Tumors of the Nervous System

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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 Circumscribed

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
- Atypia, Mitosis, Endothelial proliferation, Necrosis
- Heterogeneous both phenotypically and genetically
- Average survival of less than 1 year
Glioblastoma Multiforme
Glioblastoma Multiforme

KI67

GFAP
Giant cell GBM
Low Grade Diffuse Astrocytoma

- 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 Astrocytoma (WHO grade II)
# WHO Grading of Diffuse Fibrillar Astrocytomas

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>WHO Grade</th>
<th>Atypia</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>-</td>
<td>6-8 years</td>
</tr>
<tr>
<td>Anaplastic Astrocytoma</td>
<td>III</td>
<td>+</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>+</td>
<td>&lt; 1 year</td>
</tr>
</tbody>
</table>
Genetic Alterations in the Evolution of Primary and Secondary Glioblastoma

<table>
<thead>
<tr>
<th>Low Grade Astrocytoma</th>
<th>Primary glioblastoma</th>
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</thead>
<tbody>
<tr>
<td>-p53 mutations (65%)</td>
<td>-EGFR overexpression (60%)</td>
</tr>
<tr>
<td>-PDGF/ PDGFR overexpression (60%)</td>
<td>-LOH 10p and 10q</td>
</tr>
<tr>
<td><strong>Anaplastic Astrocytoma</strong></td>
<td>-PTEN mutations/loss (30%)</td>
</tr>
<tr>
<td>-LOH 19q (50%)</td>
<td>-P16 deletions (30%-40%)</td>
</tr>
<tr>
<td>-RB alterations (25%)</td>
<td>-MDM2 overexpression (50%)</td>
</tr>
<tr>
<td><strong>Secondary glioblastoma</strong></td>
<td></td>
</tr>
<tr>
<td>-LOH 10q</td>
<td></td>
</tr>
<tr>
<td>-DCC overexpression (50%)</td>
<td></td>
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</tbody>
</table>
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
Pilocytic Astrocytoma
Ganglioglioma

- Associated with seizures
- Children or young adults
- Cytic 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
Oligodendroglioma

Anaplastic Oligodendroglioma
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
Medulloblastoma

- 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 psamomma 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 pallisading (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**
Craniopharyngioma

Most common non-neuroepithelial intracranial tumor in children

Suprasellar mass partially cystic, focally calcified, “Machine oil”

Squamous epithelium with adamantinomatous or papillary growth pattern and nodules of “wet keratin”
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>Chromosome</th>
<th>Associated Tumors</th>
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</thead>
<tbody>
<tr>
<td>Neurofibromatosis 1</td>
<td>NF1</td>
<td>17</td>
<td>Neurofibromas, Optic gliomas</td>
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<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>22</td>
<td>Bilateral schwannomas, Meningioma, Ependymomas</td>
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<tr>
<td>Von Hippel-Lindau</td>
<td>VHL</td>
<td>3</td>
<td>Hemangioblastomas</td>
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<tr>
<td>Tuberous Sclerosis</td>
<td>TCS1</td>
<td>9</td>
<td>Subependymal Giant Cell Astrocytoma</td>
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<tr>
<td>Li-Fraumeni</td>
<td>p53</td>
<td>17</td>
<td>Astrocytoma, GBM, PNET</td>
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<tr>
<td>Cowdens</td>
<td>PTEN</td>
<td>10</td>
<td>Dysplastic gangliocytoma of the cerebellum</td>
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<tr>
<td>Turcot</td>
<td>APC</td>
<td>5</td>
<td>Medulloblastoma</td>
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<tr>
<td>HNPCC</td>
<td></td>
<td>3,7</td>
<td>GBM</td>
</tr>
<tr>
<td>Nevoid Basal cell carcinoma syndrome</td>
<td>PTCH</td>
<td>9</td>
<td>Medulloblastoma</td>
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