Brain Tumor Types and Treatment

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No disclosures
Overview

- Recognizing a brain tumor
- The landscape of neurologic deficits
- Components of diagnosis
- Histologic classification and grading
- Gliomas, a family of diseases and the intricacies of treatment
- Intro to radiation, its forms, uses, & side effects
- The role of chemotherapy in malignant tumors
- Other common brain tumors
- Tumors of the spine and ventricles
- Primary lymphomas of the CNS
- Pediatric brain tumors
Recognizing a brain tumor

- New and Persistent Headaches
- New seizure
- Neurological deficits
- Lethargy, vomiting
- Multiple office or ED visits
Progressive neurologic deficit

- Frontal lobe – Personality changes
- Parietal lobe – weakness or loss of sensation
- Temporal lobe – language problem (Aphasia)
- Occipital lobe – visual field deficit (homonymous)
- Sella – other visual field and endocrine abnormalities
- Brainstem – Cranial nerve deficits
- Spinal cord – back pain, weakness, numbness, bowel and bladder difficulties
Components of Diagnosis

• Clinical context
• Imaging
• Histology
• Molecular markers
Classifying brain tumors by histology

- Oligodendroglioma
- Astrocytoma
- Ependymoma
- Meningioma
# World Health Organization

## Grading of brain tumors

<table>
<thead>
<tr>
<th>Grade</th>
<th>Example</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO I</td>
<td>Pilocytic astrocytoma&lt;br&gt;Myxopapillary&lt;br&gt;Ependymoma/Subependymoma</td>
<td>Low proliferating, discrete, non invasive tumor</td>
</tr>
<tr>
<td>WHO II</td>
<td>Diffuse astrocytoma&lt;br&gt;Papillary, cellular and clear cell&lt;br&gt;Ependymoma</td>
<td>Modest proliferating, partly invasive tumor</td>
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<tr>
<td>WHO III</td>
<td>Anaplastic astrocytoma&lt;br&gt;Anaplastic ependymoma</td>
<td>Fast proliferating, invasive tumor</td>
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<tr>
<td>WHO IV</td>
<td>Glioblastoma multiforme&lt;br&gt;Highly malignant glioma-like&lt;br&gt;Pineoblastoma and Medulloblastoma</td>
<td>Rapidly proliferating, highly invasive tumor</td>
</tr>
</tbody>
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https://www.emaze.com/@AWFLTFO/low-grade-glioma
Gliomas

Tumors derived from supportive cells (Glial cells: Astrocytes, oligodendrocytes)

- Diffuse (infiltrative) vs Discrete gliomas

Diffuse Gliomas

High grade gliomas

• Anaplastic Oligo. or Anaplastic Astro.
  – (WHO III)
• Glioblastoma (GBM)
  – (WHO IV)
• Diffuse Midline Glioma (WHO IV)

Low grade gliomas

• Oligodendroglioma
• Astrocytoma
  – (WHO II)
Molecular pathways for diffuse gliomas

The Cancer Genome Atlas, NEJM 2015
Case

• Presentation:
  – 56 year old executive presents with intermittent confusion over the last 3 months. He also noticed new headaches of moderate severity. Finally, one day at work, he has a convulsive seizure and coworkers called EMS. Imaging reveals a right frontal enhancing mass.

• Diagnosis: Glioblastoma, WHO grade IV, IDH wildtype, MGMT unmethylated.
Initial Management - GBM

- Steroids for cerebral edema may relieve symptoms
  - Dexamethasone 4mg q6h
  - EXCEPT if primary CNS lymphoma or infection is in the differential diagnosis.

- Seizure control
  - Keppra 1000mg BID

- Neurosurgery consultation

- Maximal safe resection extends survival

Grabowski, J Neurosurg, 2014
Radiation Therapy

- Fractionated external beam
- Linear accelerator – creates high energy electrons or photons that damage DNA
- 42 divided doses over 6 weeks

Side effects:
- Short term memory and cognitive processing
- Fatigue
- Skin toxicity, alopecia
- Radiation necrosis

Gamma Knife

- Stereotactic Radiosurgery
- For lesions less than 2cm
- Effective for brain metastases

https://www.healthgrades.com/procedures/gamma-knife-surgery

http://www.aboutcancer.com/gk_brain_mets.htm
Chemotherapy

- Oral administration
- Daily treatment concurrent with RT
- Adjuvant treatment 4 weeks after RT for 6-12 cycles
  - Side effects:
    - Fatigue
    - Confusion
    - Constipation
    - Bone marrow suppression: Thrombocytopenia more likely than neutropenia
Tumor treating field

Low Grade Glioma

Oligodendroglioma, IDH mutant
• WHO grade II
• Defining chromosomal deletions in 1p and 19q

- 2/3 presents with seizure
- Nonenhancing mass with mild edema, CT often has calcifications.
- Peak incidence age 35-44
- Median OS ~15+ years
- Eventually transform to Anaplastic Oligo (grade III)
- Treatment stratified by risk:
  - Complete removal, age <40, neuro intact: observe and treat upon recurrence
  - Others may receive chemo alone vs chemoradiation upfront

https://basicmedicalkey.com/oligodendroglioma/
Low Grade Glioma

- Diffuse Astrocytoma, IDH mutant
- Presents similarly to Oligo’s, 3rd & 4th decade of life
- Median OS ~10y
- Treatment based on risk: Surveillance, chemo alone, or combined chemoradiation upfront.
- Transforms to grade III and then grade IV Astrocytoma (Secondary GBM).

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 9014
Discrete gliomas

- Pilocytic astrocytoma
- Pleomorphic Xanthoastrocytoma
- Subependymal giant cell astrocytoma
- Ganglioglioma

- Less common than diffuse gliomas and more often in children
- Surgery is primary treatment with radiation as adjunct
- Much better prognosis with some exceptions
- BRAF mutation offers possibility of targeted treatments.
Meningioma

- Derived from arachnoid cells
- Most common (36%) of all brain tumors, female bias
- Dural based enhancing mass
  - ~75% are grade I
  - ~20% grade II
  - ~1 – 6% grade III
- Treatment:
  - Surgery is the primary treatment and cures 80% of tumors
  - Up to 20% may recur within 20 years
  - Radiation can be adjunct if inaccessible to surgery or for recurrence.

Case images courtesy of P Canoll, SNO review 2016
Ependymoma

- Derived from fluid-lining (ependymal) cells, pseudorosettes on histology

- Spinal ependymoma, grade I
  - More common in adults, frequent NF2 mutation, better prognosis (over 98% survival in 5y)
  - Extramedullary and intradural, most common in the conus/filum
  - Treatment: Surgery, radiation as adjunct

- In children, ependymomas more often arise in supratentorial brain or posterior fossa and are more aggressive (grade I-III)

https://radiopaedia.org/articles/spinal-myxopapillary-ependymoma
Primary CNS lymphoma

- Diffuse large B cell lymphoma
- ~3% of all brain tumors, peak incidence 5th to 7th decade of life.
- Can occur anywhere in CNS, as well as ocular involvement
- Increased risk with immunodeficiency/AIDS
- Imaging
  - Avidly and homogeneously enhancing tumor with diffusion restriction.
  - Favors deep structures & periventricular areas
- Histology: Large B lymphocytes, stains CD 20+

http://www.pathologyoutlines.com/topic/cnstumorprimaryCNSlymphoma.html
Primary CNS lymphoma

**Diagnosis**

- CSF cytology/flow cytometry
- Biopsy
- Rule out extracranial disease: PET scan, CT, testicular ultrasound
- AVOID STEROIDS – delays diagnosis, sometimes months

**Treatment**

- No role for surgery beyond biopsy
- Whole brain radiation is toxic and OS 11.6mo
- Chemotherapy is first line
  - Best induction therapy* is a combo involving high dose methotrexate (IV), rituxumab, and temozolomide (PO).
  - followed by consolidation tx: etoposide & cytarabine
  - Estimated 4yr OS≈65%, mOS not yet reached (2013)

*Rubinstein, JCO. 2013;31(25):3061-8
Pediatric brain tumors

- Most arise in the posterior fossa (Cerebellum, brain stem)

- Treatment involves surgery, radiation, chemotherapy
  - (Radiation only if older than age 3)

- Chemotherapy for certain diseases, regimens vary:
  - Cyclophosphamide or Lomustine + Cisplatin and Vincristine
  - Ifosfamide, Cisplatin, Etoposide

Medulloblastoma

- Most common malignant brain tumor of childhood (20%).
- Majority 3-8 years old
- Highly malignant with leptomeningeal spread (up to 50%).
- Enhancing mass commonly of the vermis, protruding down from the roof of 4th ventricle
- Various molecular subgroups distinguishable by imaging with distinct prognostic implications

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 6494
Also case courtesy of Sona Partap, SNO review, 2016
Medulloblastoma

Diagnosis & workup

• Histology
• CSF and MRI spine for staging
  – Avg risk: GTR and no mets = 80+% OS 5y
  – High risk: STR, Mets, or high risk histology = 60% 5y OS
• WNT subtype is excellent prognosis: 90% 5y OS, whereas MYC is worst

Treatment

• Surgery
  – Complications include posterior fossa syndrome: Mutism, ataxia, dysphagia/dysarthria
• Craniospinal RT
  – (radiation dose based on risk, 23 vs 36 Gy with focal boost)
• Chemotherapy
  – Methotrexate, Carboplatin, etoposide, vincristine
Diffuse Intrinsic Pontine Glioma

- Stereotypic presentation – abducens palsy, ataxia, unilateral weakness
- Biopsy is often not safe, and MRI is sufficient for diagnosis
  - Minimally enhancing
  - FLAIR/T2 abnormalities in Pons
- Treat with local radiation
- Prognosis is typically 9-11 months
  - 20% 1 year
  - 5 yr overall survival 0%

https://radiopaedia.org/articles/diffuse-brainstem-gliomas-1
& Sonia Partap, SNO review, 2016
H3K27M mutant Diffuse Midline Gliomas

- New 2016 WHO classification
- Various gliomas located around the midline in children and even adults often carry a mutation in a histone gene
- New targeted therapies now possible:
  - panobinostat (histone deacetylase inhibitor)

Nat Rev Cancer. 2014 Oct;14(10)
Germ cell tumors

Presentation & Diagnosis

- Presents with:
- Hydrocephalus, endocrine dysfunction, & eye movement abnormalities
  - upgaze paralysis, convergence nystagmus
- Suprasellar and/or pineal mass
- Serum or CSF markers for BHCG & AFP may be present

Workup & Treatment

- Assess CSF and serum markers to distinguish germinoma vs non-germinomatous germ cell tumor
- Biopsy if markers negative
- RT to whole ventricles
- Chemosensitive: Carboplatin, Etoposide, +/- ifosfamide
Thank You