# Diagnostic Neuropathology

# (NB Edited version – some images removed)

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ST4 Diagnostic Neuropathology

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# Plan

- What is neuropathology?
- How does the training work?
- How did I get into it?
- What is a typical week for me?
- A few example cases
- Q&A

## Anatomy

- Brain
- Spinal cord
- Peripheral nerve
- Skeletal muscle
- Eye

## Disease process

- Tumours
- Neurodegenerative disease
- Vascular
- Inflammatory
- Autoimmune
- Infective
- Trauma
- Malformations
- Epilepsy
- Etc etc

## Diagnostic methods

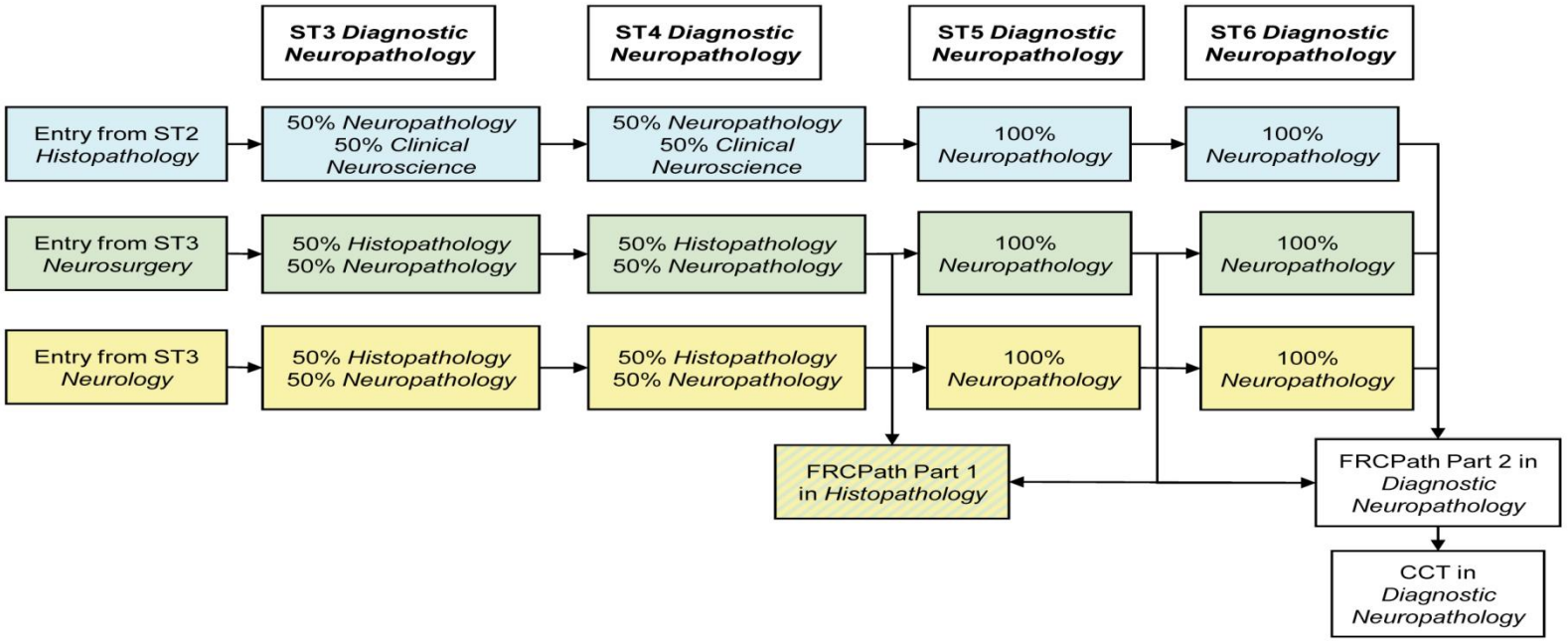
- Macroscopic
  - Surgical resections
  - Full PM
  - Referred brains
- Microscopic
  - H&E
  - IHC
  - EM
- Molecular

# Neuropathology as a specialty

- Became a separate specialty in 2012
- Higher specialty training, therefore entry point is ST3
- Routes in:
  - From histopathology, after FRCPath part 1
  - From neurology, after MRCP
  - From neurosurgery, after MRCS
- Part 2 FRCPath in neuropathology

# Neuropathology training

- 4 years
  - One year of clinical neurosciences if entering from pathology
  - One year of general histopathology if entering from clinical specialties



# Neuropathology training

- Regular BNS teaching days
- BNS meeting and conference each year
- BNS summer school alternate years
- EuroCNS courses
- Any relevant courses outside neuro e.g. autopsy

# My journey into neuropathology

- Medicine at Cardiff University
  - Initial interest in surgery with rapid change of mind…
  - Research SSU in molecular virology
  - Intercalated degree in cellular and molecular pathology
  - Elective at Harvard – GI pathology at Massachusetts General Hospital
  - Final year project – GIST case series

# My journey into neuropathology

- Foundation years
  - Taster week in F2, and occasional ad-hoc experience
  - Audits relevant to pathology
  - Attendance at pathology conferences
  - Applied to histopathology training programme

# My journey into neuropathology

- General histopathology in Wessex
  - One month blocks in neuropathology and paediatric pathology
  - FRCPath part 1

  - Case reports
  - Audits
  - Conferences – BNS meetings, autopsy courses
  - Further experience during general pathology ST3 year
  - Entered neuropathology training in August 2015

# A typical week

- Surgical specimens
  - Tumour biopsies and resections
  - Non-neoplastic biopsies
- CSF cytology
- Skeletal muscle biopsies
- Peripheral nerve biopsies
- Ophthalmic specimens

# A typical week

- Post-mortem
  - Full autopsies
  - Brain dissections (adult and paediatric)

- MDTs
- M&M meetings
- Teaching
- Research
- Supervising junior trainees

# Case 1: A typical surgical case

- 49-year-old male presents with behavioural changes for two weeks, followed by a grand-mal seizure
- No PMH/DH/FH
- Urgent MRI:

# Brain tumours: the basics

- Most common tumour in the brain?
- Primary intrinsic tumours are rare

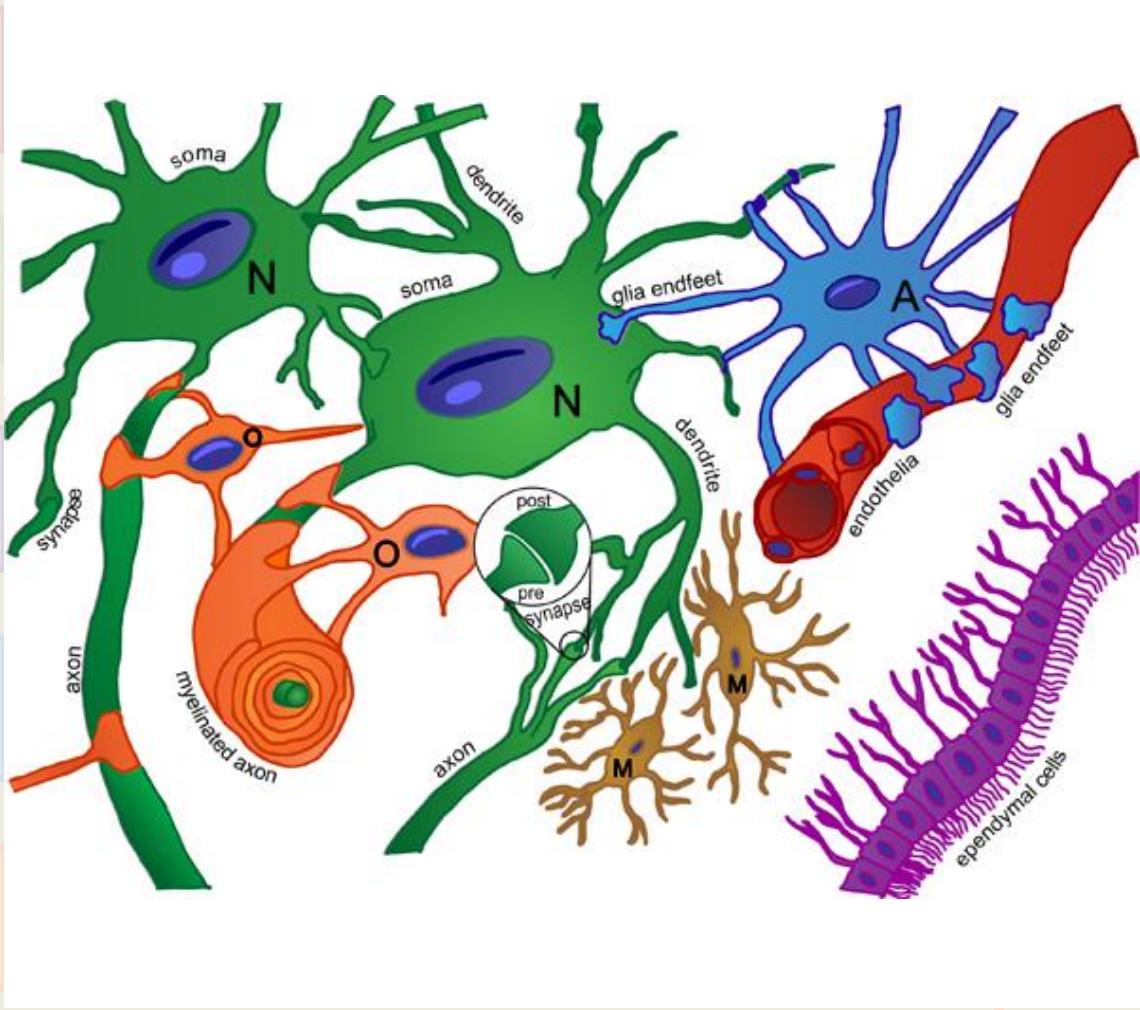
Astrocytes

Oligodendrocytes

Ependymal cells

Neurons

Arachnoidal cells



# Brain tumours: the basics

- Most common tumour in the brain?
- Primary intrinsic tumours are rare

| | |
|---|---|
| Astrocytes | • Pilocytic astrocytoma (I)<br>• Astrocytoma (II)<br>• Anaplastic astrocytoma (III)<br>• Glioblastoma (IV) |
| Oligodendrocytes | • Oligodendroglioma (II)<br>• Anaplastic oligodendroglioma (III) |
| Ependymal cells | • Ependymoma (II) |
| Neurons | • Neurocytoma |
| Arachnoidal cells | • Meningioma (I)<br>• Atypical meningioma (II) |

# Subtotal resection performed

# Histology

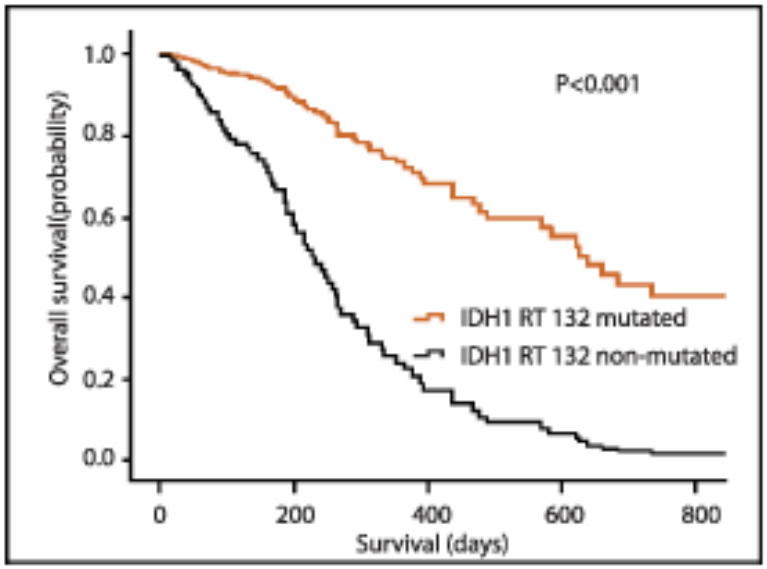
- Glial tumour
  - Astrocytic morphology
  - Mitotic activity
  - Microvascular proliferation
  - Necrosis

# IHC to confirm diagnosis

- GFAP positive confirming glial origin
- Ki67 proliferation index high

# Molecular techniques

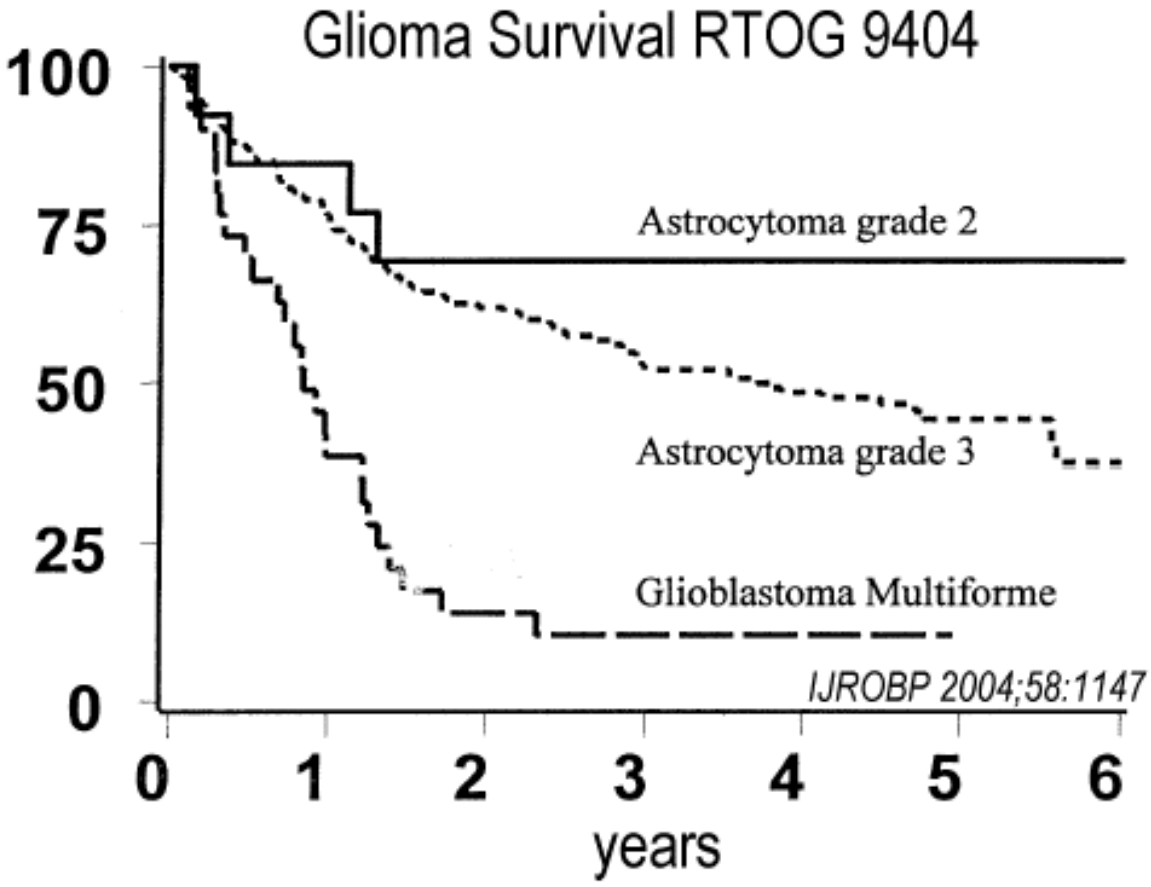
- IDH-1 (R132H) immunohistochemistry: Negative
- ATRX immunohistochemistry: Loss of staining
- MGMT promoter methylation: 50-100% methylated




Acta Neuropathologica.2010.

# Final diagnosis

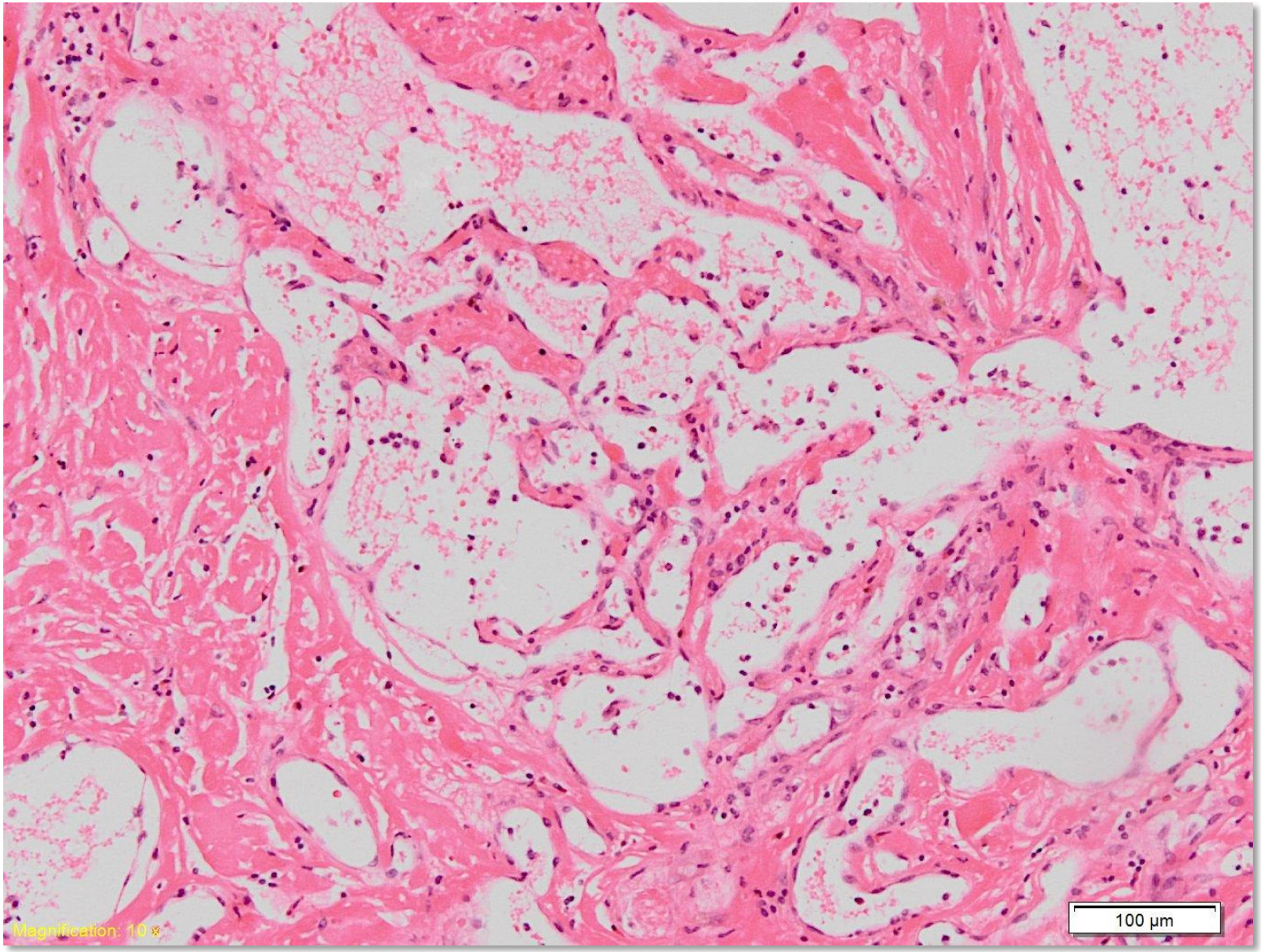
- Glioblastoma, WHO grade IV



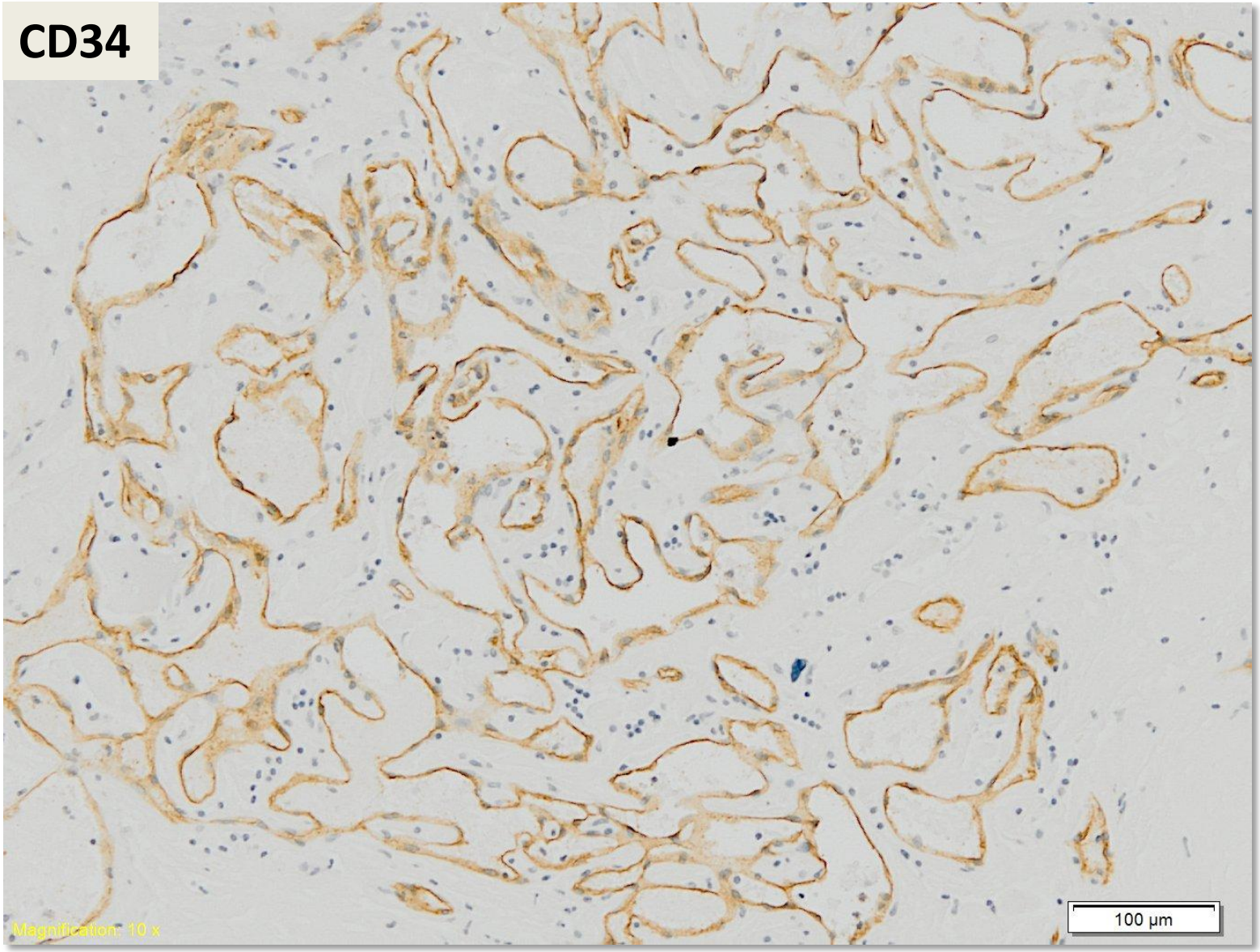
# Case 2: A less typical surgical case

- Clinical details on request form: “ICH evacuated”
- Note on request form: “Brown in colour ?melanoma”

# Histology



# Immunohistochemistry



# Diagnosis?

- Papillary endothelial hyperplasia (AKA "Masson's tumour")
- Benign reactive response by endothelial cells, for example secondary to organising thrombus

- Further history retrieved:
  - Small intracerebral haemorrhage at this site 2/12 ago
  - Subsequent seizures therefore removed surgically

# Case 3: A typical PM

- 78M
- Unwitnessed fall down stairs 3 days ago
- PMH: Hypertension, glaucoma

- CT scan showed contusions and midline shift
- Neurosurgical intervention deemed futile, best supportive care
- Died on day 3

# Questions

- PM required?
- Coroner or consented?

- Questions for PM:
  - Cause of death
  - Correlate head injury with radiological findings
  - Why did he fall down the stairs?

# External examination

- Bruising around both eyes
- Dried blood in right ear canal
- Abrasions on nose
- 6cm bruise on right elbow

# Internal examination

- Bronchopneumonia both lower lobes
- No evidence of acute myocardial ischaemia

- Skull base and temporal bone fractures
- Subdural haematoma
- Large temporal lobe contusions
- Blood, vitreous humour, urine sent for toxicology and biochemistry

# Conclusions

- Cause of death:
  - 1a Bronchopneumonia
  - 1b Traumatic head injury
  - 1c Fall

# Other recent PM cases:

- CJD
- Holoprosencephaly
- Thanatophoric dysplasia
- Colloid cyst -> hydrocephalus
- Undiagnosed mitochondrial disorder
- Intravascular lymphoma

- More regularly:
  - Traumatic head injury
  - SUDEP
  - Intracerebral haemorrhage

# Why neuropathology?

- Small specialty
- Very close clinical and academic integration
- Integration/overlap with paeds, forensics etc
- Huge variety of disease processes, most of which are rare
- Opportunity to use less common techniques e.g. EM, enzyme studies
- Huge potential in the future e.g. molecular diagnostics, neurodegenerative disease

# Top tips

- Spend time in a histopathology department, we are a friendly and welcoming specialty
  - Placements/SSU if possible
  - Follow cases to the lab if on surgical/derm placements
  - Research projects
  - Audits
  - Elective
- Attend some conferences – e.g. BNS meetings, PathSoc, BDIAP, ACP and RCPath meetings
- Enter competitions/elective scholarships – e.g. BDIAP, PathSoc
- Taster weeks in F1/2

# Questions?

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