Pre-talk Questions for Audience

1) True/False:

Most brain tumors in children are diagnosed soon after symptoms arise.
Pre-talk Questions for Audience

2) Headaches are most likely to be caused by a brain tumor or other cause of elevated intracranial pressure if:

A. They are associated with vomiting
B. They get worse as the day goes on
C. They are associated with visual changes or neurological deficits
D. All of the above
E. A and C
Pre-talk Questions for Audience

3) If you suspect the possibility of a brain tumor in your patient you should order the following test
A. CT of the brain without IV contrast
B. CT of the brain with IV contrast
C. MRI of the brain without gadolinium
D. MRI of the brain with gadolinium
Pediatric Brain Tumors

I. Introduction/Epidemiology

II. Clinical Presentation and Diagnosis: What Should the Pediatrician Know?

III. Current Management of Pediatric Brain Tumor Patients

IV. Future Directions
Pediatric Brain Tumors

- Second most common cancer in children
- Most common solid cancer and leading cause of cancer death in children
- Approximately 4000 new pediatric brain tumors diagnosed per year in U.S.
- Etiology of vast majority of tumors is unknown

(www.cbtrus.org, 2011)
Case #1

- 12 year old girl presented with morning headaches 4/2009
- Treated for sinusitis with antibiotics, headaches continued, associated with intermittent vomiting and neck pain
- Sent to chiropractor for neck pain, treated with manipulations
- 10/2009; vomiting worsened, associated with retro-orbital pain and diplopia, sent for MRI of brain
Case #2

- 8 y/o girl presents with polyuria and polydipsia in 1999; etiology not discovered; slowly progressed, parents told it was likely psychogenic
- 12/2000 – decreased appetite
- 4/2001 – daily headaches, intermittent vomiting
- 5/2001 – referred to GI specialist; endoscopy negative
- 5/2001 – Decreased vision; visual field deficit noted by ophthalmologist - imaging studies of brain ordered
Case #3

• 5 month old boy presented with intermittent twitching, sometimes with arching of the neck
• Sent to pediatric neurologist, EEG ordered (negative)
• Twitching persisted and became more frequent
• Age 11 months – vomited several times over a few days then became lethargic, stopped breathing
Case #3

Pre-op MRI

Post-op MRI
Diagnosis of Pediatric Brain Tumors

- **Signs/Symptoms of Elevated Intracranial Pressure**
  - Headache (morning, persistent)
  - Vomiting (sometimes without headache!)
  - Lethargy
  - Papilledema
  - Young children: increasing head circumference, full fontanelle
Diagnosis of Pediatric Brain Tumors

Presentation Related to Tumor Location:

**Posterior Fossa**

- Cerebellar signs (ataxia, scanning speech, nystagmus, dysmetria)
- Torticollis in young children
- Cranial neuropathies
Diagnosis of Pediatric Brain Tumors

Presentation Related to Tumor Location: Cerebral Hemispheres

- Seizures (40 to 75%)
- Focal neurologic deficits
- Behavior changes

Diagnosis of Pediatric Brain Tumors

Presentation Related to Tumor Location:

**Suprasellar**

- Endocrine dysfunction
- Visual impairment
Diagnosis

Presentation Related to Tumor Location:

**Pineal Region**

- Parinaud’s Syndrome
  - Upgaze palsy
  - Convergence Nystagmus
  - Pupils unreactive to light but respond to accomodation
Diagnosis: Imaging Studies to order

- The imaging study of choice to diagnose brain tumors in children is an MRI with gadolinium.
- Sedation is required for young children.
- Exception: Non-contrast CT should be ordered first if patient is deteriorating or if contraindication to MRI.
Diagnosis: Imaging Studies to order

Why Not Just Get a Quick Head CT first as a screening study?

1) One brain CT = 30 to 100 chest x-rays worth of radiation exposure

2) One single brain CT: 0.05% risk of death from radiation-induced malignancy

(Brenner & Hall, NEJM, 2008)
What Should Pediatrician Do if Diagnosis of Brain Tumor is Made?

• If patient is lethargic, continuously vomiting, or has rapidly progressive neurological changes – send to emergency department

• If patient is stable: call pediatric neurosurgeon to discuss timing of consultation (usually same day or the next day) and then discuss plan with family
Current Management of Pediatric Neurosurgery Patients

- CSF dissemination?
- Surgical Considerations
- Diagnostic sampling
- Hydrocephalus
Surgical Considerations: CSF Dissemination

• MRI of entire spine as part of diagnostic work-up in child with brain tumor

Example: 1 y/o boy, presented with lethargy; pathology – choroid plexus carcinoma
Surgical Considerations: Anatomy

In general, pediatric brain tumors that are in anatomic regions safe for surgical approaches should be resected as completely as possible (Duffner, et. al. Neuro-oncol., 1999).

- Baby POG I = study of 198 children < 3 with malignant brain tumors treated with surgical resection followed by chemotherapy and delayed radiation.
- Most important predictor of survival was degree of surgical resection (61.8% 5 yr survival vs. 31% for subtotal).

(Duffner, et. al. Neuro-oncol., 1999)
Pediatric Brain Tumors: Surgery
Pediatric Brain Tumors: Surgery

(Campell et al., Neurosurg. 1996)
Surgically Resectable Brain Tumors: Supratentorial

Three year old female, presented with nausea/vomiting; pathology = ependymoma

Pre-op

Post-op
Surgically Resectable Brain Tumors: Suprasellar

Four year old male, presented with visual changes – bumping into walls
Surgically Resectable Brain Tumors: Posterior Fossa

12 y/o boy, presented with headache and vomiting; pathology = pilocytic astrocytoma
Surgically Resectable Brain Tumors: Posterior Fossa

3 y/o boy presented with vomiting; pathology = ependymoma
Intraoperative Considerations

• Neuro-anesthesia
• Temperature control
• Skull fixation
• Frameless Stereotaxy
• Functional Mapping/Awake Craniotomy
• Blood loss
Intraoperative Considerations:
Skull Fixation
Intra-operative Considerations: Frameless Stereotaxy
Intra-operative Considerations: Frameless Stereotaxy
Intra-operative Considerations: Functional Mapping
Endoscopic Tumor Biopsy: Case #1

- 15 y/o female, presented with visual field deficits and diabetes insipidus
- Normal Serum bHcG and AFP
Endoscopic Tumor Biopsy: Case #1
Endoscopic Tumor Biopsy: Case #1

- Pathology: germinoma
- Treatment: chemotherapy and involved field radiation therapy
- Complete response
- Visual fields normalized; required hormone replacement therapy
Adjuvant Treatment

• Chemotherapy and Radiation Therapy
  - Can decrease recurrence rates or lengthen time to recurrence in some CNS malignancies BUT...
  - Systemic chemotherapy limited by BBB and systemic side effects
  - Technical Limitations of XRT in children (frames for stereotactic radiosurgery, anesthesia)
  - Late effects of chemotherapy and XRT: endocrinopathy, cognitive effects, 2nd malignancy
Radiation Therapy

• Risk of radiation damage to brain is inversely proportional to age; risks include cognitive damage, endocrinopathies, hearing loss, vasculopathy, second malignancy

  (Duffner, et. al. Neuro-oncol., 1999)

• In study of 20 long-term survivors of radiation therapy for tumors under 3, 85% had impaired cognition at 5 yr follow-up; 55% required special education

  (Suc, et. al., Acta Neurochir., 1990)
Advances in Radiotherapy

- Reduced dose
- Reduced fields – decreased dose to surrounding brain
  - 3D conformal RT
  - Stereotactic Radiation Therapy
    1) “Radiosurgery” – single-dose
    2) Fractionated
Stereotactic Radiation Therapy

Isodose lines of conventional external beam irradiation

Isodose lines of stereotactic radiotherapy plan
Pediatric Brain Tumors: Future Directions

• Neuro-endoscopy – better instrumentation, surgical resection of more tumors
Pediatric Brain Tumors: Future Directions

- **Molecular studies** – new tumor markers to improve tumor diagnosis, possibly generate individual tumor-specific expression profiles predicting response to therapies

- **Novel therapeutic approaches** – immunotherapy, local delivery methods
Future Directions: Local Delivery of Chemotherapeutic and other Agents

Intraoperative Images

Illustrational View
Future Directions: Local Delivery of Chemotherapeutic and other Agents
First in Humans Clinical Trials – Direct Administration of Chemotherapy Into the Fourth Ventricle
Patient Number 1: Dramatic Clinical Response in Brain!!

Pre-treatment 3/2003

After 15 cycles 2/2014

Chemotherapy Administration Directly into the Fourth Ventricle
Patient Number 1: Complete Response of 2 Spine lesions!!

Chemotherapy Administration Directly into the Fourth Ventricle
Most Recent Patient Enrolled in Dose Escalation Trial

Before Treatment  
After 3 Cycles  
After 2 more cycles in Arkansas
Post-Talk Questions for Audience

1) True/False:

Most brain tumors in children are diagnosed soon after symptoms arise

Answer: False
2) Headaches are most likely to be caused by a brain tumor or other cause of elevated intracranial pressure if:

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C. They are associated with visual changes or neurological deficits
D. All of the above
E. A and C

Answer: E
3) If you suspect the possibility of a brain tumor in your patient you should order the following test:
A. CT of the brain without IV contrast
B. CT of the brain with IV contrast
C. MRI of the brain without gadolinium
D. MRI of the brain with gadolinium

Answer: D
Thank you!