Tumors of the Central Nervous System
Financial Disclosures

- I have NO SIGNIFICANT FINANCIAL, GENERAL, OR OBLIGATION INTERESTS TO REPORT
Introduction

General:

Brain tumors are lesions that have \textit{mass effect} distorting the normal tissue and often result in increased intracranial pressure.
Introduction

• Primary neoplasms may develop from any cell type normally residing in or over the brain. Their neoplastic proliferation often is a bizarre mimic of normal morphology.
  • Meninges
  • Astrocytes
  • Oligodendroglia
  • Ependyma
  • Neurons
# Intracranial tumors

<table>
<thead>
<tr>
<th>Primary</th>
<th>Metastatic</th>
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<tbody>
<tr>
<td>• Axial: anywhere within the brain parenchyma</td>
<td>• usually at the gray/white junction (Axial location).</td>
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<td>• Extra-axial: outside the brain parenchyma</td>
<td>• May be extra-axial (dural).</td>
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<td>• Patient may have a known primary.</td>
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Metastatic Carcinoma

• Most common intracranial adult tumor.

• Primary sources:
  • Lung, Breast, Kidney, GI tract, Skin (Melanoma)
  • Sarcomas are uncommon

• Predominance of location relates to volume of blood flow to area:
  Cerebrum>Cerebellum>Spinal cord
Metastatic Carcinoma

Gross/Radiology:
- Tumor emboli most commonly found at the grey/white junction.
- May be more than one lesion.
- Often marked edema surrounding tumor.

Microscopic:
- Tumor typically looks like the primary.
Primary Extra-axial Intracranial Tumors
Meningioma

- Neoplasm derived from the brain coverings ("meninges").
- Incidence:
  - 20% of primary CNS tumors
- Age:
  - adult; 40 - 65 yrs.
- Gender Predominance:
  - Female (2:1) symptomatic tumors
Meningioma

• Clinical:
  • slow progression
  • clinical symptoms depend on location of tumor

• Sites:
  • Parasagittal, sphenoid ridge, spinal cord

• Treatment:
  • Surgical excision

• Prognosis:
  • Good; 25% recurrence
Meningioma

Surgical excision is the usual treatment.

Some may be asymptomatic and found at autopsy.
While meningiomas are benign neoplasms, they can be locally aggressive, invading bone as in this case.
Meningioma

General

- slow growing, benign
- arises from cells forming surface coverings of brain
- compresses rather than invades brain
- well-circumscribed
- may be focally mineralized

Brain & Normal Meninges

Arachnoid

PIA
Meningioma

Microscopic

- arachnoid-like cells with vacuolated nucleus.
- sheets of cells without distinct borders (syncytium)
- spindle-shaped cells
- cellular whorls of arachnoid cells
- concentric laminated calcifications (psammoma bodies)
CNS Nerve Sheath Tumors

Schwannoma
Schwannoma

Benign tumor of schwann cells

**Incidence:** 10% of primary CNS tumors

**Age:** 35-60 years; younger age and multiple if part of Neurofibromatosis complex

**Sites:** cranial nerves (especially CNVIII), sensory spinal roots, peripheral nerves

**Prognosis:** favorable; benign, slow growing tumors

**Rx:** surgical excision
Schwannoma

Bilateral schwannomas located at the cerebello-pontine angle (CPA tumor)
Schwannoma

**Gross**: nerve focally enlarged and rubbery. The tumor grows by expansion and is encased within the nerve. It can usually be shelled out sparing remaining nerve.
SCHWANNOMA

**Micro:** spindle-cell proliferation with wavy appearance;

Biphasic architecture: cellular with palisading nuclei (Antoni A) admixed with loose, less cellular areas (Antoni B).
Schwannomas may show a peculiar palisading of nuclei in parallel rows with intervening anuclear zone known as the **VEROCAY BODY**.
Tumors of the CNS Parenchyma

- **Astrocytoma**
  - Oligodendroglioma
  - Ependymoma
  - Medulloblastoma
Classification of Astrocytomas

**Circumscribed astrocytoma**

- Relatively well-circumscribed or cystic.
- Usually low grade (WHO Grade I).
- Low tendency to have anaplastic progression.
- Favorable prognosis

**Diffuse Astrocytoma**

- Infiltrative margin.
- Three histologic grades II-IV.
- Tendency to progress to more anaplastic forms.
- Unfavorable prognosis
Circumscribed Astrocytoma

• Incidence: 10% of primary CNS tumors
• Age: childhood tumor
• Clinical: slowly progressive.
• Site: Midline (esp. cerebellum, optic nerve)
Circumscribed Gliomas - Juvenile Pilocytic Astrocytoma

• Rx: surgical
• Gross: well-demarcated, effacing adjacent structures; grey-white, rubbery to gelatinous; may be cystic (esp. cerebellar tumors)
Juvenile Pilocytic Astrocytoma

Microscopic

- elongated spindle-shaped astrocytes (piloid)
- biphasic pattern of hyper and hypodense areas with microcysts
Circumscribed Astrocytoma

Rosenthal fibers are common (pink beaded arrangement of astrocytic glial filaments).
Diffuse Astrocytomas

- Infiltrative tumor with ill-defined margins
Astrocytic tumors show a histologic continuum from nearly normal looking neuropil in low grade tumors (Grade II/IV) to highly cellular proliferations with necrosis in high grade tumors (Grade IV/IV). Usually stain positively for the presence of the intermediate cytoskeletal filaments, GFAP (Glial Fibrillary Acidic Protein).
Grade IV Astrocytoma - Glioblastoma *Multiforme* (GBM)

• High cellularity, pleomorphism, hyperplastic vascularity, mitoses and necrosis are features of glioblastoma.
Transformation of a low grade tumor to high grade is well-known and can be traced by cumulative gene abnormalities including p53 mutations and LOH of chromosome 10.
Diffuse Astrocytoma- Treatment

• Surgical debulking when possible.
• Radiation
• Chemotherapy- poor response
• Prognosis:
  • Low Grade tumors: Good, 10-15 years.
  • High Grade tumors: Poor; usually 6-12 months
Tumors of the CNS Parenchyma (Gliomas)

- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Medulloblastoma
Oligodendroglioma

• Incidence: 5% of CNS tumors
• Age: 25-50 years
• Clinical: progressive course over several years
• Site: Cerebral hemispheres
• Prognosis: 40%, 5 year survival
• Treatment: Surgical
• Gross: poor circumscription, infiltrative, hemorrhage, focal calcification
Oligodendroglioma

- Immunohistochemistry:
  - No good positive marker; GFAP- Negative.
  - Often mutated IDH-1.
- Molecular marker:
  - 1p 19q co-deletion
Oligodendroglioma

Microscopic: Uniform, cellular pattern of oligodendrocytes with “fried egg” perinuclear halo appearance and calcifications.
Oligodendroglioma

- The chicken-wire vascular pattern is an important clue to histogenesis and can be identified with Factor VIII antibody against endothelial cells.
- Oligodendroglia with halos are negative for GFAP.
Tumors of the CNS Parenchyma (Gliomas)

- Astrocytoma
- Oligodendroglioma
- **Ependymoma**
- Medulloblastoma
Ependymoma

• Incidence: 5% of CNS tumors
• Age: 5-25 yrs (brain); 20-50 years (spinal cord)
• Clinical: Present with symptoms of CSF obstruction.
• Site: fourth ventricle, cerebrum; distal spinal cord
• Prognosis:
  • 40% 5 yr (brain); 60% 5 yr (spinal cord)
• Rx: Surgery; radiation
Ependymoma

• Gross: Many are intraventricular; granular and friable.

These factors give this tumor a greater tendency to seed the CSF pathways.
Ependyma

• Ependymomas arise as neoplastic proliferations of ependymal cells which normally line ventricular spaces.

Ependymal cells line the ventricles
Ependymoma

- Vascular tumor with uniform sheets of cells with small dark round nuclei in a glial fibrillary background.
- Perivascular pseudorosettes are key diagnostic feature
Tumors of the CNS Parenchyma

• Astrocytoma
• Oligodendroglioma
• Ependymoma
• Medulloblastoma
Medulloblastoma

• 5% of primary tumors
• 5-20 yrs
• rapid progressive cerebellar symptoms
• Site: Cerebellar vermis (young); lateral hemisphere (older)
• Prognosis: 75% 5 year; CSF seeding is common
• Rx: Surgery and radiation
• Micro: “Small, round blue cell tumor” comprising Primitive neuroectodermal cell precursors of glia and neurons (PNET); Homer Wright rosettes
Medulloblastoma
Medulloblastoma

- Rosette formation is a classic feature of Medulloblastoma and tend to be of the Homer Wright type.
- Other rosette formations are seen in primitive neuroectodermal tumors found elsewhere.
Lecture Objectives

• Know the histologic features of meningioma, schwannoma, oligodendroglialoma, astrocytomas (pilocytic and diffuse Grades II-IV), ependymoma, medulloblastoma

• Know the differences in behavior of the tumor types noted above.

• Be aware of age distribution of the tumor types discussed.
THE END