Approach to Neuropathological Disorders at Autopsy

Histopathology trainees
January 2017
Prof S B Wharton
Session Aims

• Appreciating the context of the examination
• Approach to Dissection
• Describing abnormalities
• Block selection
• Clinicopathological synthesis
Context

- Clinical context
- At autopsy or brain referral
- Formal neuropath – 3/52 fixation vs fresh
- Autopsy type
  - Coronial
  - Consent
  - Research donation
- Consent / permissions/ disposal instructions
- Proper records and tissue tracking
External 1: Coverings of the Brain

• Skull
• Meninges
  – Spaces
  – Venous sinuses
Vessels

- Lesions
- Lumen
- Layout
Brain surface

- Swelling
- Softening
- Discolouration
- Herniation
Assessment of focal Lesions

• Neuroanatomy
• Mass effect
• Tissue loss
• Effect of a mass on the brain
• Relationship to cause of death
Anatomical Effects of a Mass Lesion

• Local deformity and shift of structures
• Decreased volume of CSF
• Pressure gradients - internal herniation
  – Lateral tentorial with secondary haemorrhage
  – Cerebellar tonsillar
  – Central transtentorial
  – Subfalcine cingulate
The autopsy for stroke

- What is the vascular pathology?
- What has caused the vascular pathology?
- How does it relate to other pathology?
- How does it explain the patient’s symptoms?
- How has it contributed to death?
Issues in the young (<45)

- Structural cardiac defects
- Premature atherosclerosis
- Oral contraceptives and pregnancy
- Arterial dissection
- Vasculitis
- Fibromuscular dysplasia
- Hereditary disorders
- Smoking and alcohol
- Recreational drugs
Cerebral Embolism

- Thromboembolism
- Septic
- Air
- Fat
- Amniotic fluid
Global ischaemia

• Diffuse brain swelling
• CA1 ischaemic neuronal change
• Purkinje cells ischaemic neuronal change
• Cortical laminar necrosis
• Boundary zone infarcts
• Note effects of fixed arterial obstructions
Pathology of Head Injury
Primary Pathology

• Focal
  – Extradural haematoma
  – Subdural haematoma (acute and chronic)
  – Intraparenchymal haematomas / contusions

• Diffuse
  – Diffuse axonal injury
  – Diffuse brain swelling
  – Diffuse vascular injury
Extradural Haematoma

• Most have skull fracture
• May have lucid interval
• Classically due to tearing of the middle meningeal artery
Chronic Subdural Haematoma

- Often elderly
- Associations
  - Cerebral atrophy, alcohol, coagulopathy
- Injury may be trivial
- Haematoma may be encapsulated in membrane
- May be repeated small bleeds
Diffuse Axonal Injury

- Small haemorrhages – corpus callosum, dorsolateral rostral brainstem
- Often associated with gliding haemorrhages in cerebral white matter
- Diffuse axonal damage
  - Eosinophilic, argyrophilic bulbs on axons appear 15-18hrs post injury
  - Followed by reactive changes in microglia and astrocytes
  - Beta APP up-regulated from 3 hrs
Secondary Effects of Head Injury

- Ischaemia
- Brain swelling
- Infection
- Raised intracranial pressure
Late Complications of Head Injury

- Severe disability
- Persistent vegetative state
  - DAI and diffuse ischaemic brain damage
- Post-traumatic epilepsy (early or late)
- Concentration /memory impairment
- Hydrocephalus
- Progressive neurological disease
- Chronic traumatic encephalopathy
Atrophy – the Brain in Neurodegeneration

- Disorders of Cognition
- Disorders of Motor Function
- Atrophy – location
- Pigment loss
  - Substantia nigra Parkinson’s
  - Locus ceruleus Parkinson’s, Alzheimer’s
- Other pathologies – e.g. vascular
Dementia - causes

• Neurodegenerative Diseases
  – **Alzheimers**
  – **Dementia with Lewy Bodies**
  – Picks Disease
  – MND inclusion dementia
  – FTDP-17
  – Dementia lacking distinctive histology
  – Progressive supranuclear palsy
  – Argyrophilic grain disease
  – Corticobasal degeneration
  – Huntington’s disease Etc.

• Vascular Diseases
  – **Vascular dementia**

• Infectious/Inflammatory/Immune
  – Prion diseases
  – Neurosyphilis, AIDS
  – Multiple sclerosis

• Toxic and Metabolic

• Others
### Braak Staging for Neurofibrillary Tangle Formation

<table>
<thead>
<tr>
<th>Location</th>
<th>Stage:</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trans ERC Pre-alpha</td>
<td></td>
<td>i-+</td>
<td>+</td>
<td>++</td>
<td>+++g</td>
<td>+++g</td>
<td>+++g</td>
</tr>
<tr>
<td>Entorhinal pre-alpha</td>
<td>0-i</td>
<td>+</td>
<td>++</td>
<td>+++g</td>
<td>+++g</td>
<td>+++g</td>
<td></td>
</tr>
<tr>
<td>Entorhinal pri-alpha</td>
<td>0</td>
<td>i</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++g</td>
<td></td>
</tr>
<tr>
<td>CA1 pyramidal</td>
<td>0</td>
<td>i-+</td>
<td>+</td>
<td>++</td>
<td>+++g</td>
<td>+++g</td>
<td></td>
</tr>
<tr>
<td>CA4 non-pyramidal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>i-+</td>
<td>+</td>
<td>+++g</td>
<td></td>
</tr>
<tr>
<td>CA4/3 pyramidal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>i-+</td>
<td>+</td>
<td>+++g</td>
</tr>
<tr>
<td>Subiculum</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>I</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Association cortex</td>
<td>0</td>
<td>0</td>
<td>i</td>
<td>+</td>
<td>+++g</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Parastriate area</td>
<td>0</td>
<td>0</td>
<td>0-i</td>
<td>i-+</td>
<td>+</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Striate area</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0-i</td>
<td>i-+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

### Groups
1. Entorhinal – stages I-II
2. Limbic – stages III-IV
3. Isocortical – stages V-VI
CERAD Protocol

- Semi-quantitative assessment of plaques and tangles in several neocortical areas
- Determination of an age-related plaque score
- Integration with clinical information – dementia +/- to determine a level of certainty of diagnosis.
Neuropathological diagnosis of neurodegenerative disease

- Classification is increasingly complex
- Diagnosis requires demonstration of characteristic cytopathology AND neuroanatomical distribution
- Diseases may and often do co-exist

Therefore, the CNS needs to be widely examined – ideally the whole brain post-fixation or, at least, multiple sampling based on understanding the likely neuroanatomical distributions of pathology
Autopsy approach

• Pre-autopsy
  – Clinical history
  – Family history
  – Consent

• Frozen sample for genetic studies

• Sampling of relevant anatomical areas
Sampling – either in fixed or fresh

BLOCKS
- Frontal cortex
- Superior temporal gyrus
- Inferior parietal
- Medial occipital
- Cingulate
- Hippocampus/parahippocampal gyrus
- Basal ganglia
- Thalamus
- Midbrain
- Pons
- Cerebellum

Is spinal cord required?
Conclusions

• Pre-exam: establish the context
  – Clinical context
  – Type of autopsy – establish consent, permissions and discuss the effect of limitations if required

• Plan sampling
  – Brain retention or block selection
  – ?Need for spinal cord or other tissues
  – Is frozen tissue required

• Neuropathology
  – Diagnosis – what is the pathology
  – Describe the effect on the brain
  – Explain the neurology of the case
  – Integrate with general pathological findings
  – Clinicopathological synthesis
  – How does the neuropathology relate to cause of death