CENTRAL NERVOUS SYSTEM

Pathology of raised intracranial pressure and cerebrovascular disease

Intracranial pressure (ICP)

Definition: Pressure of the CSF within the cranial cavity
Normal range: Less than 10 mmHg (150 mm water)
Increased ICP: Defined as elevation of the mean CSF pressure above 15 mmHg (200 mm water) when measured with the patient in the lateral decubitus position

Increased ICP

Considerations on cause
1. Rigid cranium (exception: infant)
2. Space occupying lesions
   • e.g. haematoma, tumour, abscess, etc.
3. Secondary effects
   • Brain edema, obstruction to CSF flow (hydrocephalus)

Considerations on effect
1. Age – elderly (cerebral atrophy), infant (separation of sutures)
2. Stage of spatial decompensation
   • An initial phase of spatial compensation can be achieved by a reduction in the CSF volume and venous space (intracranial veins)
   • If the rate of development of a SOL is slow, there can be compensatory cerebral atrophy, erosion of skull bone etc.
   • When all the available space has been utilised, there is a critical point at which a further slight increase in the volume of the intracranial contents causes an abrupt increase of intracranial pressure.
3. Rate – e.g. a haematoma versus a meningioma
4. Pressure gradient
   • The dural folds (falx cerebri, tentorium cerebelli) separate the brain into compartments (right and left cerebral hemispheres, posterior cranial fossa). The posterior cranial fossa is connected to the spinal cord through the foramen magnum.
   • Expanding lesion in one compartment of the brain will cause distortion and displacement of the brain towards the other compartments (herniation) – a live-threatening situation!

Herniations

Classified based on the part that is herniated and the structure which it has been pushed.
1. Transtentorial or uncal herniation*
2. Cerebellar tonsil herniation (coning)*
3. Subfalcine or supra callosal herniation
4. Reverse tentorial herniation
5. Transcalvarial or fungus herniation
Transtentorial herniation – effects, complications and clinical manifestations

1. Compress ipsilateral oculomotor nerves – fixed and dilated pupils, eye deviates laterally due to unopposed action of VI nerve
2. Compress posterior cerebral artery – infarction of ipsilateral occipital cortex (cortical blindness) (bilateral in severe case)
3. Contra lateral cerebral peduncle pushed against free edge of the tentorium - hemiplegia in same side of body as the space occupying lesion (false localising sign)
4. Compress vital structures – haemorrhage and infarction of midbrain and pons (loss of consciousness, depression of heart rate, changes in respiration, elevated blood pressure due to increased sympathetic activity)
5. Compress aqueduct of Sylvius – hydrocephalus
6. Compress optic nerve and retinal vein – papilloedema

Tonsillar herniation – Downward displacement of the cerebellar tonsils through the foramen magnum causes compression and distortion of the medulla and frequently results in apnoea.

Other earlier signs of raised intracranial pressure includes headache (stretching of the meninges), projectile vomiting (distortion of brainstem). In infants and children, the early sign of raised ICP is often separation of the sutures of the vault. Erosion of skull bone occurs in long sustained moderate increase in ICP.

Brain swelling

Cerebral edema occurs when there is an increase in CNS water content. It is classified as vasogenic, cytotoxic and hydrocephalic

1. Vasogenic edema results from increased filtration pressure and/or permeability of the capillaries and venules. The blood-brain-barrier is defective and water, sodium and protein are extravasated into the extracellular space. It is often prominent in the tissue around cerebral contusions, recent infarcts, brain abscess and tumours.
2. Cytotoxic edema results from metabolic derangements and following acute hypoxia with disturbance of cellular osmoregulation. The edema is intracellular.
3. Hydrocephalic edema results from increased resistance of CSF absorption with collection of CSF in the periventricular white matter.

Congestive brain swelling due to vasodilatation alone may occur in hypoxia, hypercapnia or result from loss of vasomotor tone, which may complicate acute brain damage.
Pathology of stroke

1. Stroke or cerebrovascular accident is a clinical term that describes the rapid onset of a focal disturbance of cerebral function of presumed vascular origin and of more than 24 hours' duration with structural brain damage.

2. Transient ischaemic attack (TIA) is a fully reversible neurological deficit lasting less than 24 hours with no structural brain damage.

3. Stroke comprises infarction (84%) and haemorrhage (16%) in Western countries. Figures for stroke in Hong Kong Chinese: infarction (70%), haemorrhage (30%).

Cerebral infarction

Cerebral infarction is due to inadequate blood supply to the involved areas causing tissue necrosis

Common causes:

1. occlusion or stenosis of extracranial or intracranial or deep penetrating arteries by atherosclerosis or lipohyalinosis
2. emboli from atheroma plaques especially in the carotid bifurcation, or from mural thrombi formed in the heart, e.g. in patients with chronic rheumatic heart disease
3. hypotension e.g. boundary zone infarcts
4. vasculitis e.g. in tuberculous meningitis
5. vasospasm as in subarachnoid haemorrhage
6. venous occlusion causing haemorrhagic infarcts
7. vascular complication of raised intracranial pressure
8. other causes: sickle cell anaemia, polycythaemia rubra vera, migraine, hyperlipidaemia

Atherosclerotic arterial disease: Occlusion or stenosis of the carotid, the vertebral arteries and the intracranial cerebral arteries is a major cause of cerebral infarction. Atherosclerosis is the chief predisposing factor. One commonest site is the origin of the internal carotid artery at the carotid bifurcation. Angiographic studies in stroke patients show more extracranial vascular occlusion in Caucasians while African-Americans, Japanese and Chinese have more intracranial vascular occlusions.

Small vessel disease: The basal ganglia, thalamus and pons are supplied by deep penetrating arteries, which are small arteries and take off at a sharp angles from the large cerebral arteries. Degenerative change in these vessels is known as lipohyalinosis, which is characterised by hyalinization and fibrinoid degeneration of the vessel wall with lipid deposition and accumulation of foamy macrophages. This type of degenerative changes is especially severe in patients with hypertension. There can be progressive narrowing of the lumen causing a small deep cerebral infarct in the region supplied by it (lacunar infarct) or weakening with progressive dilatation of the lumen giving rise to microaneurysm. Rupture of these microaneurysms leads to the hypertensive cerebral haemorrhage. Lacunar infarcts are small infarcts of 3-20 mm in diameter that lie deep within the cerebral hemisphere and brain stem. Though they are of small size, involvement of the internal capsule or brain stem may result in significant neurological deficit.
Boundary zone infarcts: The zone between two arterial beds becomes maximally deficient in blood supply and usually undergoes progressive and gradual ischaemia and necrosis. They are most often seen in the borders between the anterior and middle cerebral arterial beds. The usual cause is diffuse intracranial atherosclerosis in combination with a drop in systemic blood pressure or congestive heart failure. Clinically, these patients do not produce clear focal neurological signs.

Infarcts due to vasculitis: This is most commonly due to purulent meningitis with vasculitis. Haemophilus influenzae and tuberculous meningitis are typical examples.

Morphologic changes in cerebral infarct: A pale infarct is initially swollen and slightly softened. This is followed by cracking and liquefaction in 4 to 5 days. Resorption with replacement by fluid filled cavities as seen in an old infarct takes weeks to months. Microscopically, between 6 to 8 hours, the neurons undergo ischaemic necrosis. Macrophages appear in the next 6 to 12 hours. At the end of the first week, the typical infarct will show heavy infiltration of macrophages with astrocytic proliferation around the border.

**Intracranial Haemorrhage**

3 major pathological types:
1. intracerebral haemorrhage
2. subarachnoid haemorrhage
3. extradural and subdural haemorrhage

**Intracerebral Haemorrhage**

Common causes:

1. Abnormalities of blood vessels:
   - microaneurysm in hypertension
   - saccular aneurysm
   - arterio-venous malformation (AVM)
   - congophilic angiopathy
   - arteritis

2. Blood disorders:
   - thrombocytopenia
   - coagulopathies
   - anti-coagulants

3. Abnormalities of brain tissue:
   - infarcts
   - tumour

4. Traumatic

5. Miscellaneous e.g. drugs (amphetamine), alcohol

6. Idiopathic
Hypertensive cerebral and cerebellar haemorrhage:

Spontaneous intracerebral haemorrhage associated with hypertension are particularly likely to occur in the basal ganglia, pons and cerebellum. This is due to the small vessel disease in the deep penetrating arteries in patients with hypertension. There is lipohyalinosis with microaneurysm formation. Rupturing of these microaneurysms results in massive intracerebral haemorrhage, which tends to dissect through the brain tissue and extends into the ventricular system. Secondary oedema of the surrounding brain tissue, obstructive hydrocephalus and herniation will follow.

Congophilic angiopathy: Amyloid is deposited in the pial and intra-cortical arterioles. The incidence increases with age. It is found in 10% of Caucasians over 70. It is an increasing important cause of cerebral haemorrhage, especially in lobar sites and in elderly people.

Blood disorders: In thrombocytopaenia, the haemorrhage is often multifocal and lobar in location. Patients with coagulation factor deficiencies more often bleed into the subdural space. Another important cause is anti-coagulant therapy especially in patients with prosthetic heart valves.

Brain tumors: Massive haemorrhage can occur in both primary and secondary intra-parenchymal tumours. Metastatic choriocarcinoma is a typical example.

Vascular Malformations (Angiomas)

These are congenital malformations of vessels, consisting of 4 main types: arteriovenous malformations (AVM), venous angiomas, cavernous angiomas and capillary angiomas. The venous type is the most common. The arteriovenous malformation is the most aggressive. The major clinical effects are rupture with massive haemorrhage, steal and mass effect. The cause of rupture is not known and appears to be unrelated to physical activity, hypertension or trauma. The adjacent neural tissue is often deprived of normal blood supply by an angioma, (often an AVM), i.e. steal which gives rise to epilepsy and neurological dysfunction.

Subarachnoid Haemorrhage

It is usually due to rupture of a berry (saccular) aneurysm (65%) but may also result from bleeding from AVM (5%), blood dyscrasia or other causes. In up to 20% of patients no cause is found even after angiography or autopsy. The bleeding may occur only in the subarachnoid space or occurs both in the subarachnoid space and into the brain.
Saccular intracranial aneurysms (berry aneurysms, medial defect aneurysms).

Prevalence: They occur at all ages past puberty, estimated to 1-2%. 25% have multiple aneurysms which are often bilateral as mirror image aneurysms.

Location: These occur at arterial bifurcations, 90% in anterior circulation, most often in 3 sites:

1. the middle cerebral artery - origin of first main branches within the Sylvian fissure
2. the origin of anterior communicating artery from the anterior cerebral artery
3. the internal carotid artery - terminal bifurcation and origin of posterior communicating artery

Co-existing disorders: These include adult polycystic kidneys and coarctation of aorta.

Size: Aneurysms less than 5 mm in diameter seldom rupture. The critical range in size of ruptured aneurysms is between 5 and 10 mm. Those larger than 3 cm will cause mass effects rather than rupture.

Outcome: The majority (60%) have no symptoms. For those with symptoms, 90% are due to rupture and 10% due to mass effect of the aneurysm.

Those ruptured will be followed by one of the followings:

1. spontaneous closure (but the risk of rebleeding is high)
2. progressive hydrocephalus due to obliteration of subarachnoid space by organizing haematoma
3. cerebral infarction due to spasm of the cerebral artery harbouring the ruptured aneurysm
4. expanding haematoma
5. epilepsy

Etiology: There is no satisfactory explanation. Theories include congenital defects of the media, and origin from vestigial remnants of embryonic vessels.