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Pathology: the science behind the cure

Neuropathology autopsy practice: post mortem examination in patients with traumatic brain injury

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Coordinators: Dr C Smith, Department of Pathology, University of Edinburgh, Edinburgh
Dr T Dawson, Neuropathology Department, Lancashire Teaching Hospital NHS Trust, Preston, Lancashire
Dr S al-Sarraj, Department of Clinical Neuropathology, King's College Hospital, London

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| Produced by | Dr C Smith, Department of Pathology, University of Edinburgh, Edinburgh, Dr T Dawson, Neuropathology Department, Lancashire Teaching Hospital NHS Trust, Preston, Lancashire, Dr S al-Sarraj, Department of Clinical Neuropathology, King's College Hospital, London |
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The Royal College of Pathologists
2 Carlton House Terrace, London, SW1Y 5AF
Tel: 020 7451 6700
Fax: 020 7451 6701
Web: www.rcpath.org

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1 The role of the post mortem examination

Traumatic brain injury (TBI) is an umbrella term for a range of focal and diffuse pathologies which can be associated with trauma. In cases of death related to traumatic brain injury, the post mortem examination can serve a range of roles:

- Providing a detailed description of the intracranial, intracerebral and spinal pathology associated with trauma.
- In cases of criminality, potentially providing additional information relating to the mechanism and timing of the injuries.
- Providing accurate national statistical information regarding the incidence of the various pathologies seen in traumatic brain injury.
- Supporting research into the mechanisms of pathology seen in traumatic brain injury.

Virtually every traumatic brain injury-related death will fall under the authority of the Coroner/Procurators Fiscal and post mortem examination will be under their instruction. As such, in many instances, the brain (and spinal cord) is examined by the general and/or forensic pathologist. However, involving a neuropathologist in the brain examination may give more information about the nature of trauma, mechanism and timing.

2 Brain pathology encountered at post mortem examination

A range of pathologies may be seen in traumatic head injury. Pathologies can best be considered to fall into either the focal or diffuse groups.

2.1 Focal

2.1.1 Scalp

The distribution of bruising and lacerations is important to document in relation to the face and cranium. In addition, there may be surgical incision if there has been neurosurgical intervention.

2.1.2 Skull

Fractures are commonly seen in fatal traumatic head injury.

2.1.3 Haematomas

Haematomas can be extradural, subdural, subarachnoid or intracerebral. Intracerebral haemorrhages may be superficial, associated with contusions or more deeply seated, particularly in cases of high velocity impact.

The size (volume) and site of the extradural (usually associated with skull fracture) and subdural haematoma should be measured. A volume exceeding 40–50 ml is usually associated with a pressure effect on the brain. More than 100–120 ml is usually fatal and associated with macroscopic brain midline shift with herniation.

In cases of traumatic basal subarachnoid haemorrhage, a comprehensive examination of the cerebral blood vessels is essential and should be done at the time of autopsy examination to exclude any aneurysm or vascular malformation. The intracranial and intraspinal parts of the vertebral arteries should then be examined for any traumatic tear or damage. The vertebral arteries are best examined *in situ* by careful dissection of the vertebral canal in the cervical spinal column, the dissection extending all the way upwards to the point where the artery enters through the dura at the foramen magnum, and downwards to the subclavian artery (Bromilov and Burns 1985). Any fresh blood should be

carefully cleared. The arteries should be carefully removed and processed for serial sectioning.

2.1.4 Contusions and lacerations

Contusions and lacerations are typically found on the inferior surfaces or poles of the frontal and temporal lobes. These are common for what are called contre-coup contusions. Direct or coup contusions can be anywhere in the brain, depending on the site of the impact, and are usually associated with some scalp bruising and sometimes with skull fracture.

2.2 Diffuse

A range of diffuse injuries may be seen, some of which are obvious macroscopically while others require microscopy.

2.2.1 Diffuse traumatic axonal injury

Axonal damage may be a consequence of rotational injury. The forces result in secondary axotomy, although clinical effects may be almost immediate. Microscopy is required to make this diagnosis.

2.2.2 Diffuse vascular injury

This is an extreme form of rotational injury in which small white matter vessels are damaged, particularly in the frontal white matter, but often more extensively. White matter petechial haemorrhage is seen macroscopically. The clinical picture is often that of immediate unconsciousness with only short survival.

2.2.3 Diffuse ischaemic brain injury

This is a common finding in fatal TBI and results from reduced or absent cerebral perfusion. This may be secondary to cardiac arrest associated with other injuries, or may be secondary to raised intracranial pressure preventing adequate cerebral perfusion. If there has been survival of at least several days, laminar necrosis may be seen macroscopically. If there has been a survival of less than a few hours, microscopic examination is unlikely to show any definite neuronal ischaemic injury.

2.2.4 Diffuse brain swelling

Most commonly swelling is secondary to ischaemic injury, although swelling may also be seen in relation to contusions or in the setting of diffuse traumatic axonal injury.

As can be seen from the above discussion, the diagnosis of head injury, while sufficient for national data, gives little information regarding the actual pathology responsible for, or significantly contributing to, the death of the individual.

3 Clinical information relevant to the post mortem examination

Most of the information will come from the Coroner's/Procurators Fiscal's Office and through the police reports. In some circumstances this may be supplemented by access to GP and hospital records.

As with any post mortem examination, knowledge of past medical history is important. It is useful to have details in relation to the following:

- *Previous head injury:* it is useful to know if there have been one or many episodes of previous head injury, their significance and whether they required neurosurgical intervention. Chronic subdural membranes are more prone to bleed with lesser trauma due to the fragile macro-capillaries found within these membranes.

- *Social and medical history*: recurrent falls are more common amongst the alcoholic population. In addition, a range of bruises and cuts to the face are not uncommon amongst individuals leading a chaotic lifestyle. Patients on warfarin treatment or with liver disorder are more prone to greater bleeding. Any significant medical history, such as hypertension, should be noted.
- *Circumstances at the time of death*: it is important to have as much detail as possible relating to the incident that caused the fatal head injury. In the setting of a road traffic accident, for example, was the deceased a passenger, a driver or a pedestrian? If within a vehicle, was the deceased wearing a seatbelt? It is important to be aware of other injuries documented at the time of autopsy examination, and the results from any studies during life, including any radiological and neurosurgical interventions.
- In criminal cases, information via the police about witnesses or other findings may be very important. All available information should be documented or recorded in the neuropathology report.

4 Autopsy procedure

The post mortem examination should be performed in the standard way. If tissue is referred for further neuropathological examination, a draft copy of the autopsy report should be provided. If available, a set of photographs of the autopsy may be informative and neuroradiology, if available, should be examined.

The Royal College of Pathologists has produced a useful document outlining an approach to medicolegal specimens and preserving the chain of evidence (http://www.rcpath.org/resources/pdf/g047_chainofevidence_jul08.pdf).

4.1 External examination

In road traffic accidents there may be bruising indicating that a seatbelt was worn or there may be bruising related to the head or face indicating a point of impact. In cases of assault or fall, again, document the site, size and pattern of bruises on the body, particularly the head and neck regions. Any signs of surgical intervention should be documented. Photography is strongly recommended for future reference, particularly in criminal cases.

4.2 Internal examination

There should be a standard macroscopic description for each organ system, including measurement of the organ weights. Morbid anatomical causes of death that are visible at the time of post mortem should be sought and where necessary supported by histological confirmation. For example, a road traffic accident may have been secondary to a myocardial infarct. It is important to realise that cases of head injury are frequently associated with injury to other organs, soft tissue and bone. All these should be carefully recorded.

5 Specific significant organ systems

5.1 Head and neck

The scalp and skull should be carefully examined for signs of impact injury. Any skull fractures should be carefully documented and if appropriate an illustration should be recorded, either photographic or drawn. When reflecting the dura, the bridging veins should be studied and any obvious tears documented. The spinal column and in particular the cervical spine should be carefully examined. Any soft tissue haemorrhages or fractures to the spinal column should be documented and the underlying cord should be examined.

Imaging of the neck in cases of suspected bony injury is to be encouraged.

6 Organ retention

Whereas previously retention and prolonged fixation of the brain was the normal procedure, current practice requires a modified approach. In all cases of criminality involving significant head injury, the recommendation remains that the brain is retained for prolonged fixation prior to examination. The Coroner (or Procurator Fiscal), and through their office the deceased's family, should be informed that a completed neuropathological examination will be provided within a period of 3 months from the time of death. 10% formalin is the standard fixative used.

The following are offered as compromises in situations where there is no consent for retention of the brain for prolonged fixation.

- Macroscopic examination only. There are many situations where the macroscopic pathology alone is informative and allows a confident discussion of the pathophysiology of the cause of death. An example would be an accidental fall with subdural haemorrhage (SDH) and mass effect associated with axial displacement.
- The brain may be retained in fixative for a period of no longer than 24 hours and then sliced in the standard way and samples taken for histological analysis. This provides a reasonable degree of fixation and makes sectioning of the brain easier than in the fresh state. The brain can then be returned to the body for burial.
- Retention of a mid-region coronal section of brain and sections of brainstem and cerebellum. In this scenario the brain is examined and sectioned in the fresh state. A single section of the cerebrum beginning approximately 1 cm caudal to the mamillary bodies is retained. This section should be approximately 1 cm in thickness. A block of anterior corpus callosum, a section of left and right cerebellar hemispheres and sections of midbrain, pons and medulla should also be retained for histological examination. It should be made clear to the Coroner/Procurator Fiscal that all tissue retained in this slice will be processed for histological examination and that no tissues will be retained outwith paraffin blocks, or that any retained small fragments of tissue will be disposed of in line with Human Tissue Authority (HTA) guidelines. Histological blocks should also be taken from any other pathological lesion. If the spinal cord has been retained, representative sections of cervical, thoracic, lumbar and sacral regions should be put directly into histology clips for fixation.

In any method, it is preferable that the brain is photographed. The photographs should be labelled and stored with the case file for future reference.

7 Minimal blocks for histological examination

In many cases histology is not required as the macroscopic examination can provide all the information required. Histology is most useful in the assessment of diffuse injury, or where assessment of a focal lesion may provide additional information regarding timing of an injury. The following is suggested for a minimum approach to the investigation of traumatic brain injury.

7.1 General histology

Representative histology should be taken as felt appropriate and determined by the findings at the post mortem examination. For example, myocardium may be taken if there has been a suspected myocardial infarct.

7.2 Neuropathology

7.2.1 Focal pathology

Any focal pathology identified at the time of post mortem may be examined microscopically. Extradural or subdural haemorrhages should be sampled in the form of a dural roll. This requires a section of dura to be rolled up and cut to a thickness of no more than 1 cm before being placed into a histology clip. Sampling of these lesions may allow a rough estimate at timing if the clinical history is incomplete. Take extra blocks from different regions if more than one episode of bleeding is suspected by the history or gross examination.

7.2.2 Diffuse lesion

Diffuse lesions should always be considered when the patient has been unconscious in the absence of any focal mass lesion. The commonest diffuse pathologies are global ischaemic injury and diffuse traumatic axonal injury. The following is recommended as part of the assessment of diffuse lesions within the brain. The blocks should be taken from both the right and left side (see Appendix 1):

- Block 1: Frontal to include parasagittal white matter areas and anterior corpus callosum at the level of the head of the caudate nucleus;
- Block 2: Basal ganglia, including the internal capsule;
- Block 3: Hippocampus (at the level of the lateral geniculate body);
- Block 4: Thalamus, including the internal capsule;
- Block 5: Posterior corpus callosum and parietal parasagittal white matter;
- Block 6: Parietal convexity;
- Block 7: Pons, including the superior cerebellar peduncle;
- Blocks 8 and 9: Cerebellum, including the middle cerebral peduncle.

Other blocks such as medulla and midbrain may be useful.

If large blocks cannot be processed in a particular lab, two or more smaller contiguous samples could be taken from a particular region.

7.2.3 Spinal cord

The most common scenario where the spinal cord is examined is in the setting of cervical spine injury with damage to the underlying cord. Only a small segment of cervical cord should be examined in this setting, and the sampling should be related to the areas of bony injury.

7.3 Staining

The blocks should be stained with H&E, and when required with beta amyloid precursor protein (β APP) and CD68 (to investigate microglial cells).

Diffuse axonal injury is best demonstrated by β APP immunohistochemical staining. The β APP staining for traumatic axonal injury should be differentiated from that associated with ischaemic injury (vascular axonal injury), such as that seen in cases of space-occupying lesion (like subdural haematoma) with increase in the intracranial pressure and brain shifting (see Further reading, Reichard *et al* 2005).

The dura and extra/subdural haematoma are stained with H&E, Perl's and CD68, which are useful stains to age the haematoma.

8 Paediatric head injury

Neuropathologists may face cases of paediatric head injury, including non-accidental child death with head injury. The same rules of examination of the brain in child head trauma as in adults should be followed with the following additional recommendations:

- The dura should be examined thoroughly and sampled from different locations if SDH is present.
- The brainstem and cervicomedullary region should be sampled extensively to investigate axonal injury.
- The spinal cord should be examined and sampled thoroughly (blocks are taken as mentioned in 7.2.3) and examined for focal lesions, axonal injury in the white matter and spinal nerve roots. Subdural and subarachnoid haemorrhage in the spinal cord also needs to be documented.

9 Other samples required

Toxicology may be required, again in discussion with the Coroner/Procurator Fiscal. In deaths following assaults or road traffic collisions, alcohol and other drugs may need to be assessed.

10 The clinicopathological summary

The clinicopathological summary needs to be clear and concise and the pathologist must remember that this is likely to form part of a medicolegal document. Therefore, only statements of fact should be provided. The pathologist should clearly outline their macroscopic and microscopic observations. This should be considered in light of the clinical history provided. An overall summary should be made to correlate the pathological findings with the clinical history provided and in particular to highlight consistencies or inconsistencies between the two. It is important for the pathologist to highlight areas of certainty and of uncertainty, in particular in relation to the mechanism and timing of injuries.

11 Summary of post mortem brain examination with head injury

- 1 Subarachnoid haemorrhage:
 - Distribution (diffuse or localised);
 - If basal, exclude possibility of berry aneurysm and examine vertebral arteries (intracranial and intraspinal courses) for traumatic tear.
- 2 Contusions:
 - Site: temporal, frontal, other site (coup and countre-coup);
 - Measurement: may be related to severity of head injury.
- 3 Brain herniation [\uparrow intracranial pressure (ICP)]:
 - Uncal herniation (remove brainstem and cerebellum for better assessment), bilateral or unilateral;
 - Tonsillar herniation, usually associated with haemorrhage and necrosis rather than only bulging;
 - Supracallosal (or subfalcine) herniation;
 - Brain shifting – corpus callosum and lateral ventricle.
- 4 Brain swelling – flattening of gyri, bilateral or one cerebral hemisphere.
- 5 Corpus callosum and fornix: small areas of haemorrhage may be a sign of diffuse traumatic axonal injury (lateral), or may be secondary to supracallosal herniation (midline).
- 6 Infarction and ischaemia:
 - Site;

- Arterial territory.
- 7 Intracerebral haemorrhage:
- Related to an expanding contusion;
 - Deep structure of brain like white matter and basal ganglia.
- 8 Brainstem:
- Diffuse traumatic axonal injury (small bleeding: dorso-lateral quadrants and superior cerebellar peduncle);
 - Diffuse vascular injury (small bleeding: subependymal and around fourth ventricles and aqueduct);
 - ↑ ICP (haemorrhage in midline).

12 Further reading

Bromilow A, Burns J. Technique for removal of the vertebral arteries. *J Clin Pathol* 1985;38:1400–1402.

Geddes JF, Vowles GH, Beer TW, Ellison DW. The diagnosis of diffuse axonal injury: implications for forensic practice. *Neuropathol Appl Neurobiol* 1997;23:3947.

Geddes JF, Whitwell HL, Graham DI. Traumatic axonal injury: practical issues for diagnosis in medico-legal cases. *Neuropathol Appl Neurobiol* 2000;26:105–116.

Geddes JF, Hackshaw AK, Vowles GH, Nickols CD, Whitwell HL. Neuropathology of inflicted head injury in children. I: Patterns of brain damage. *Brain* 2001;124:1290–1298.

Geddes JF, Vowles GH, Hackshaw AK, Nickols CD, Scott IS, Whitwell HL. Neuropathology of inflicted head injury in children. II: Microscopic brain injury in infants. *Brain* 2001;124:1299–1306.

Graham DI, Smith C. The pathology of head injury. *CPD Bull Cellular Pathol* 2001;3:148–151.

Graham DI, Smith C, Reichard R, Leclercq PD, Gentleman SM. Trials and tribulations of using β APP immunohistochemistry to evaluate traumatic brain injury in adults. *Forensic Sci Int* 2004;146:89–96.

Reichard RR, Smith C, Graham DI. The significance of β APP immunoreactivity in forensic practice. *Neuropathol Applied Neurobiol* 2005;31:304–313.

Appendix 1 Recommended blocks to assess diffuse brain injury

