Neuro-oncology Update
2013

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DISCLOSURES
Nothing to disclose
Case 1

58 year old man with recent facial droop and HA’s
• Thin, cachectic
• Drives a semi-trailer
• 48 pack-year history
• Progressive cough
Case 2

68 year old woman
New onset visual field cut, visual obscurations, blurring vision
Unsteadiness
Confusion
Case 2

- No significant PMH
Case 3

26 year old woman
Present to ER with HA’s, sense of impending doom
Short lived bout of fatigue a few years ago
Morbid obesity
EPIDEMIOLOGY OF BRAIN TUMORS

77,801 Primary brain tumors are diagnosed in the US (malignant and benign)
- 5,177 in children
- 72,624 in adults

24,766 neuroepithelial tumors (mostly malignant)
- 1,746 lymphomas
- 28,591 meningiomas
- 12,391 sellar tumors

6,486 tumor of cranial and spinal nerves

180,000-210,000 metastatic brain tumors
Adult Brain Tumor Histology

- Meningioma: 36%
- Glioblastoma: 16%
- Pituitary: 14%
- Astrocytoma: 6%
- Ependymoma: 2%
- Oligodendroglioma: 2%
- Embryonal: 1%
- Craniopharyngioma: 1%
- Nerve Sheath Tumors: 8%
- Lymphoma: 2%
- Germ Cell Tumors: 1%
- All Other: 11%
Adult Gliomas

- Most common primary brain tumor arising in the brain
- Estimated 24,766 gliomas are diagnosed / year in the US
- 2nd most common tumor and most fatal tumor in children
- <5% hereditary, risk factors otherwise unknown
## Glioma incidence at various ages

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Age Range</th>
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<tbody>
<tr>
<td>Pilocytic astrocytoma</td>
<td>5-25</td>
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<tr>
<td>Ependymoma</td>
<td>5-30</td>
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<tr>
<td>Oligodendroglioma</td>
<td>30-55</td>
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<tr>
<td>Low-grade Astrocytoma</td>
<td>25-55</td>
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<tr>
<td>Glioblastoma Multiforme</td>
<td>45-65</td>
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</tbody>
</table>
Clinical Presentations of Intra-axial Neoplasms

- Progressive focal neurological deficit 68%
- Non-localizing CNS symptoms 54%
  - Headache 8% only
    - classic triad: AM, associated with bending, coughing, nausea, vomiting
  - Behavioral changes
  - Increased ICP
- Seizures 26%
  - New onset seizure in an adult should be considered a brain tumor until proven otherwise
Supratentorial Tumors

Focal sensory / motor deficits
Neurobehavioral symptoms
  Aphasia
  Apraxia
  Neglect
  Personality change
Posterior Fossa Tumor

- Increased Intracranial Pressure
  - Headache
  - Nausea or vomiting
  - Papilledema
- Focal Findings
  - Brainstem compression
    - Cranial nerve deficits
    - Long tract signs
  - Cerebellar hemisphere: Ataxia, dysmetria
  - Cerebellar vermis: Ataxia, Gait disturbance
Special Clinical Syndromes

- CP angle tumors
  - Progressive unilateral hearing loss, tinnitus
- Pineal region tumors
  - Abnormalities of vertical gaze
  - Hydrocephalus
- Anterior hypothalamus
  - Diabetes insipidus
  - Precocious puberty
- Endocrinopathies from pituitary adenomas
  - Prolactinomas - PRL
  - Cushing’s disease - ACTH
  - Acromegaly - GH
- Bifrontal tumors - Abulia / anhedonia
Histopathology

• WHO classification
  • I- hypercellularity
  • II- hypercellularity + cytoplasmic atypia
  • III- hypercellularity, nuclear anaplasia, mitotic activity
  • IV- + microvascular proliferation and/or necrosis
WHO classification: Neuroepithelial tumor lineage

- Astrocytoma
- Oligodendroglioma
- Mixed Oligoastrocytoma
- Ependymomas
- Choroid plexus tumors
- Pinealocytomas
- Embryonal
  - Medulloblastoma
  - PNET
Low Grade Astrocytoma
# Tumor Markers

<table>
<thead>
<tr>
<th>Neoplasm</th>
<th>GFAP</th>
<th>Cytokeratin</th>
<th>EMA</th>
<th>S100</th>
<th>Synaptophysin</th>
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<tbody>
<tr>
<td>Astrocytoma</td>
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<td>Pituitary adenoma</td>
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<td>Meningioma</td>
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Treatment Modalities

Symptoms

- **EDEMA:** steroids effective only in enhancing tumors
  - Vasogenic - Steroid-responsive
  - Cytotoxic - Not steroid-responsive
  - Ischemic - Not steroid-responsive

- **SEIZURES**
  - 20-40% have seizures. AED’s indicated
  - Prophylactic AED use
    - Level 1: No evidence
    - Level II: Safe to use in pts undergoing craniotomy, taper off starting 1 week postop
Treatment

- Surgery: Treatment of choice if feasible
  - Biopsy: for diagnosis, nearly always indicated
  - Resection: indicated if “significant” resection can be achieved safely, without new deficits
- Radiation: one of most effective treatments
  - Focal 60 Gy targeting T2 + 2 cm
  - Not WBXRT
  - Radiosurgery not indicated
Therapeutic Treatment Modalities

- Chemotherapy
  - Nitrosoureas like BCNU, CCNU
  - Alkylating agents: temozolamide, procarbazine
  - Nitrogen mustard: CP, cytoxan
  - Vinca alkyloids: Vincristine
  - Anti-angiogenics: Bevacizumag
- Other promising but unproven treatments
  - Vaccines
  - Gene therapy
Brain Metastases

• Common
  • Lung, breast, melanoma, GI, renal, unknown primary

• Rare
  • Esophagus, oropharynx, non melanoma skin cancer, prostate
Treatment Goals

- Prevent or relieve neurologic symptoms
- Extend life
- Improved quality of life remaining
- Diagnosis
- Cure?
Therapeutic Options

• Location, size, and number of brain mets
• Extent of systemic cancer
• Patient age, performance score, and neurologic status
• Tumor type and responsiveness to therapy
Therapeutic Options

• Surgery
• Whole Brain Radiation
• Stereotactic Radiosurgery
Surgery for Solitary Brain Metastasis

- 48 patients with solitary metastases randomized to surgery + WB vs WB alone

- Addition of surgery to WB reduced the local recurrence rate in these patients from 52 to 20%

- Length of survival was improved in the surgical group from 15 to 40 weeks

- Patients in the surgery and WB arm also remained functionally independent for a longer period of time, 38 weeks vs 8

Patchell, RA. NEJM, 1990
Metastatic Breast Cancer
Whole Brain Radiation for Cerebral Metastases

- Different levels of radioresistance vs. radiosensitivity
- Provides 2-3 month survival benefit
- Considered for palliation especially for those with multiple mets or surgically unresectable disease or can’t perform SRS
- Side effects: Cognitive dysfunction
- Convenience lacking
- Usual dose of 30 Gy in 10 fractions
  - Severe dementia in 11% of 1 yr survivors and 50% of 2 yr survivors
- Prophylactic WBXRT in small cell lung cancer patients
- Role following craniotomy for mets
Radiosensitivity of brain metastases to WBXRT

Radiosensitive
Small cell lung cancer
Germ cell tumors
Lymphoma
Leukemia
Myeloma
Breast (moderately)

Radioresistant
Colon
Nonsmall cell lung cancer
Thyroid
Renal cell
Melanoma
Adenocarcinoma
Stereotactic Radiosurgery

- Steep dose gradient which limits the volume of normal brain being exposed to high doses of radiation
- Suitable for tumors 3 cm or less
- Even effective for radioresistant cancers
- Multiple tumors
Stereotactic Radiosurgery

- Large meta-analyses show local tumor control rate 70-96%
- Median survival 7-12 months
- Excellent improvement in quality of life, minimal morbidity

Oncology 1999
Curr Opin Oncl 2003
Metastatic tumors treated worldwide from 1991-2011
Gamma Knife Radiosurgery alone
cumulative, in thousands
Multiple lesions from breast cancer
Cerebellar Hemangioblastoma of Von-Hippel Lindau Disease
Radioresistant renal cell carcinoma
Lung Adenocarcinoma
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Final thoughts

- We have a long road ahead of us for our patients
- Treatments continue to struggle to extend quality years
- Better coordination of care
- Increase the focus on treatments extending a better quality of life