Central Nervous System Tumors of Childhood and Adolescence

Chris Conrady, PNP & Kellie J. Nazemi, MD
March 10, 2012
Objectives

• Describe common CNS tumors of childhood
• Define underlying treatment principles
• Review exam findings relevant to CNS tumors
Signs & Symptoms

• Increased intracranial pressure
• Localized symptoms
Ventricular System & CSF Flow
Hydrocephalus

Patient with hydrocephalus

Patient with normal pressure
Increased intracranial pressure

- Headaches
- Vomiting
- Papilledema
- **Mental status changes**
- **Cushing’s Triad**
  - Bradycardia
  - Irregular respirations
  - Hypertension

Beware: risk of tonsillar herniation with lumbar puncture!!!
QUESTION

• What is the approximate prevalence of headache in children?

**ELEMEN TARY age**

A. Under 10%
B. 10 - 20%
C. 20 - 30%
D. 40 - 50%
E. Over 60%

**HIGH-SCHOOL age**

A. Under 10%
B. 10 - 20%
C. 20 - 30%
D. 40 - 50%
E. Over 60%
Headache in brain tumor patients

- Overall: gradually worsening
- Timing: when recumbent
- Associated symptoms:
  - Vomiting with relief
  - “Dizziness” (unsteady or vertigo)
  - Personality change or school problems
  - Triggered by straining
  - Numbness or weakness
Headache in brain tumor patients


• > 98% have abnormal:
  • Mental status
  • Optic discs
  • Eye movement
  • Motor exam (hemiparesis)
  • Tandem gait OR
  • Deep tendon reflexes

• The rest have seizures!
Increased ICP in young children

Growth Chart
Head Circumference-for-Age Percentiles (Girls, Birth to 36 Months)
Localized Signs & Symptoms
• **PEARLS:**
  
  • Non-urgent neuroimaging should be seriously considered in any child **under 1 year of age** with new-onset of seizures
  
  • A child with history and EEG findings consistent with absence seizure does not require neuroimaging
  
  • A child with a simple febrile seizure does not need neuroimaging
  
  • If a neuroimaging study is needed, **MRI of the brain with & without contrast** is the preferred modality
  
  • Emergent neuroimaging is needed in a child with a **post-ictal focal deficit that does not resolve** within “several hours”
Febrile Seizures

• Generally accepted criteria:
  ➢ A convulsion associated with an elevated temperature greater than 38ºC
  ➢ A child younger than six years of age
  ➢ No central nervous system infection or inflammation
  ➢ No acute systemic metabolic abnormality that may produce convulsions
  ➢ No history of previous afebrile seizures

• Two categories:
  ➢ SIMPLE (BENIGN): these are most common
    ➢ last less than 15 minutes
    ➢ have no focal features, AND
    ➢ if they occur in a series, the total duration is less than 30 minutes
  ➢ COMPLEX:
    ➢ last more than 15 minutes
    ➢ have focal features or postictal paresis
    ➢ occur in a series with a total duration greater than 30 minutes
Eye Movements

• INFANTS: ABNORMALITIES BEYOND 2 - 3 MONTHS OF AGE SHOULD...
  – Be seen by an ophthalmologist
  – Be evaluated with MRI
Eye Movements

• ANY CHILD WITH AN ACQUIRED EYE MOVEMENT DISORDER SHOULD...
  – Be seen by an ophthalmologist
  – Undergo neuro-imaging (MRI)
Back pain in children

• Abnormal in children
• Complaint in 80% of patients with cord compression
• Compression originating from:
  – intrinsic CNS tumor
  – bony disease originating in a vertebral body
  – paraspinous soft tissue tumor infiltrating through an intervertebral foramina
• Etiology:
  – sarcomas, lymphoma, leukemia, neuroblastoma, germ cell tumors, spinal cord tumors, and metastatic brain tumors
Back pain in children

• Urgent MRI of entire spine indicated when:
  – Child has known or suspected cancer
  – Fecal or urinary incontinence
  – Refusal or inability to walk
  – Neurologic abnormality on exam
    • Attention to strength, reflexes, sensory abnormalities, tone (musculoskeletal and sphincter)
      – Tenderness to percussion of vertebral column
• Paraplegia or quadriplegia can occur rapidly
• Only urgent decompression can reverse
### WHO grades of CNS tumours

<table>
<thead>
<tr>
<th>Astrocytic tumours</th>
<th>I</th>
<th>II</th>
<th>III</th>
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<tbody>
<tr>
<td>Subependymal giant cell astrocytoma</td>
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<td>Diffuse astrocytoma</td>
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<td>Glioblastoma</td>
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<td>Giant cell glioblastoma</td>
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<td>Myxopapillary ependymoma</td>
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<td>Ependymoma</td>
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<td>Anaplastic ependymoma</td>
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<tr>
<td>Choroid plexus papilloma</td>
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<td>Atypical choroid plexus papilloma</td>
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<td>Choroid plexus carcinoma</td>
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<td>Angiocentric glioma</td>
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<td>Choroidal glioma of the third ventricle</td>
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<td>Ganglioglioma</td>
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<tr>
<td>Anaplastic ganglioglioma</td>
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<td>Desmoplastic infantile astrocytoma and ganglioglioma</td>
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<td>Dysmyeloplastic neuroepithelial tumour</td>
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<td>Pineal parenchymal tumour of intermediate differentiation</td>
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<td>Pineoblastoma</td>
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<td>Papillary tumour of the pineal region</td>
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<td>Medulloblastoma</td>
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<tr>
<td>CNS primitive neuroectodermal tumour (PNET)</td>
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<tr>
<td>Atypical teratoid / rhabdoid tumour</td>
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<th>Tumours of the cranial and paraspinal nerves</th>
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<td>Schwannoma</td>
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<td>Neurofibroma</td>
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<td>Perineuroma</td>
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<td>Malignant peripheral nerve sheath tumour (MPNST)</td>
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<th>Meningeal tumours</th>
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<td>Anaplastic / malignant meningioma</td>
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<td>Haemangiopericytoma</td>
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<td>Anaplastic haemangiopericytoma</td>
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<tr>
<td>Haemangioblastoma</td>
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<th>Tumours of the sellar region</th>
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<td>Craniopharyngioma</td>
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<td>Granular cell tumour of the neurohypophysis</td>
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<td>Pituitaryoma</td>
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<td>Spindle cell oncocytoma of the adenohypophysis</td>
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CNS Cell Types

- Neurons
- Glia
- Choroid Plexus
CNS Tumor Classification

**Glial**
- Astrocytoma
- Oligodendroglioma
- Ependymoma

**Neuronal**
- Medulloblastoma
- Pineoblastoma
- sPNET

**Choroid Plexus**
- Choroid plexus papilloma
- Choroid plexus carcinoma

**Germ-cell Tumors**
- Germinoma
- Non-germinoma (NGGCT)

**Craniopharyngioma**

*Note: this is extremely un-official & only applies to common childhood tumors*
Common Infratentorial CNS Tumors

- Pilocytic astrocytoma
- Medulloblastoma
- Ependymoma
Initial Management

• Neurosurgical service
• Hydrocephalus
  – Dexamethasone
  – EVD placement or ETV
  – +/- VP shunt placement
• Definitive surgery
• Neuro-oncology consult
Pilocytic Astrocytoma

• First described in 1924

Percival Bailey, MD
Harvey Cushing, MD

www.aneuroa.org
history.library.ucsf.edu
Clinical Presentation

- Mean age: 7 years
- Duration of symptoms: 3 – 5 months
  - Indolent course
  - More compensation
- Headaches & vomiting
- Cerebellar dysfunction
Pilocytic Astrocytoma: MRI Findings
Pilocytic Astrocytoma
Pilocytic Astrocytoma

- Complete resection is curative  ...almost always
- Role for chemotherapy
- Role for radiation therapy

- Treatment approach same for all low-grade gliomas
Glioma, astrocytoma, what the heck?

- Low-grade glioma
- High-grade glioma
- Optic glioma
- DIPG
- Brainstem glioma
- Oligoastrocytoma
- Glioneuronal tumors
- Ganglioglioma

- ASTROCYTOMA
  - Grade I (JPA = pilocytic)
  - Grade II (diffuse / fibrillary)
  - Grade III (anaplastic astro)
  - Grade IV (GBM = glioblastoma multiforme)
Medulloblastoma

• First described in 1924
  – Percival Bailey, MD
  – Harvey Cushing, MD

• “...we were impressed by the frequency with which there has been encountered (in the large majority of cases in childhood) a very cellular tumor of a peculiar kind, apparently arising over the roof of the fourth ventricle and projecting into the center of the cerebellum.”
Typically short history

- Clinical presentation
  - Nearly uniform 2 – 4 week history
    - Initial headaches, vomiting
    - Progressive worsening
    - Development of localizing signs
      - cerebellar dysfunction
      - cranial nerve dysfunction

www.fleshandbones.com
Diagnostic Evaluation

• **Radiographic Imaging**
  - solid, homogeneous, contrast-enhancing mass

• **Predilection for spread**
Medulloblastoma sub-types

- Classic
- Desmoplastic
- Anaplastic

Normal layers of cerebellum

* pale island
## Classic risk stratification

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<tr>
<th></th>
<th>Standard-risk</th>
<th>High-risk</th>
<th>Infant-risk</th>
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<tr>
<td><strong>Age</strong></td>
<td>&gt; 3y</td>
<td>&gt; 3y</td>
<td>&lt; 3y</td>
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<tr>
<td><strong>Mets</strong></td>
<td>M0</td>
<td>M1 – M4</td>
<td>M0 – M4</td>
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<tr>
<td><strong>Residual disease</strong></td>
<td>&lt;1.5cm²</td>
<td>&gt;1.5cm²</td>
<td>Any size</td>
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Radiotherapy is important

- **Craniospinal irradiation**
  - Necessary to prevent relapses
  - 1992: France Bouffet et al., *Int J Radiat Oncol Biol Phys*
  - **3600cGy** (old “standard-dose”, now “high-dose”) vs. **2400cGy** (old “reduced-dose”, now “standard-dose”)
    - 2000: POG 8631 / CCG 923 Thomas et al., *Journal of Clinical Oncology (JCO)*
    - 1999: CCG – role of adjuvant chemotherapy Packer et al., *JCO*
  - **1800cGy**
    - Current COG study – further reduction of dose
      - Pilot study 1999 CHOP Goldwein et al., *Int J Radiat Oncol Biol Phys*

- **Posterior fossa boost** (total dose 5500cGy)
  - Volume reduction
Chemotherapy is important

- Medulloblastoma is chemo-sensitive
- Alkylators & platinum
  - Single agents
    - Cisplatin
    - Cyclophosphamide
  - Combinations
    - Cisplatin / etoposide
    - Cyclophos / vincristine
Standard Therapy


- Maximal surgery, then...
  - **Standard-risk** (>3yo: <1.5cm² residual AND M0)
    - 2400cGy CSI + posterior fossa boost
    - Adjuvant chemotherapy
    - Clinical trial goals to lower CSI (1800cGy)
    - 80% 5yr OS
  - **High-risk** (>3yo: >1.5cm² residual OR M1-M4)
    - 3600cGy CSI + posterior fossa boost
    - Adjuvant chemotherapy
    - Clinical trial goals to improve survival
    - 60% 5yr OS
  - **Infant-risk** (age <3y)...

Doernbecher Children’s Hospital
A division of Oregon Health & Science University
Medulloblastoma in “Infants”

- Sequelae of craniospinal radiotherapy unacceptable
- Modest success with conventional chemotherapy alone
  - 1993: Baby POG I
    Duffner et al., *N Engl J Med* → 5y PFS 32%
  - 1994: CCG
    Geyer et al., *J Clin Oncol* → 3y PFS 22%
  - 1999: CCG 921
    Zeltzer et al., *J Clin Oncol* → 5y PFS 32%
Treatment approaches in infants

• High-dose chemotherapy with stem-cell rescue (autologous "transplant")
  – Also used in high-risk and relapsed settings

• Focal radiation

• Intrathecal therapy
Ependymoma

• First described in 1924
  – Percival Bailey, MD

• Clinical Presentation
  – Majority intracranial
    • Peak age 0 – 4 years
  – Increased ICP
  – Localizing Signs/Symptoms
  – Duration 1 – 2 months
Ependymoma: MRI findings
Complete resection is critical

• Prognosis
  – Complete resection (~50%)
    • Overall survival: 75%
    • Progression-free: 50 – 75%
  – Sub-total resection
    • Overall survival: 20 – 50%
    • Progression-free: 0 – 25%

• Role for radiation therapy
• Limited role for chemotherapy
Posterior Fossa Tumors

- Signs / symptoms
  - Increased intracranial pressure
  - Localizing signs
- Pilocytic astrocytoma
  - cured with complete resection
- Medulloblastoma
  - requires all 3 modalities of treatment
- Ependymoma
  - prognosis dependent on extent of resection
Neurofibromatosis Type I

Table 2 - Diagnostic criteria for Neurofibromatosis type 1 (NF1) established by the National Institutes of Health Consensus Development Conference (1988)\textsuperscript{15}

Individual is affected with NF1 if two or more of the following conditions are met:

- Six or more café au lait macules over 5 mm in greatest diameter in pre-pubertal individuals and over 15 mm in greatest diameter in post-pubertal individuals.
- Two or more neurofibromas of any type, or one plexiform neurofibroma.
- Freckling in the axillary or inguinal regions.
- Optic glioma.
- Two or more Lisch nodules (iris hamartomas).
- A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex, with or without pseudoarthrosis.
- A first-degree relative with NF1 by the above criteria.
Neurofibromatosis Type I

- Up to 20% develop intracranial tumors
- Typically low-grade
- Optic nerve most common
- Can spontaneously resolve
- Treat only those with progressive symptoms
- Screen with ophtho exam
- No screening MRIs please 😊
Cases to remember

• Father noted that cranial sutures of this 3yo boy had re-opened

• Review of systems
  – Progressive increase in head size
  – Running into walls

• Choroid plexus carcinoma
Cases to remember

- 4-day history:
  3yo child tilting his head way back when playing video games

- Pineal region
- Immature teratoma
Cases to remember

• 9yo with “few days” of double vision and eyes deviated down

• PRECOCIOUS PUBERTY
  – Tanner IV hair
  – Deep voice
  – Testosterone 900!

• Pineal region
• Malignant germ cell tumor
Cases to remember

• Vision problems first noted @ 4 mo

• At 2.5yrs, visit to optometrist for glasses, referred immediately to ophtho

• Difficult exam due to NYSTAGMUS

• MRI done at 5yo

• **Extensive low-grade astrocytoma**
Cases to remember

• **Pre-natal detection of hydrocephalus**
  – Neurosurgery consult
  – Suspected aqueductal stenosis
  – Induced at 36wks for shunt placement

• **Well-appearing infant with normal exam**
  – Head circumference 34cm
  – Fontanel soft/flat
  – Face symmetric
  – Moved extremities equally, normal tone
Cases to remember

- **Atypical teratoid/rhabdoid tumor (AT/RT)**
Cases to remember

• The common story
  – 2 - 4wk history
  – Suspected common illness with vomiting +/- headaches
  – PROGRESSION instead of resolution
  – New localizing finding
    • Eye movements
    • Ataxia

• Medulloblastoma
Cases to remember

- 11yo male with 6-month history of headaches
- Gradually worsening
  - Increase in frequency & severity over several weeks
- Ataxia noted on exam

• **Pilocytic astrocytoma**
Cases to remember

- Healthy 15yo with 8-month history of intermittent left hip pain, exacerbated by jarring
- No limitation of activity
- “X-rays & CT” normal
- Physical therapist noted left leg weakness, inability to flex or extend ankle, difficulty standing on left foot

- Ependymoma
Best references


