Brain Tumors and Treatment

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Idaho Society of Health-System Pharmacists
Spring Conference
Saint Luke’s Regional Medical Center
Boise, Idaho
April 7th 1030-1130

Learning Objectives

› List the signs and symptoms of a brain tumor.
› Describe the general treatment modalities of treating brain tumors.
› Name the oral chemotherapy agent used in treating brain tumors.

What is a brain tumor?

› Primary Brain Tumor
  › Group of abnormal cells that start in the brain
  › Malignant or benign
  › Generally, will not spread to the body
    › The CNS does not have a lymph system
› Metastatic Brain Tumor
  › Metastasize to the brain from a systemic cancer
  › Most common are breast and lung

Epidemiology

› Primary brain tumors are more prevalent in children
  › 4,300 children younger than 20yo will be diagnosed
    › 3,050 children will be <15yo
  › 22,910 cases of primary tumors will be diagnosed in the US (adult and children)
    › Responsible for 13,700 deaths
  › Incidence has been increasing over the last 30 years
    › More common in males than females
    › Represent 2% of all cancers
› Metastatic brain tumors are more prevalent in adults
  › Occurs 10 times more than primary brain tumors
  › 20-40% of patients with systemic cancer
Type of Brain Tumor

- There are more than 120 types of tumors in the brain and central nervous system.
- The type of tumor depends on the type of tissue and where the abnormal cells began to grow.

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningioma</td>
<td>Astrocytoma</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>Glioblastoma (GBM)</td>
</tr>
<tr>
<td>Pituitary Adenoma</td>
<td>Oligodendroglioma</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>Primary CNS Lymphoma</td>
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Incidence Rates

Pathology

- Radiation
- Ionizing radiation
- Significant increase in risk after irradiation as a child
- Latency period of 10-20 years
- Genetics
  - 5% of primary brain tumors
    - Li-Fraumeni Syndrome, p53 mutations, Von Hippel-Lindau disease, Turcots Syndrome
- Environmental Exposure
  - Oil refining, rubber manufacturing and chemists
**Signs and Symptoms**

- Seizures
- Changes in speech, hearing
- Changes in vision
- Balance problems
- Problems with walking
- Problems with memory
- Personality changes
- Inability to concentrate
- Weakness in one part of the body
- Numbness or tingling in the arms, legs

**Diagnosis**

- Magnetic resonance imaging (MRI)
- Positron-emission tomography (PET) scan

**Staging (WHO)**

- **Grade I**: The tissue is benign. The cells look nearly like normal brain cells, and cell growth is slow.
- **Grade II**: The tissue is malignant. The cells look less like normal cells than do the cells in a grade I tumor.
- **Grade III**: The malignant tissue has cells that look very different from normal cells. The abnormal cells are actively growing. These abnormal-appearing cells are termed anaplastic.
- **Grade IV**: The malignant tissue has cells that look most abnormal and tend to grow very fast.

**General Treatment**

- **Surgery**: Regardless of tumor type, remove as much as possible, provides an accurate diagnosis
- **Radiation therapy**: Standard fractionated external beam radiation therapy
  - Primary brain tumors
  - Whole brain radiation
  - Metastatic brain tumors
- **Chemotherapy**: May or may not be an option
- **Will need to cross the blood brain barrier**
Benign Primary Tumors

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Meningioma (WHO Grade 1)

- Not technically a brain tumor, originate in the arachnoid
- Slow growing
- More common in women
- Higher incidence in women with breast cancer

Treatment
- Active Surveillance
- Surgery
- High risk of recurrence
- Adjuvant radiation therapy
- Radiation alone
- No role for chemotherapy

Schwannoma

- Arises from a nerve cell
- Most commonly affect the 8th cranial nerve
- Vestibulocochlear nerve
- Affect people between ages of 50-60

Treatment
- Active Surveillance
- Surgery
- Stereotactic Radiation
- No role for chemotherapy

Pituitary Adenoma

- Inappropriate pituitary hormone secretion
- Type of tumor depends on the cell type the tumor is derived from
  - Proactin (PRL)
  - Adrenocorticotropic (ACTH)
  - Growth Hormone (GH)
  - Thyroid

Treatment
- Surgery
- Radiation Therapy
- Medical Hormone Therapy
- Combination
### Pituitary Adenoma

<table>
<thead>
<tr>
<th>Secreting Hormone</th>
<th>Treatment by Type</th>
<th>1st Line</th>
<th>2nd Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proloactin (PRL)</td>
<td>Dopamine agonists: cabergoline and bromocriptine</td>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Adrenocorticotropic (ACTH)</td>
<td>Surgery +/- Radiation</td>
<td>Steroidogenesis inhibitors: mitotane, metyrapone, ketoconazole, aminoglutethimide</td>
<td></td>
</tr>
<tr>
<td>Growth Hormone (GH)</td>
<td>Surgery, and Medical Therapy</td>
<td>GH-receptor antagonist: pegvisomant</td>
<td>Adjunctive radiation therapy</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Surgery +/- Radiation</td>
<td>Medical Therapy: somatostatin analogues (octreotide)</td>
<td></td>
</tr>
<tr>
<td>Non Functioning</td>
<td>Surgery</td>
<td>Radiation Therapy</td>
<td></td>
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### Craniopharyngiomas
- Arise from cells in the pituitary stalk and project into the hypothalamus
- Occurs most commonly in children 5-14yo, some men and women, 50-60 yo
- Growth failure, sexual dysfunction and visual loss
- Slow growing

### Treatment
- Surgery
- Radiation Therapy

### Transsphenoidal Surgery

### Craniotomy
Malignant Primary Tumors

- Astrocytoma
- Glioblastoma (GBM)
- Oligodendroglomoas
- Primary CNS Lymphoma

Atrocytoma

- Arise from astrocytes, star shaped, supportive tissue
- Classified by grade – WHO
- Slow to fast growing
- Most common in the cerebral hemisphere

Treatment

- Grade I & II – Surgery + Radiation
- Grade III & IV – Surgery, Radiation, Chemotherapy
  - Procarbazine, lomustine, vincristine, temozolamide

Glioblastoma Multiform (GBM)

- Most common and lethal
- Classified as a Grade IV astrocytoma
- Cerebral hemisphere, brainstem and spinal chord

Treatment

- Surgery
- Radiation
- Chemotherapy
  - Temozolamide, carmustine, Gladel® (carmustine wafers), irinotecan, bevacizumab, thalidomide, procarbazine, tamoxifen, cisplatin, gefitinib, erlotinib

- Needs to cross the BBB

Oligodendroglomoas

- Less aggressive, indolent, majority are low grade
- Survival of 5 years
- Arise in cerebral hemispheres, distributed in the frontal, parietal, temporal and occipital lobes

Treatment

- Surgery
- Radiation Therapy
- Chemotherapy
  - Procarbazine, lomustine, vincristine
Primary CNS Lymphoma
- Arise from histiocytes, limited to the cranial-spinal axis
- Affect immuno-compromised patients: HIV, EBV, transplant
- Presents around 60-70yo
- Infiltrate the deep structures of the brain: CSF, eye
- Treatment
  - Surgery for biopsy only
  - Radiation therapy if <60yo
  - Chemotherapy
    - Good performance status, adequate renal function
    - High dose methotrexate, vincristine, procarbazine, cytarabine

Brain Metastasis
- Most common in adults
- Occur 10x more frequently than primary brain tumors
- Metastasize from the lung, melanoma and breast cancers
- Occur in cerebral hemispheres
- Treatment
  - Surgery
  - Whole Brain Radiation
  - Chemotherapy
    - Depends on the histology of the primary tumor
    - Carmustine wafers, temozolamide, high dose methotrexate, platinum drugs, etoposide, capecitabine, lapatinib

Questions?