Pediatric Brain Tumors: Current Concepts

Nalin Gupta
Division of Pediatric Neurosurgery
Departments of Neurosurgery and Pediatrics
University of California San Francisco

Introduction
• Brain and spinal cord tumors are the second most common malignancy in children
• Outcome is often dependent on several factors
  **Degree of resection**
  Location. Benign tumors in critical locations are often unresectable
  Histological grade

Epidemiology
• Uncommon. Incidence is 2-5/100,000 ~3000 new cases in the US annually
  • No sex predominance, although variations exist between histological types
  • Metastatic lesions are very rare

Clinical Features
• Children have different patterns of clinical presentations; often a function of location
  I Posterior fossa tumors
  II Low grade hemispheric tumors
  III Sellar region

I - Posterior Fossa
• Signs and Symptoms
  Headache (morning)
  Nausea
  Projectile vomiting
  Drowsiness and lethargy
  Diplopia
  Ataxia
  Papilledema

POSTERIOR FOSSA SYNDROME
Epidemiology

- Distribution varies between different cranial compartments
  - supratentorial 54%
  - infratentorial 41%
  - spinal 5%

Posterior Fossa Tumors

- PNET (medulloblastoma) 25-30%
- Cerebellar astrocytoma (JPA) 25%
- Ependymoma 15%

Cerebellar Astrocytoma (JPA)

- Peak incidence is between 6-8 yrs of age
- No sex predilection
- Headache is the presenting symptom in ~90% of cases; vomiting in ~80%
- Histologically benign
- Gross surgical resection is curative

Surgical Principles

Gross Total Resection
Pre-op surgical considerations
  a) symmetric vs. asymmetric
  b) cystic vs mainly solid
  c) relationship to vermis (rostral to caudal)
  d) relationship to 4th ventricle

Craniotomy
  - two burr holes either side of midline and two at foramen magnum
  - superior edge at inferior edge of transverse sinus (extend craniectomy above)
  - width: at least 4 cm

Drain the cyst early
Maintain the boundary!
If the cyst wall is substantial, resect
Preserve the vermis
Other Considerations

Fourth ventricle
Non-enhancing cyst wall
Differential diagnosis
  PNET
  ganglioglioma
  ependymoma
  hamartoma

Complications

Vermian injury (mutism)
New neurological signs in up to 40%
CSF leak
Hydrocephalus
Brainstem injury

* Residual tumor

Residual Disease

If resection is possible, re-operation warranted
If small residual, unresectable, close observation warranted

Similar strategy for recurrent disease

Grade II Astrocytomas

Infrequently in cerebellar location
(I: 85-90%; II: 10-15%; III-IV: <5%)
GTR preferred, only achieved in a minority of cases
Summary

- GTR is achievable in most cases
- Tailor surgical approach to anatomic location
- Treat Grade II astrocytomas like their supratentorial cousins

Medulloblastoma

- Belong to a group of neoplasms designated as primitive neuroectodermal tumors (PNET)
- Median age of diagnosis is 5-7 yrs
- 80% of tumors occur < 15 years of age
- Typically occur in the midline; can occur in the cerebral hemispheres

Medulloblastoma

- ‘Standard risk’ stage
  - <1.5 cm residual, >3 yrs of age, no spread
- Treatment
  - surgical resection
  - craniospinal radiation (2340 cGy to CSA with boost to 5340)
  - chemotherapy

Gross Total Resection

![Graph showing probability vs. years postoperatively with dotted and solid lines representing residual tumor sizes.](image)

Dotted line ≤ 1.5 cm$^2$; solid line > 1.5 cm$^2$ residual tumor


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**Ependymoma**

- Peak incidence between birth and 4 yrs
- Male:female :: 1.4:1
- Majority are histologically benign
- Locally invasive and difficult to resect entirely
- Controversies exist regarding role of adjunctive radiotherapy and/or chemotherapy

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**Brainstem Tumors**

- 5-10% of all brain tumors in children
- Clinical presentation:
  - ataxia, cranial nerve deficits, nausea and vomiting
- Diffuse brainstem tumors are malignant astrocytomas and are uniformly fatal (20% survival at 2 yrs)
- Adjunctive therapies are not effective
Brainstem tumors traditionally separated by location
Less 10% of all pediatric brain tumors
Location = pathology (but perhaps not always)
Technically challenging locations

### Location

<table>
<thead>
<tr>
<th>Location</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midbrain</td>
<td>Tectal Glioma</td>
</tr>
<tr>
<td>Pons</td>
<td>Diffuse infiltrative</td>
</tr>
<tr>
<td>Medulla</td>
<td>JPA</td>
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</table>

### Midbrain Location

Tectal lesions usually display an indolent profile
Tegmental lesions are usually JPA but can also resemble a thalamic profile
Patterns of growth are unpredictable and surgery may be required

### Technical Considerations

- Relationship to key structures; complication avoidance
- Anatomical corridor
- Working distance

### Case 1

6 y/o girl presenting with progressive left-sided weakness
Clumsiness, weakness of left side with upper motor neuron features. No cranial neuropathy
Management

Diagnosis?
Favor stereotactic biopsy to exclude the diagnosis of PNET

Comparison - OZ Approach

Pros
- OZ craniotomy
- Shorter reach
- Familiar anatomy

Cons
- Obstructing vessels and nerves
- Upward and downward reach is reduced

Management

Diagnosis?
Favor stereotactic biopsy to exclude the diagnosis of PNET

Biopsy > JPA

Comparison - Transcallosal

Transcallosal
- Long axis of tumor
- "Pure" anatomy
- Long reach
- Limits of large tumor difficult to reach
Case 2

3 y/o girl with progressive difficulty walking and right sided weakness
Case 3
11 y/o boy with progressive right-sided weakness
Stereotactic biopsy: grade II astrocytoma

Summary
High brainstem tumors are surgically accessible
Safe decompression is possible
Gross total resection is difficult with large tumors
Tools are suboptimal
II - Hemispheric Tumors

- **Signs and Symptoms**
  - seizures
  - headache, nausea, vomiting
  - focal weakness or hemiparesis
  - personality change
  - visual loss (common sign is papilledema)

Hemispheric Tumors

- 30% are low grade astrocytomas
  - incidence is 5/1 million children
- 30% are a conglomerate of low grade glial, neuronal, and mixed tumors
  - gangliogliomas, DNET
- 20% are malignant tumors (*PNET*)
- Other (*ependymomas*)

Hemispheric Astrocytoma

- Outcome determined by:
  - tumor histology, extent of resection, location
- 5 yr survival with subtotally resected low grade gliomas is 90%
  - low grade tumors may remain quiescent
- Controversies
  - adjuvant therapy (chemotherapy before radiotherapy)
  - treatment of epilepsy
  - radiotherapy modality

Hemispheric Astrocytoma

- Current approach
  - Deferral of radiation in children < 5 years

  Randomized study of chemotherapy (CCG-A9952)
  - Carboplatin/Vincristine vs.
  - 6TG/CCNU/Procarbazine/Vincristine

High Grade Glioma

- Graph showing progression of disease
III - Sellar Region

• Signs and Symptoms
  Visual change (field deficits, blindness)
  Endocrine abnormalities
  - growth failure
  - failure of secondary sexual maturity
  - hypothyroidism
  - diabetes insipidus
  - Drowsiness and lethargy
  - Papilledema

Sellar Region

• Optic pathway gliomas can be indolent and long term survival is common
• 65% occur in first 5 years of life
• Majority involve the chiasm and hypothalamus
• Strongly associated with NF1
• Excellent results reported with certain chemotherapy regimes

Surgical Adjuncts

Neuronavigation
  Greatly improved imaging

Functional Mapping and Imaging

Intraoperative monitoring
  - facial nerve, hypoglossal nerve
  - SSEP, MEP
Subcortical Motor Tractography

MRI with MRS grid

MR Spectroscopy

MRI with MRS grid

MRI with MRS Map

MRS Map

Brain Mapping - Subdural Grids

Brain Mapping

Brain Mapping
Molecular Features

<table>
<thead>
<tr>
<th>TUMOR TYPE</th>
<th>CHROMOSOMAL ALTERATIONS</th>
<th>IMPLICATED GENES</th>
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</thead>
<tbody>
<tr>
<td>Pilocytic astrocytoma</td>
<td>del 17q</td>
<td>NF1</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td>LOH 17p (GBM)</td>
<td>EGFR, PTEN, PTEN, CDK4, Rb, AGT, AMMR</td>
</tr>
<tr>
<td>Brainstem glioma</td>
<td>LOH 17p</td>
<td>p53</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>del 9p22</td>
<td>P16, CDK4, Rb, AGT, MMR</td>
</tr>
<tr>
<td>Atypical Teratoid/Rhabdoid</td>
<td>LOH 10p</td>
<td>p53</td>
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Summary

- Outcome is better than in adults (due to biology rather than treatment)
- Development of ‘rational’ therapeutics
- Cognitive outcome after treatment is a major concern
- Second malignancy rate - 11.3%