction, but only 5–11% are due to parenchymal brain haemorrhage.[2,3] The mortality from stroke has also declined over the past two decades due to reduced incidence, lesser severity and improved management.[2,4–6] There are several risk factors associated with stroke, of which age, gender, race, genetic, vascular, haematological and metabolic diseases are non-modifiable; hypertension, hyperlipidaemia, heart disease, cigarette smoking, diabetes mellitus, oral contraceptive use and heavy alcohol consumption are modifiable to certain extent. This review starts with a brief overview of vascular anatomy, discusses the neuropathology of common cerebrovascular diseases and concludes with the role of autopsy in evaluating cerebrovascular diseases.

Vascular anatomy

The brain is supplied by two pairs of large arteries, the internal carotid arteries (anterior circulation, 70–80%) and the vertebral arteries (posterior circulation, 20–30%). The internal carotid arteries give rise to two main branches, the anterior cerebral arteries which supplies the medial aspects of frontal and parietal lobes, anterior limb of internal capsule and corpus callosum, and the middle cerebral arteries which supplies most of the lateral aspect of the brain and the deeper grey nuclei. The two vertebral arteries join to form the basilar artery which then divides into two posterior cerebral arteries which supply the inferior-medial aspects of temporal and occipital lobes, thalamus and posterior limb of internal capsule. The connections between posterior cerebral and internal carotid arteries (post communicating artery), and between two anterior cerebral arteries (anterior communicating artery) complete the circle of Willis (Figure 1). Branches from the posterior circulation supply the brainstem and cerebellum. The spinal cord is supplied by a single anterior spinal and two posterior spinal arteries. Anastomoses occur within the circle of Willis which allows collateral supply of blood in the event of arterial blockage. The border zone between territories of two major arteries is vulnerable to ischaemic injury and result in '*watershed infarction*' (Figure 2). Watershed infarcts are usually wedge-shaped with their base towards the pial surface. The superior sagittal sinus, cavernous sinuses and the transverse sinuses collect blood from the superficial and deep cerebral veins and drains them into sigmoid sinus, internal jugular vein and then to the heart through brachiocephalic vein and superior venacava. The anterior and posterior spinal veins drain blood from the spinal cord into vertebral venous plexus which then drains into lumbar, azygos and hemiazygos veins.

Cerebral infarction and haemorrhage

The basic pathology of cerebrovascular diseases can be divided into two categories – 1) blockage of the blood vessel resulting in *ischaemia or infarction*, and 2) rupture of the blood vessel causing *haemorrhage*.

Ischaemia and/or infarction results from interruption of blood supply to the brain, which can be either focal (confined to a defined vascular territory) or global (blood flow to the whole brain is reduced). The most common cause of ischaemia and/or infarction is atherosclerosis. Other causes include – cardiac emboli, arterial dissection, vasculitis, haematological disorders, hypotension and neoplasms. Amongst the cells of nervous system, neurons are most vulnerable to hypoxia/ischaemia. The morphology of ischaemia/infarction depends largely on the severity and duration of vessel occlusion. Broadly, three different stages of evolution of cerebral ischaemia are recognized – acute (~1–4 days), subacute (~5–30 days) and chronic (weeks to months or years). The acute stage is characterized by mild softening and swelling of the affected area (best appreciated by palpation), blurring of grey-white matter junction and dusky discolouration which later becomes well demarcated from the normal tissue (Figure 3). Histology in the early stage (few hours to 1 day) shows neuronal eosinophilia (red neurons) with pyknosis, neuropil vacuolation and polymorph neutrophil infiltration (Figure 4). This is followed by macrophage infiltration (2 days) which persists for months. In the subacute phase, tissue shrinkage and

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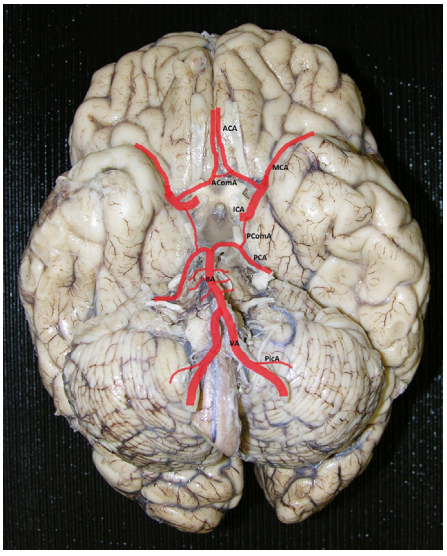

Figure 1 Basal view of the brain showing major branches of the circle of Willis. ACA – anterior cerebral artery, AComA – anterior communicating artery, MCA – middle cerebral artery, ICA – internal carotid artery, PComA – posterior communicating artery, PCA – posterior cerebral artery, BA – basilar artery, VA – vertebral artery, and PicA – posterior inferior cerebellar artery.

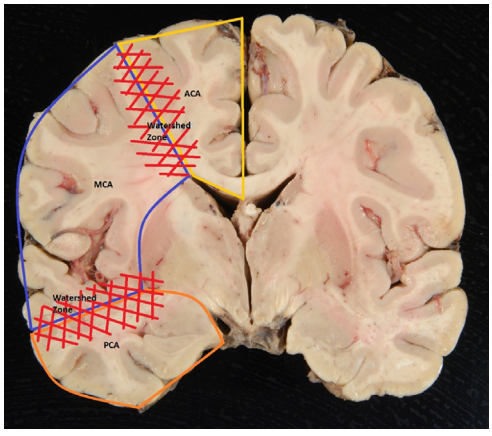

Figure 2 Coronal slice of brain at the level of mamillary bodies showing the distribution of major cerebral arteries and the '*border or watershed zones*' between them. ACA – anterior cerebral artery, MCA – middle cerebral artery, and PCA – posterior cerebral artery.

partial cystic changes appear. Polymorph neutrophils disappear, macrophages predominate, astrocytes and new blood vessels appear (Figure 5). The tissue undergoes necrosis. A long standing infarct shows extensive cystic changes surrounded by atrophic tissue (Figure 6). Occasional macrophages, haemosiderin (if there is haemorrhage), scattered small blood vessels and fibrillary gliosis are present in the adjacent tissue[7,8] (Figure 7).

Haemorrhage accounts for approximately 18–48% of all deaths from stroke.[9] Chronic hypertension and cerebral amyloid angiopathy (CAA) are the two most common causes of intracerebral haemorrhage in the elderly. Other causes include –

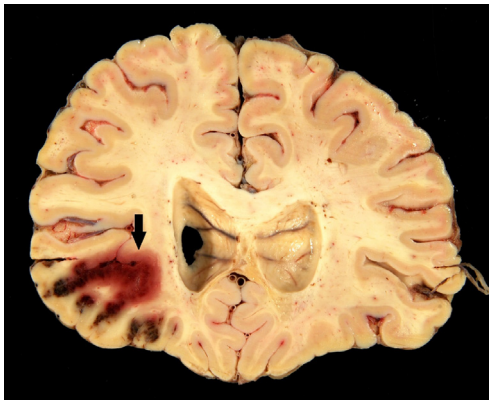

Figure 3 Acute cerebral infarction. Coronal slice showing haemorrhagic discolouration and blurred grey-white matter junction (*arrow*).

ruptured aneurysm, vascular malformation, neoplasms, coagulopathies, drugs, vasculitis and trauma. Hypertensive haemorrhages are usually single and are commonly located in the basal ganglia (putamen), thalamus, cerebellum, or pons. CAA-related haemorrhages are lobar, mainly in the frontal and frontoparietal lobes, and rarely in the posterior fossa. In the early stage, a liquid or semiliquid mass of blood with surrounding oedema is present (Figure 8). The haematoma changes in consistency after a few days and appear brown in colour. A cystic cavity with yellow-brown discolouration is all that is left after several months or years. Microscopic examination shows red blood cells which subsequently lyse and polymorph neutrophils appear. This is followed by infiltration of macrophages which phagocytose blood products and necrotic tissue. Months to years later a gliotic cyst bordered by residual macrophages and haemosiderin is all that remains.

The important causes for cerebrovascular disease are listed in Table 1.

Atherosclerosis is the leading systemic vascular disease causing brain infarcts and mainly affects large and medium-sized muscular and elastic arteries. The internal carotid artery and basilar artery are the two most commonly affected blood vessels in the intracranial compartment. There are several risk factors associated with atherosclerosis which include – increasing age, male gender, strong family history, hyperlipidaemia, hyperhomocystinaemia, hypertension, cigarette smoking and diabetes mellitus. Several gene polymorphisms have been linked to atherosclerosis (*ABCA1, MMP-3, IL-6*)[10]. The atherosclerotic process begins as a yellow flat lesion also known as '*fatty streak*' containing lipid-filled foam cells, and can even be seen in children as young as 10 years. The fatty streak then changes to plaque or *atheroma* (Greek word for '*gruel*') and appear as white to pale yellow raised lesion containing a lipid core and white fibrous covering. These plaques can narrow the vascular lumen and can also undergo rupture, ulceration or erosion, haemorrhage, thrombus formation or aneurysmal dilatation (complicated plaque). The most favoured mechanism for atheroma genesis is the 'vascular injury or response to injury theory' wherein the vascular endothelium is injured first, which then attracts inflammatory cells and results in release of several

