Tumors of the Nervous System

Peter Canoll MD. PhD.

What I want to cover

• What are the most common types of brain tumors?
• Who gets them?
• How do they present?
• What do they look like?
• How do they behave?

Epidemiology of Brain Tumors

• Annual incidence of 10-20 per 100,000
• 2.5% of all cancer deaths
• 20% of childhood tumors

Common Nervous System Tumors

• Gliomas
  – Diffuse Astrocytoma-Glioblastoma Multiforme
  – Pilocytic Astrocytoma
  – Oligodendroglioma
  – Ependymoma
• Medulloblastoma
• Meningioma
• Schwannoma
• Metastatic

Different types of growth patterns

Well Circumscribe    Diffusely Infiltrating

Glioblastoma Multiforme

• Most common adult primary brain tumor
• Peak incidence is between 45 and 70
• Often present with seizures or subtle deficits
• MRI shows ring-enhancing lesion
• Glioma cells diffusely infiltrate the brain,
• But almost never metastasize to other organs
• Anaplasia, Mitosis, Endothelial proliferation, Necrosis
• Heterogeneous both phenotypically and genetically
• Average survival of less than 1 year
Glioblastoma Multiforme

- Peak age of incidence is 3rd and 4th decade
- Frequently present with seizures or subtle cognitive abnormalities
- MRI shows an ill-defined non-enhancing lesion, most commonly in the cerebrum
- Moderate nuclear atypia, very few mitotic figures
- Glioma cells diffusely infiltrate the brain, but almost never metastasize to other organs
- Recur and progress to Anaplastic Astrocytoma and Glioblastoma Multiforme

Low Grade Diffuse Astrocytoma

- WHO Grading of Diffuse Fibrillary Astrocytomas

<table>
<thead>
<tr>
<th>WHO grade</th>
<th>Anaplasia</th>
<th>Mitoses</th>
<th>Endothelial Proliferation</th>
<th>Necrosis</th>
<th>Average Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocytoma</td>
<td>II</td>
<td>+</td>
<td>+/−</td>
<td>−</td>
<td>6-8 years</td>
</tr>
<tr>
<td>Anaplastic Astrocytoma</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
<td>2-3 Years</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>&lt; 1 year</td>
</tr>
</tbody>
</table>
Genetic Alterations in the Evolution of Primary and Secondary Glioblastoma

**Low Grade Astrocytoma**
- p53 mutations (65%)
- PDGF/PDGFR overexpression (60%)

**Anaplastic Astrocytoma**
- LOH 19q (50%)
- RB alterations (25%)

**Secondary glioblastoma**
- LOH 10q
- DCC overexpression (50%)

**Primary glioblastoma**
- EGFR overexpression (60%)
- LOH 10p and 10q
- PTEN mutations/loss (30%)
- P16 deletions (30%-40%)
- MDM2 overexpression (50%)

Pilocytic Astrocytoma
- Relatively benign (WHO grade I)
- Typically occurs in children and young adults
- Often presents with focal neurological signs or increased intracranial pressure
- Common locations are cerebellum, optic nerve, cerebrum, brainstem
- Often cystic with an enhancing mural nodule
- Composed of bipolar cells with “hairlike” process
- Rosenthal fibers are often present
- Molecular genetics are distinct from diffuse fibrillary astrocytomas
- Good prognosis after complete resection

Pilocytic Astrocytoma
- Cystic with an enhancing mural nodule in the cerebellum

Ganglioglioma
- Associated with seizures
- Children or young adults
- Cystic with enhancing mural nodule
- Often involves temporal lobe
- Neoplastic neurons and glia
- Malignant progression involves the glial component

Oligodendroglioma
- Most common in forth and fifth decade
- Usually involve cerebral hemispheres
- Usually present with seizures and/or headache
- Composed of sheets of cells with round regular nuclei and clear cytoplasm (fried egg appearance)
- Dense network of branching capillaries
- Diffusely infiltrate the cortex and white matter
- Anaplastic oligodendroglioma shows atypia, mitoses, endothelial proliferation and necrosis
- Tumors with LOH of 1p and 19q are responsive to chemotherapy
Ependymoma

- Most common in children and young adults
- Arise adjacent to the ventricular system, most commonly in the posterior fossa and spinal cord
- Often present with signs of increased intracranial pressure, ataxia, motor or sensory deficits
- Distinctive histologic features include perivascular pseudorosettes and ependymal rosettes
- Tumor cells are usually GFAP+
- Ultrastructural features include cilia, microvilli and junctional complexes
- 5 year survival of about 50% after surgical resection

Ependymoma

- Malignant, poorly differentiated tumor of the cerebellum
- Predominantly seen in children
- Present with ataxia and intracranial hypertension
- Composed of densely packed cells with hyperchromatic nuclei and scant cytoplasm
- Homer-Wright (neuroblastic) rosettes
- High mitotic activity
- Tumor cells may express neuronal or glial markers
- Often disseminates through the CSF (drop mets)
- Responsive to radiation and chemotherapy
- 5 year survival rate as high as 75%

Medulloblastoma

MRI and gross images of a tumor in the vermis with CSF metastasis to the dura and cauda equina

Medulloblastoma invading the cerebellar cortex.

Note the difference between the tumor cells and granule cell neurons.
Meningioma

- Slow growing, benign tumors (WHO grade I)
- Most occur in adults
- Female bias
- Imaging shows dural based enhancing mass
- Grow as well demarcated, firm-rubbery mass
- Attached to dura and compress adjacent brain
- Frequently invades dura and bone
- Invasion into brain indicates malignant behavior

Meningioma

- Meningothelial meningiomas have whorls and psammoma bodies
- Fibroblastic meningiomas

Schwannoma

- Benign tumor of peripheral nerve (WHO grade I)
- Frequently arise from the spinal or cranial nerves
- Biphasic growth pattern hypercellular (Antoni A) and hypocellular (Antoni B)
- Nuclear palisading (Verocay bodies)
- Most are cured with surgery

Metastatic Carcinoma

- Account for about 30% of adult brain tumors
- One or more discrete lesions, usually ring enhancing
- Frequently located in cerebrum or cerebellum
- Noninfiltrative growth pattern
- Shows histologic features of the primary tumor
- Most patients survive less than 1 year

Origin of Brain Metastases

- Lung (50%)
- Breast (15%)
- Skin/melanoma (10%)
- Kidney
- GI carcinoma

Lots of Bad Stuff Kills Glia

Other Tumors of the Nervous System

- Pineal Parenchymal Tumor
- Germ Cell Tumor
- Primary CNS Lymphoma
- Pituitary Adenoma
## Familial Cancer Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurofibromatosis 1</td>
<td>NF1</td>
<td>Neurofibromas</td>
</tr>
<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>Optic gliomas</td>
</tr>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL</td>
<td>Hemangioblastomas</td>
</tr>
<tr>
<td>Tuberous Sclerosis</td>
<td>TSC1</td>
<td>Subependymal Giant Cell Astrocytoma</td>
</tr>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL</td>
<td>Astrocytomas, GBM</td>
</tr>
<tr>
<td>Cowden</td>
<td>PTEN</td>
<td>Dysplastic gangliocytoma of the cerebellum</td>
</tr>
<tr>
<td>Tuberous Sclerosis</td>
<td>TSC2</td>
<td>Subependymal Giant Cell Astrocytoma</td>
</tr>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL</td>
<td>Astrocytomas, GBM</td>
</tr>
<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>Malignant peripheral nerve sheath tumors</td>
</tr>
<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>Malignant peripheral nerve sheath tumors</td>
</tr>
<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>Malignant peripheral nerve sheath tumors</td>
</tr>
</tbody>
</table>