Brain tumor terms and definitions

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Overview

- Brain tumors
  - Definitions
  - Epidemiology
  - Classification of brain tumors
- Anatomy
- Tests
- Treatments
  - Surgery
  - Radiation
  - Chemotherapy
Introduction

Brain Tumors

- **Brain tumors**
  - Abnormal mass of cells that grow uncontrollably in the brain
  - Can grow slowly or quickly
  - Can invade critical parts of the brain
  - Can cause life-threatening damage
Introduction

- Two types of brain tumors: *Primary* and *Metastatic*

- Primary brain tumors
  - Tumors start in the brain
  - Most commonly arise from the brain’s support cells, aka glial cells
    - Astrocytes - astrocytomas
    - Oligodendrocytes - oligodendrogliomas
    - Ependymal cells - ependymomas
  - Some tumors, more commonly seen in children, arise from primitive neuroectodermal cells
    - Primitive neuroectodermal cell tumors (PNETs)
Introduction

• **Metastatic** brain tumors
  – By definition, malignant
  – Formed by cancer cells that originate elsewhere in the body then travel to the brain, usually by hematogenous spread
  – Common cancers that metastasize to the brain:
    • lung, breast, and melanoma
  – Stage IV
Cells of the Brain

- Astrocytes
- Neurons
- Oligodendrocytes
- Ependymal cells
- Choroid plexus
- Pineal cells
- Pituitary gland
- Schwann cells
- Lymphocytes
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Incidence of Brain Tumors

- Brain tumors account for 2% of all cancers.
- Incidence rate of primary brain tumors
  - 14 per 100,000 persons (malignant and benign)
- ~40,000 people are diagnosed with a new primary brain tumor each year (NIH)
- ~190,000 people in the US are diagnosed with a metastatic brain tumor each year (NBTF)
Figure 5. Distribution of All Primary Brain and CNS Tumors by Histology (N=295,986)

CBTRUS Statistical Report: NPCR and SEER Data from 2004-2008

- Meningioma: 34.7%
- Pituitary: 13.5%
- Nerve Sheath: 8.5%
- Craniopharyngioma: 0.9%
- Lymphoma: 2.3%
- Other Neuroepithelial: 5.0%
- Germ Cell Tumor: 0.5%
- All Other: 6.7%
- Glioblastoma: 16.3%
- Astrocytomas: 6.8%
- Ependymomas: 1.8%
- Oligodendrogliomas: 1.9%
- Embryonal, including Medulloblastoma: 1.1%

Gliomas (ICD-O-3: 9380-9384, 9391-9460, 9480) account for 30% of all tumors and 80% of malignant tumors
Figure 7. Distribution of All Primary Brain and CNS Gliomas* by Histology Subtypes (N=89,617)

CBTRUS Statistical Report: NPCR and SEER Data from 2004-2008

- Glioma Malignant, NOS: 7.1%
- Ependymoma: 5.8%
- Oligodendroglioma: 6.4%
- Pilocytic Astrocytoma: 5.2%
- Protoplasmic and Fibrillary Astrocytoma: 1.8%
- Anaplastic Astrocytoma: 6.7%
- All Other Astrocytoma: 8.8%
- All Other Glioma: 4.3%

Glioblastoma: 53.9%

Astrocytomas and glioblastomas account for 76% of all gliomas*

*ICD-O-3 codes = 9380-9384, 9391-9460, 9480
Possible Risk Factors?
Tumor Grading

- **Low Grade**
  - Few dividing cells (mitoses)
  - May have bizarre nuclei
  - No vascular proliferation
  - No necrosis

- **High Grade**
  - Many dividing cells (mitoses)
  - Bizarre nuclei
  - Vascular proliferation
  - Necrosis
Grading Scheme

• Grade I (benign)
  – Well-circumscribed
  – Rosenthal fibers, eosinophilic granular bodies, calcification

• Grade II (low grade)
  – Infiltrating, bizarre nuclei
  – Can progress to malignant

• Grade III (anaplastic astrocytoma, AA)
  – Mitoses, bizarre nuclei, vascular proliferation
  – Increasing DNA abnormalities

• Grade IV (glioblastoma, GBM)
  – Mitoses, bizarre nuclei, vascular proliferation, necrosis
Tests- CT

• Computerized tomography (CT or CAT) scan
  – Typically requires contrast injection
  – Low density or same density as brain
  – May have enhancement
  – Swollen gyrus
  – Calcifications if low grade
  – May be cystic
Tests- MRI

- Magnetic resonance imaging (MRI)
  - Decreased signal attenuation on T1
  - Increased on T2
  - Little or patchy enhancement to significant enhancement
    - Enhancement can be a sign of a low grade tumor but is more often consistent with malignancy
  - May be cystic or necrotic
MRI

- Low grade astrocytoma grade I/grade II
  - Little, or no enhancement
    - Pilocytic astrocytomas –
      - Contrast enhancing
        often cystic with mural nodule
    - Little, if any edema
    - Little, or no mass effect
Low Grade Gliomas

- Grade I and Grade II
  - Surgery
    - Complete surgical resection if possible
    - At least biopsy or partial resection is recommended in almost all cases to determine pathology
Neuronavigation

- Thin-cut pre-operative MRI
- Incision and craniotomy planning
- Planning tumor resection, estimating extent of resection
- Brain shift
- Small amounts of tumor cannot be visualized, not all tumors can be readily seen
Surgical decision-making

- If tumor is localized
- If no major medical problems which make surgery risky
- Eloquence
  - Motor
  - Language
  - Vision
- Deep vs superficial
Low Grade Glioma Treatment

• Grade I and Grade II
  – Surgical resection
  – Radiation Therapy
    • Fractionated XRT to residual tumor postop
  – Chemotherapy
    • Usually with tumor progression of if significant residual tumor/ biopsy only
    • Often Temozolomide
Common Brain Tumors – *Astrocytomas*

- **Malignant Astrocytomas**
  - Constitute over 40% of all primary intracranial tumors
  - Widely infiltrate adjacent brain
  - Growth is rapid
  - Anaplastic astrocytoma (Grade III)
  - Glioblastoma Multiforme (Grade IV)
Imaging

- Anaplastic astrocytoma grade III/GBM grade IV
  - Complex enhancement on contrast imaging
  - Areas of hemorrhage
  - Mass effect
  - Irregular ring enhancement with hypointense center represents necrosis
    - GBM
  - Cerebral edema
High Grade Glioma Treatment

- Depends on a number of factors:
  - Site of lesion
  - Degree of malignancy
  - +/- Elevated ICP
  - Degree of disability and effect of steroid therapy
  - Suspected nature of tumor on imaging
  - Patient’s age
  - Patient’s wishes
Principles of Medical Management for Brain Tumors

• **Surgery**
  – Craniotomy for tumor resection
    • To reduce mass effect/decrease tumor burden
    • Diagnostic tissue sampling
  – Stereotactic biopsy
    • Tissue sampling to make a diagnosis
      – When removal of tumor unsafe
    • Requires head frame or frameless navigation
    • Burr hole
Malignant Glioma Treatment

- Grade III and Grade IV
- Surgical resection vs biopsy
- Followed by external beam radiation (EBRT)
  - 40 Gy whole brain + 15-20 Gy to tumor bed = 60 Gy
- GBM- Median survival of
  - One month w/o treatment
  - 14+ mos w/ surgery, xrt, chemo
Principles of Medical Management for Brain Tumors

- **Radiation therapy**
  - (WBRT)
  - Focal radiation
  - SRS (stereotactic radiosurgery)
    - Focused radiation as if to replace surgery
    - X-knife – linear accelerator
    - Gamma Knife – cobalt 60
    - (Proton beam)

- **(Brachytherapy)**
  - Implantation of radioactive seeds
  - 125-Iodine
  - Gliasite
LT Frontal, 18Gy @ 80%, 5 Arcs, 370 degrees
Common Brain Tumors – *Astrocytoma* - Treatment

- **Chemotherapy**
  - Alkylating agent
  - Temozolomide (Temodar)
    - FDA approved for treatment of initial relapse of AA and progression
    - Used (off label) for newly dx’d GBM and AA
  - Carmustine (BCNU)
  - Cisplatinum (Cisplatin)
**Common Brain Tumors – *Astrocytoma* - Survival**

- **Approximate survival for astrocytomas after receiving “optimal treatment”:**

<table>
<thead>
<tr>
<th>WHO Grade</th>
<th>Median Survival</th>
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<tbody>
<tr>
<td>I</td>
<td>?</td>
</tr>
<tr>
<td>II</td>
<td>7-8 years?</td>
</tr>
<tr>
<td>III</td>
<td>≈ 3-4 years</td>
</tr>
<tr>
<td>IV</td>
<td>≈ 14 months</td>
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</table>
Prognostic Factors

- **Prognosis is based on:**
  - Type of tumor
  - Tumor grade
  - Location
  - Spread (if any)
  - Age of the patient
  - How long the patient had symptoms before it was diagnosed
  - How much the tumor has affected the patient’s ability to function
  - Extent of surgery if surgery was performed
  - Type of therapy

- **Favorable prognostic factors**
  - Lower pathologic grade
  - Young age (<60)
  - High Karnofsky performance status
    (standard way of measuring the ability of cancer patients to perform ordinary tasks/ADLs)
Mixed tumors

• Oligoastrocytomas

• More oligodendroglial component
  – Better prognosis

• Oligoastro Gr III > oligoastro Gr IV > AA > GBM

Antigen presentation from tumor cells
Immunotherapy/ Vaccine

- T-cell mediated antitumor immunity
- Pt’s with gliomas demonstrate impaired immune function.
- Glioma cells down regulate surface expression of MHC molecules, depriving infiltrating immune cells of signals needed to recognize and clear tumor cells.
- Dendritic cells (antigen presenting cells) are pulsed with tumor protein to make a vaccine.
- DC introduces tumor associated antigen (TAA) to T-cells.
- Activation of T-cells to eliminate tumor cells.