Understanding general brain tumor pathology, Part I: The basics

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plan of attack

• what IS a pathologist, anyway?
• what’s so special about neuropathology?
• what do brain tumors look like under the microscope?
• how has genetic testing changed the way these tumors are diagnosed?
what is a pathologist?
popular perceptions of pathologists
pathology is a black box, even to other doctors
to be a pathologist, you have to:

1. complete college (4 years), pass the MCAT
2. complete medical school (4 years), pass USMLE steps I, II, and III
3. complete pathology residency (3-4 years), pass the general pathology board exam
   a) anatomic pathology—surgical pathology
   b) clinical pathology—laboratory medicine
4. do a subspecialty fellowship (1-2 years)
subspecialty options in pathology

**board-certified**
- blood banking/transfusion medicine
- chemical pathology
- cytopathology
- dermatopathology
- forensic pathology
- hematopathology
- medical microbiology
- molecular genetic pathology
- pediatric pathology
- **neuropathology**

**non board-certified**
- head & neck pathology
- gastrointestinal pathology
- thoracic pathology
- renal pathology
- breast/GYN pathology
- urologic pathology
- soft tissue pathology
- transplant pathology
- coagulation medicine
- pathology informatics
our basic tool
H&E stain

hematoxylin
• from logwood tree bark
• blue-purple
• binds negatively-charged structures (e.g. the DNA in cell nuclei)

eosin
• artificial dye
• orange-red
• stains positively-charged structures (e.g. proteins in the cell)
what’s so special about neuropathology?
things a neuropathologist does: teaching

• medical students
• other physicians and physician residents
  – general pathology
  – neurosurgery
  – ophthalmology
  – neurology
things a neuropathologist does: research

• neurodegeneration
  – Alzheimer’s
  – Parkinson’s
  – ALS
  – multiple sclerosis

• tumors
  – pediatric
  – adult

• infectious diseases
  – mad cow disease
  – viral illnesses

• development
  – autism

• forensics
  – trauma
things a neuropathologist does: **clinical**

- evaluate tissue specimens → provide diagnoses for neurooncologists, neurosurgeons, neurologists, rheumatologists, and ophthalmologists
  - brain and spinal cord tumors
  - other diseases of the central nervous system
  - muscle and nerve diseases
  - eye

- **postmortem exams**
  - hospital-based cases
  - degenerative cases for banking and research
  - medical examiner cases (SIDS, abuse, trauma)
what do brain tumors look like under the microscope?
neurons

http://physicsworld.com
astrocytes

http://www.abcam.com
oligodendrocytes
astrocytes and oligodendrocytes help neurons do their job

all three kinds of cells derive from a common stem cell “ancestor”
brain factoids

• About 100 billion neurons in the brain
• 1-5 trillion glial cells in the brain
• Number of synapses in brain = 60-200 trillion
• Membrane surface area of 100 billion neurons = 25,000 m², the size of four soccer fields
• % brain utilization of total resting blood and oxygen = 20%
oligodendrocyte
neuron
capillary
astrocyte
brain tumors ALSO arise from stem cells

- glial stem cell
  - self-renewal
  - neoplastic progenitor cell
    - neuronal/glioneuronal
    - astrocytoma
    - oligodendroglioma
glial tumors

astrocytoma
oligodendroglioma
neuronal/glioneuronal
## glioma WHO grading

<table>
<thead>
<tr>
<th>astrocytomas</th>
<th>oligodendrogliomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. pilocytic astrocytoma (PA)</td>
<td>1. no such thing</td>
</tr>
<tr>
<td>2. diffuse astrocytoma (DA)</td>
<td>2. oligodendroglioma (O)</td>
</tr>
<tr>
<td>3. anaplastic astrocytoma (AA)</td>
<td>3. anaplastic</td>
</tr>
<tr>
<td>4. glioblastoma (GBM)</td>
<td>oligodendroglioma (AO)</td>
</tr>
</tbody>
</table>
pilocytic astrocytoma

- mostly children
- mostly cerebellar
- classic radiology: **cyst with nodule**
- classic histology
  - **biphasic** denser and “looser” areas
  - rosenthal fibres

http://www.neuropathologyweb.org
pilocytic astrocytoma distribution
pilocytic astrocytoma
rosenthal fibres
diffusely infiltrative gliomas

astrocytoma, grades 2-4

oligodendroglial, grades 2-3
diffuse astrocytoma

- WHO grade 2
- most patients over 20 years old
- frontal and temporal lobes most common sites
- non-enhancing on MRI with contrast

From Louis et al., WHO Classification, 4th ed., pg. 25
diffuse astrocytoma
anaplastic astrocytoma

- WHO grade 3
- grade 2 plus mitoses
- most over 20 years old
- enhancing mass on MRI

mitosis
anaplastic astrocytoma
glioblastoma

- WHO grade 4
- grade 3 plus either necrosis OR microvascular proliferation
- enhancing mass on MRI
glioblastoma
glioblastoma
oligodendrogloma

- WHO grade 2
- associated with seizures
- #1 site: frontal lobe white matter

From Louis et al., WHO Classification, 4th ed., pg. 25
oligodendroglioma—“fried egg” look
also an oligodendroglioma
neuronal tumors

ganglioglioma
ganglioglioma

• WHO grade 1
• mostly under age 50
• #1 site: temporal lobe
• solid mass or cyst with nodule

http://radiographics.rsna.org/content/20/1/257/F46.large.jpg
ganglioglioma
ganglioglioma
embryonal tumors

medulloblastoma
medulloblastoma

- WHO grade 4
- mostly under age 20
- midline of cerebellum
- rapid growth → hydrocephalus
- dissemination into cerebrospinal fluid
  - monitor recurrences via spinal tap
- radiosensitive

http://www.neuropathologyweb.org/chapter7/chapter7cMedulloblastoma.html#medullo
medulloblastoma
meningeal tumors

meningiomas
meningioma

• *very* common CNS tumor
• **F:M ~2:1**
• induced by radiation
• most are WHO grade 1
• radiologic: extra-axial tumor with “dural tails”
meningioma
in summary

• pathology is a great field
• neuropathology is the most important part of pathology
• our impact on your care is ENORMOUS
pathology is a black box NO LONGER!