Brain Tumors and Treatment

Megan R. Flood PharmD
PGY2 Oncology Resident
Mountain States Tumor Institute

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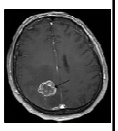
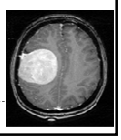
Learning Objectives

- 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

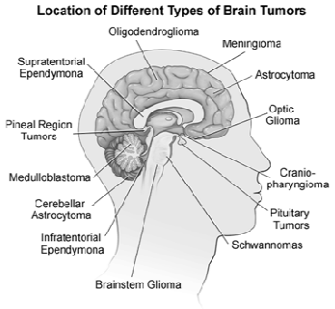
- Primary brain tumors are more prevalent in children
  - 4,300 children younger than 20yo will be diagnosed
    - 3,050 children will be <15yo
  - 22, 910 cases of primary tumors will be diagnosed in the US (adult and children)
    - Responsible for 13,700 deaths
  - Incidence has been increasing over 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

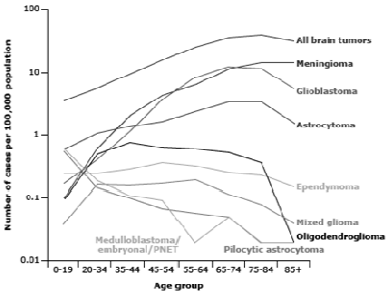
- There are more than 120 types of tumors in the brain and central nervous system
- The type of tumor depends on the type of tissue and where the abnormal cells began to grow

Benign	Malignant
Meningiomas	Astrocytoma
Schwannoma	Glioblastoma (GBM)
Pituitary Adenoma	Oligodendroglimoas
Craniopharyngiomas	Primary CNS Lymphoma

Type of Brain Tumor



Incidence Rates



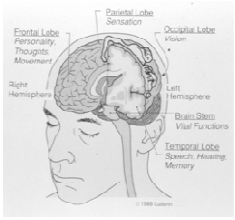
1992-1997

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

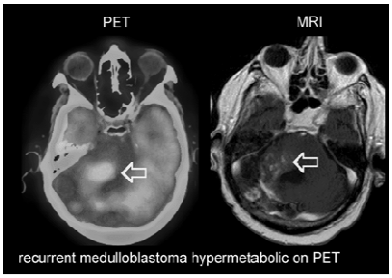
Signs and Symptoms

- 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

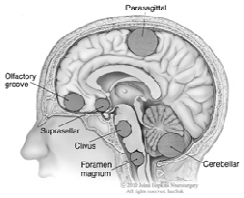
- Surgery
  - Regardless of tumor type, remove as much as possible, provides an accurate diagnosis
- Radiation therapy
  - Standard fractionated external beam radiation therapy
    - Primary brain tumors
  - Whole brain radiation
    - Metastatic brain tumors
- Chemotherapy
  - May or may not be an option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

Benign Primary Tumors

Meningiomas
Schwannoma
Pituitary Adenoma
Craniopharyngiomas

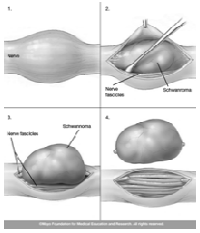
Meningioma (WHO Grade 1)

- 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



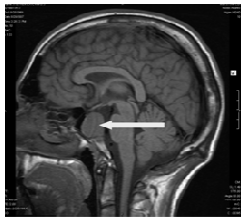
Schwannoma

- 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
  - Proloactin (PRL)
  - Adrenocorticotropic (ACTH)
  - Growth Hormone (GH)
  - Thyroid
- Treatment
  - Surgery
  - Radiation Therapy
  - Medical Hormone Therapy
  - Combination

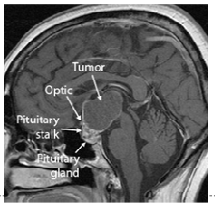


Pituitary Adenoma

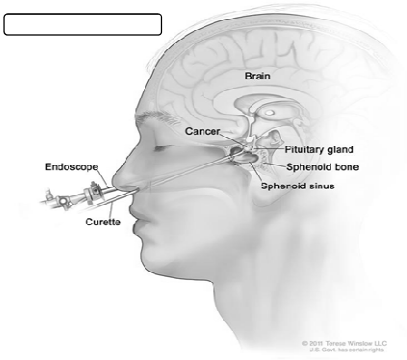
Treatment by Type		
Secreting Hormone	**1st Line**	**2nd Line**
Proloactin (PRL)	Dopamine agnoists: cabergoline and bromocriptine	Surgery
Adrenocorticotropic (ACTH)	Surgery +/- Radiation	Steroidogenesis inhibitors: mitotane, metyrapone, ketoconazole, aminoglutethimide
Growth Hormone (GH)	Surgery, and Medical Therpay Medications: Dopamine analogues (bromocriptine), Somatostatin analogues (octreotide)	GH-receptor antagonist: pegvisomant Adjunctive radiation therapy
Thyroid	Surgery +/- Raditation	Medical Therapy: somatostatin analogues (octreotide)
Non functioning	Surgery	Radiation Therapy

Craniopharyngiomas

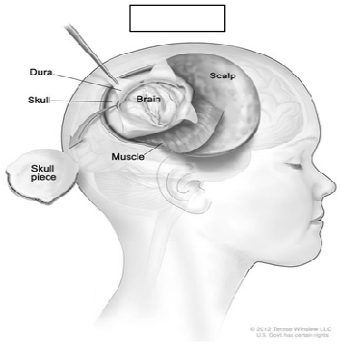
- Arise from cells in the pituitary stalk and project into the hypothalamus
- Occurs most commonly in children 5-14yo , some men and women, 50-60 yo
- Growth failure, sexual dysfunction and visual loss
- Slow growing
- Treatment
  - Surgery
  - Radiation Therapy



Transsphenoidal Surgery



Craniotomy

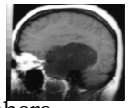


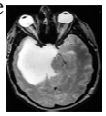
Malignant Primary Tumors

Astrocytoma
Glioblastoma (GBM)
Oligodendroglimoas
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

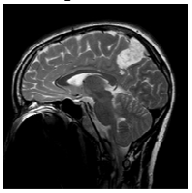
Glioblastoma Multiform (GBM)

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

- Treatment
  - Surgery
  - Radiation
  - Chemotherapy
    - Temozolamide, carmustine, Gliadel® (carmustine wafers), irinotecan, bevacizumab, thalidomaide, procarbazine, tamoxifen, cisplatin, gefitinib, erlotinib
    - Needs to cross the BBB

Oligodendrogliomas

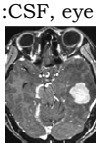
- Less aggressive, indolent, majority are low grade
- Survival of 5 years
- Arise in cerebral hemispheres, distributed in the frontal, parietal, temporal and occipital lobes



- Treatment
  - Surgery
  - Radiation Therapy
  - Chemotherapy
    - Procarbazine, lomustine, vincristine

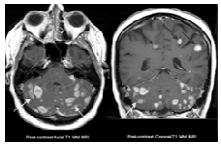
Primary CNS Lymphoma

- 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?