

The Pathology of Raised Intracranial Pressure

Under normal circumstances intracranial pressure (ICP) is maintained in the range 5-15mmHg with continuous, small fluctuations reflecting physiological variations in arterial or venous pressure such as arterial pulsation, coughing and straining. Maintenance of intracranial pressure at these levels is critical to safeguarding adequate cerebral perfusion. Inside the unyielding box that is the skull, expansion of intracranial contents may precipitate a rise in ICP with potentially serious consequences. In this article a brief review of the historical concepts contributing to our understanding of raised ICP is provided followed by detail on the neuropathological findings in circumstances where ICP has been elevated in life.

Historical background

Initial observations on the consequences of raised ICP were influenced by the doctrine of Monro¹ (1783) and Kellie² (1824) which holds that, once the fontanelles have closed, the incompressible intracranial contents, comprising brain and blood, are contained within the rigid skull. Omitted from their description, but subsequently added by Burrows³ was the contribution of cerebrospinal fluid (CSF). The interaction of these components in the context of an expanding, intracranial tumour subsequently formed the basis for the description of the clinical stages of raised intracranial pressure by Theodor Kocher⁴ (Table 1). In stage 1, the increase in tumour volume is compensated for by a reduction in volume of blood and CSF resulting in no increase in ICP. However, as these compensatory mechanisms become exhausted ICP starts to rise slowly with clinical symptoms beginning to manifest (stage 2). In stage 3, the compensatory mechanisms are overwhelmed such that relatively small rises in tumour volume result in a large rise in ICP. Eventually, unchecked, intracranial pressure may rise to equal arterial blood pressure with resultant failure of cerebral perfusion, vasomotor paralysis, coma and, ultimately, death.

A number of intracranial pathologies may precipitate a rise in intracranial pressure which may be summarised in the 'four lump' concept comprising the mass, accumulation of CSF, vascular congestion and cerebral oedema (Table 2). In the majority of cases the pathology is

localised and, together with surrounding brain swelling, produces distortion of the brain with eventual herniation and pressure gradients between CSF spaces. For example a supratentorial mass lesion may lead to a pressure gradient between supratentorial and infratentorial compartments by occlusion of the subarachnoid space as the medial temporal lobe impinges on the tentorium. Coincident with this shift, the blood supply to the brain may be compromised by direct compression of cerebral blood vessels. This compounds vascular compromise as a consequence of rising ICP and falling cerebral perfusion pressure.⁵ A further consequence, therefore, of raised ICP is hypoxic/ ischaemic damage, both localised and diffuse.

Neuropathology findings in raised intracranial pressure

To the Neuropathologist the pathology of raised ICP is a function of the causative pathology, any associated, localised deformation of the brain, a reduction in CSF volume, shift of the brain and herniation with the associated vascular consequences (Figure 1). To these features can be added the consequences of any intervention to alleviate raised ICP.

Figure 1: Autopsy findings in raised intracranial pressure

- Tight dura
- Flattened gyri
- Compressed sulci
- Asymmetry of cerebral hemispheres
- Midline shift
- Internal herniation
 - subfalcine/supracallosal
 - tentorial
 - tonsillar
- External herniation
- Posterior cerebral artery infarction
- Posterior inferior cerebellar artery infarction
- Diffuse hypoxic/ischaemic injury
- Brainstem haemorrhage/ infarction



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Table 1: Clinical stages of raised intracranial pressure

	Intracranial response	Clinical symptoms/ signs
Stage 1	increase in tumour volume; compensatory reduction in CSF and blood volume; no rise in ICP	none
Stage 2	compensatory mechanisms exhausted; slow rise in ICP	drowsy, headache
Stage 3	rapid rise ICP; falling cerebral perfusion pressure	deteriorating conscious level; intermittent elevations in blood pressure and bradycardia
Stage 4	cerebral vasomotor paralysis; ICP equals mean arterial blood pressure; cerebral perfusion ceases	coma; fixed dilated pupils; death

Table 2: Causes of raised intracranial pressure

Mechanism	Example
Mass effect	tumour, haemorrhage, infarction, contusions, abscess
Brain swelling	diffuse traumatic brain injury, metabolic/ hypertensive encephalopathy, meningitis
Increased venous pressure	venous sinus thrombosis, heart failure, depression fractures over major venous sinuses causing obstruction
Obstructed CSF circulation and/or absorption	hydrocephalus, meningeal infiltration
Increased CSF production	meningitis, choroid plexus tumour



Figure 2: View of the head following removal of the calvarium. The dura is taut reflecting raised intracranial pressure as a consequence of diffuse brain swelling.



Supratentorial expanding lesions

A consequence of an expanding mass lesion in a cerebral hemisphere is compression and distortion of adjacent structures resulting in swelling of the brain. With this, the vertex may become compressed against the dura with obliteration of the subarachnoid space, flattening of the gyri and compression of the sulci. This can be demonstrated at autopsy by careful reflection of the calvarium, leaving the dura intact. Where brain swelling is present the dura are taut with the brain compressed against the inner surface such that reflecting the dura without damaging the underlying brain can be difficult (Figure 2). On removal of the brain the extent of distortion and displacement is often most evident on inspection of the base where tentorial herniation, brainstem ischaemia, third nerve compression and the consequences of vascular compromise may be present (Figure 3).

The extent of displacement and any secondary vascular complications are optimally demonstrated on sectioning the brain. Ipsilateral to an expanding mass lesion the lateral ventricle may become compressed whilst the contralateral ventricle may be enlarged as a result of obliteration of the foramen of Monro (Figure 4). Further expansion of the mass lesion then produces shift in the brain with associated internal herniation.

Supracallosal/ subfalcaline herniation – lateral displacement of the cingulate gyrus under the free edge of the falx cerebri (Figure 4). With this there may be associated pressure necrosis of the cingulate gyrus in addition to ischaemia of the parasagittal cortex as a consequence of compression of the pericallosal arteries. Estimation of the degree of displacement of the herniated cingulate gyrus may serve as an indicator of the degree of midline shift.

Tentorial/ uncal herniation (Figure 4) – displacement of the medial temporal lobe structures downwards through the tentorial incisura. With this the midbrain may become distorted and displaced, compressing the contralateral cerebral peduncle against the free edge of the tentorium and the ipsilateral third nerve against the adjacent posterior cerebral artery. Clinically these manifest as dilatation of the pupil and hemiparesis ipsilateral to the expanding mass lesion. A further complication of tentorial herniation is necrosis of the inferomedial temporal cortex, which may be compressed over the tentorial edge. Similarly the posterior cerebral arteries are at risk of being compressed with associated vascular compromise of the medial and inferior occipital lobe (Figure 5).

Tonsillar herniation (cerebellar cone) – downward displacement of the cerebellar tonsil through the foramen magnum. This is recognised at autopsy as grooving of the inferomedial surface of the cerebellum associated with haemorrhagic necrosis of the tonsils and flattening of the medulla. This distortion of the caudal brainstem may be associated clinically with apnoea. Occasionally the posterior inferior cerebellar arteries may become compressed resulting in infarction of the inferior cerebellar hemispheres.

Brainstem haemorrhage (Duret haemorrhages) and infarction – representing the terminal events as a consequence of raised ICP. At autopsy these are recognised as small foci of haemorrhage and/ or infarction in the paramedian parenchyma of the rostral brainstem (pons and midbrain) towards the anterior aspect⁶ (Figure 3). Originally described by Duret, their pathogenesis remains unclear with compromise of the perforating branches of the basilar artery through downward displacement of the brainstem favoured.^{7,8}

Infratentorial (posterior fossa) expanding mass lesions

Mass lesions in the posterior fossa may lead to obstruction of CSF flow resulting in lateral and third ventriculomegaly as a consequence of displacement of the aqueduct and fourth ventricle. As with a supratentorial mass lesion, tonsillar herniation may occur with the associated vascular complications. Upwards displacement of the superior cerebellar hemispheres and vermis through the tentorial incisura may also occur

Figure 3: Base of the brain. As a consequence of an expanding supratentorial mass lesion, in this case a large, right-sided subdural haematoma, there is ipsilateral tentorial herniation (arrows) with haemorrhagic necrosis of the involved medial temporal cortex. Shift in the brainstem has also resulted in compression of the contralateral cerebral peduncle against the free edge of the tentorium (arrowhead). Finally, haemorrhagic necrosis is present in the midline of the midbrain (Duret haemorrhages).

resulting in reverse tentorial herniation, recognised at autopsy as upwards displacement of the superior vermis with associated distortion of the medial temporal lobes. This may be exacerbated by supratentorial decompression in the presence of a pressure gradient across the tentorium from infra- to supratentorial spaces. Clinically the result is rapid onset, bilateral extensor rigidity and loss of pupillary light reflexes.

External cerebral herniation

As noted above, as a rigid, closed box the skull, though ideally constructed for the protection of the delicate intracranial contents, is 'flawed' when the volume of those contents rises resulting in a rise in intracranial pressure. To address this in circumstances such as diffuse traumatic brain injury or malignant middle cerebral artery infarction, where medical interventions may have met with limited success, decompressive craniectomy has been utilised as a means to permit the intracranial contents to expand and so reduce ICP.^{9,10} Where there is a defect in the calvarium, either by such surgical intervention or through trauma, segments of cortex may herniate resulting in external herniation. Pressure necrosis of the cortex at the margins of the hernia may then ensue with further ischaemic damage of the herniated cortex following.

Conclusion

To the Neuropathologist the consequences of an expanding mass lesion within the rigid, closed skull are readily evident at autopsy as a constellation of findings revealing the degree of distortion of the intracranial contents in an attempt to accommodate the added volume of the mass lesion and the subsequent rise in ICP which follows as these compensatory adjustments fail. An awareness, therefore, of the range of abnormalities and their often inconspicuous appearance serves to inform the neuropathology autopsy examination where raised ICP is suspected from removal of the calvarium to review of the histology for the subtleties of early, acute hypoxic/ ischaemic damage.

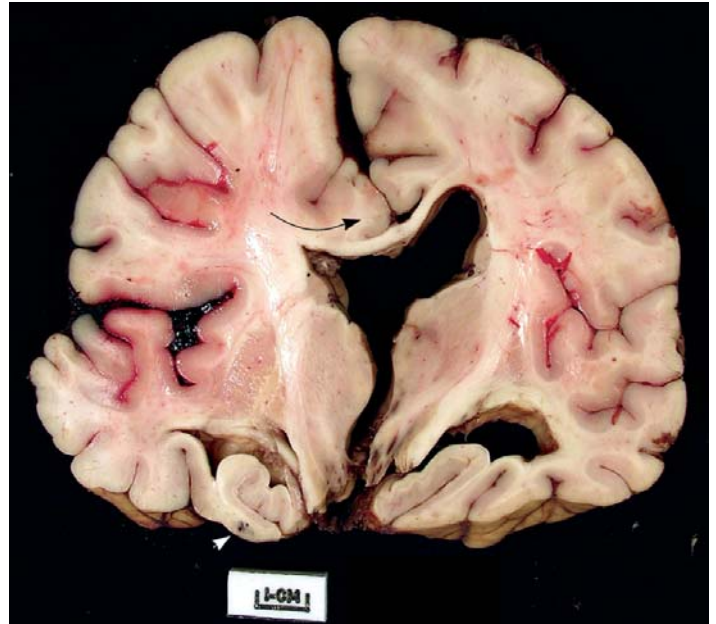


Figure 4: Coronal section of cerebral hemispheres. As a consequence of a subdural haemorrhage on the left hand side there has been midline shift, demarcated by supracallosal herniation from left to right (arrow), tentorial herniation with pressure necrosis of the inferomedial temporal lobe (arrowhead) and contralateral ventriculomegaly arising from obstruction of the foramen of Monro.

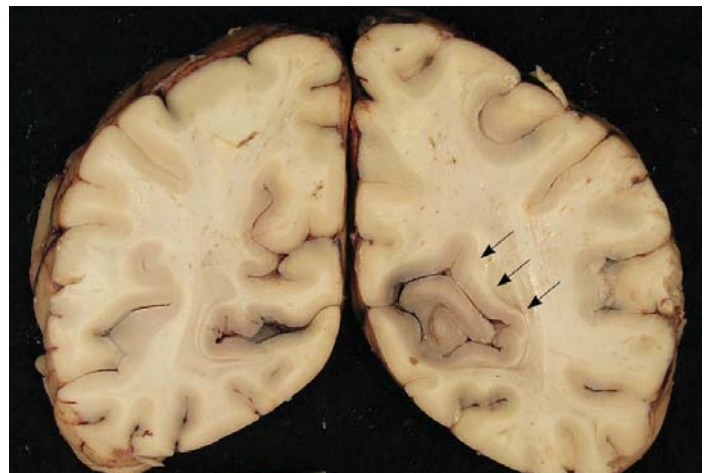


Figure 5: Coronal slices of the occipital lobes. Compression of the posterior cerebral arteries with tentorial herniation may lead to ischemia of the medial occipital lobes (arrows).

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