Approach to Neuropathological Disorders at Autopsy

Histopathology trainees

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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 Stageing for Neurofibrillary Tangle Formation

Location	Stage:	I	II	III	IV	V	VI
Trans ERC Pre-alpha		i - +	+ - ++	++	+++g	+++g	+++g
Entorhinal pre-alpha		0 - i	+	++	+++	+++g	+++g
Entorhinal pri-alpha		0	i	+	+ - ++	++	+++g
CA1 pyramidal		0	i - +	+ - ++	++	+++	+++g
CA4 non-pyramidal		0	0	0	i - +	+ - ++	+++g
CA4/3 pyramidal		0	0	0	0	i - +	+ - ++
Subiculum		0	0	0	I	+	+ - ++
Association cortex		0	0	i	+	+++	+++
Parastriate area		0	0	0 – i	i - +	+	++
Striate area		0	0	0	0 – i	i - +	+

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?

S Love
Histopathology
2004; 44:309-317

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