Pediatric Chiasmatic/Hypothalamic Gliomas: Understanding the Management Dilemma

Peter S. Amenta, MD
Department of Neurosurgery
Jefferson University Hospital
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The Presentation

- Case Presentations
- The Disease
- The Natural History
- The Literature
- Treatment
  - The Role of the Neurosurgeon
  - Chemotherapy and Radiation
- Case Discussion
- Study Design and Goals
Patient Presentation #1

- 8-year-old girl from Ghana with no past medical history presents to the CHOP emergency room via a charity medical organization

- Progressive blindness and proptosis of the left eye

- Referred to ophthalmology
  - Minimal light perception in left eye
  - Normal ophthalmologic exam in right eye
  - Normal visual fields in right eye

- MRI ordered
What to do?
Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
Patient Presentation #2

- 9-month-old healthy male with no past medical history

- Patient presents to general pediatrician after father notices “shaking” right eye for five days

- Referred to ophthalmology
  - Horizontal nystagmus noted in right eye
  - Otherwise normal ophthalmologic exam
  - CT ordered

- Presents to the CHOP emergency room
Head CT on Presentation
What to do?

Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
Patient Presentation #3

- 5-year-old female with no past medical history presents to an outside ophthalmologist after parents complained that the patient was walking into walls for several months.

- Patient complained that she was unable to see animals at the zoo.

- Visual acuity
  - OD 20/100
  - OS 20/125

- Fundoscopic exam: Optic atrophy
What to do?

Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
Traditionally, all three patients would be characterized as having “optic pathway gliomas” …
What I intend to show . . .

1. These tumors are different disease processes

2. Low-grade gliomas of the optic chiasm/hypothalamus are a unique and distinct disease entity

3. What we need to do as neurosurgeons
   - To deconstruct the literature
   - Define the disease and its actual prognosis
   - Establish a multidisciplinary treatment plan
The Patients
Symptoms at Presentation

- Visual disturbances (29%)
- Headache (23%)
- Failure to thrive (20%)
  - Diencephalic syndrome
- Nausea and vomiting (14%)
- Abnormal eye movement (14%)
- Symptoms of endocrine dysfunction (14%)
Clinical Signs at Presentation

- Decreased visual acuity (33%)
- Visual field deficit (33%)
- Optic atrophy (21%)
- Abnormal extraocular muscle exam (21%)
- Signs of endocrine abnormalities (21%)
- Ataxia (12%)
- Papilledema (9%)
Diencephalic Syndrome

- Emaciation
  - Multiple authors note complete absence of subcutaneous fat
  - Multiple theories as to underlying mechanism, but none have been proven

- Overactivity and pleasantness
  - Escalating to euphoria

- Initial growth acceleration

- Autonomic disturbance
  - Skin pallor, erratic temperature control, diaphoresis, heat intolerance

The Disease
Epidemiology

- 75% of optic pathway tumors occur in patients <12 years of age
  - 60% of these tumors involve the chiasm and hypothalamus

- OCHGs compose 2-5% of pediatric intracranial tumors\(^1\)
  - 65% occur in the first five years of life

- Anterior lesions (20-40%)
  - Involve the chiasm with or without the optic nerves

- Posterior lesions (33-60%)
  - Involve the chiasm and hypothalamus with or without the optic tracts\(^3\)
Imaging Characteristics

- **General characteristics**
  - Solid, cystic, or combination
  - Classically described as globular/exophytic suprasellar mass

- **CT**
  - Low-density to isodense
  - Intense enhancement with contrast

- **MRI**
  - T1: Low-intensity with marked gadolinium enhancement
  - T2: Hyperintense mass

- Found to grow postero-superiorly with invagination of the third ventricle

- With lateral progression, may involve the Circle of Willis
Histology: Low-grade Gliomas

- **Juvenile pilocytic astrocytomas (60%)**
  - WHO grade I circumscribed astrocytomas
  - Biphasic pattern
    - Rosenthal fibers
    - Loose-textured astrocytes and microcysts
    - Frequently not cystic in the optic pathway and medulla

- **Fibrillary astrocytomas (40%)**
  - WHO grade II diffuse astrocytomas
  - Well-differentiated
  - Hypercellularity and nuclear atypia
  - Expand the white matter
  - May undergo malignant transformation
Verhoeff defines three histologically distinct categories of pilocytic astrocytomas:

- **Coarsely Reticulated**
- **Finely Reticulated**
  - Can be confused with Grade II astrocytomas
- **Coarsely Fibrillated**
  - Most common variant of adult pilocytic astrocytomas

**Histology: Low-grade Gliomas**
## Histology of Tumors Found at the Hypothalamus and Optic Chiasm Arranged by Study

<table>
<thead>
<tr>
<th>Study by Author</th>
<th>Number of Patients</th>
<th>Pilocytic Astrocytoma</th>
<th>Fibrillary Astrocytoma</th>
<th>Ganglioglioma</th>
<th>Low Grade Astrocytomas (NOS)</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahn '06</td>
<td>33</td>
<td>19</td>
<td></td>
<td></td>
<td>14</td>
<td></td>
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<tr>
<td>Cappelli '98</td>
<td>27</td>
<td>16</td>
<td></td>
<td></td>
<td>8</td>
<td>3</td>
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<tr>
<td>Chamberlain '95</td>
<td>8</td>
<td>3</td>
<td></td>
<td></td>
<td>5</td>
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<tr>
<td>Guillamo '03</td>
<td>8</td>
<td>5</td>
<td></td>
<td></td>
<td>3</td>
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<tr>
<td>Hoffman '93</td>
<td>43</td>
<td>25</td>
<td>17</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>Horwich '85</td>
<td>16</td>
<td>12</td>
<td>4</td>
<td></td>
<td></td>
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<tr>
<td>Laithier '03</td>
<td>50</td>
<td>38</td>
<td>6</td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Suarez '06</td>
<td>14</td>
<td>13</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sutton '95</td>
<td>32</td>
<td>13</td>
<td>11</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Tow '03</td>
<td>25</td>
<td>21</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wisoff '90</td>
<td>16</td>
<td>2</td>
<td>1</td>
<td>10</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Wright '89</td>
<td>14</td>
<td>11</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>286</td>
<td>178 (62%)</td>
<td>54 (19%)</td>
<td>3 (1%)</td>
<td>45 (16%)</td>
<td>6 (2%)</td>
</tr>
</tbody>
</table>
Coronal brain slice through the hypothalamus. A large soft tissue mass is shown expanding the hypothalamus. Histology exhibited juvenile pilocytic astrocytoma. (Images courtesy of Roy H. Rhodes, MD, PhD. Robert Wood Johnson University Hospital. Department of Pathology.)
Histology: Juvenile Pilocytic Astrocytoma

Images courtesy of Roy H. Rhodes, MD, PhD. Robert Wood Johnson University Hospital. Department of Pathology.
OCHGs and Dissemination

- 5% rate of CNS dissemination in 150 patients with low-grade gliomas
  - 50% of these patients had OCHGs

- When compared to low-grade gliomas in other locations
  - Estimated 20-fold increased risk of developing multicentric spread with OCHGs
  - Prevailing theory
    - Invagination of the floor of the third ventricle eventually breaches the ependymal lining
    - CSF dissemination
T1-weighted MRI with gadolinium demonstrating multiple areas of metastatic disease
OCHGs and Neurofibromatosis type 1

- Associated with neurofibromatosis type 1 (NF-1)
  - 14-40% of NF-1 patients will develop OCHGs

- Vast majority of tumors arise prior to six years of age

- Traditionally
  - Tumors associated with NF-1 are considered to behave less aggressively
  - Higher incidence of spontaneous regression

- NF-1 not necessarily protective

Possible Signs of Neurofibromatosis

- Optic Glioma (tumor of the visual nerve)
- Lisch nodules (benign freckles in the iris)
- Cafe-au-lait spots (similar to tan birthmarks and may occur anywhere)
- Spinal cord tumors
- Scoliosis of the spine (abnormal curvature)

Educational Challenges
- Learning difficulties
- Speech difficulties
- Development delay

Psychological Challenge
- Emotional adjustment
- Impact on family
- Uncertainty

While it is unlikely that any one person diagnosed with NF will experience all of these symptoms, it is difficult to predict the severity or progression of the disorder in any individual case.
Natural History
Natural History

- Natural history of OCHGs is erratic and highly variable

- Debate in the literature
  - Congenital, non-neoplastic, self-limiting, hamartomatous lesions
  - Progressive, prone to recurrence, associated with significant morbidity and mortality

- Ambiguity and inconsistency in the literature
  - Failure to classify tumors with a consistent/reproducible system
The existing literature is derived from a wide range of sources:

- NF-1 clinics predominately see indolent tumors
- Neuro-oncologists and radiation oncologists see mostly those children with progressive disease
- Neuro-ophthalmologists primarily see intra-orbital optic nerve tumors
- Neurosurgeons
  - Typically, patients present to neurosurgical service following the first diagnostic CT or MRI
  - Broad spectrum of disease prior to the evolution of the natural course
Problems in the Literature: The Importance of Anatomic Location

- Tumors grouped together regardless of anatomic location
  - Tumors of the optic apparatus
  - Optic pathway gliomas

- Survival in relation to involvement of the chiasm
  - Gliomas confined to the optic nerve are amenable to complete resection with limited morbidity and mortality
  - Low-grade gliomas confined to the optic nerve
    - 85% long-term survival
  - Low-grade gliomas involving the optic chiasm
    - 44% long-term survival

Rush et al
Problems in the Literature: The Importance of Anatomic Location

Survival at 5 and 10 Years in Patients with Low-Grade Optic Pathway Gliomas Initially Treated With Radical Resection

<table>
<thead>
<tr>
<th>Tumor Location</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 years</td>
</tr>
<tr>
<td>Type I (Retrobulbar-prechiasmatic lesions)</td>
<td>100%</td>
</tr>
<tr>
<td>Type II (Optic tract lesions)</td>
<td>75%</td>
</tr>
<tr>
<td>Type IIIa (Chiasmatic lesions)</td>
<td>87.5%</td>
</tr>
<tr>
<td>Type IIIb (Chiasmatic-hypothalamic lesions)</td>
<td>22.2%</td>
</tr>
</tbody>
</table>
The Dodge Classification Systems for Optic Pathway Gliomas

- The DC breaks down tumors into pre-chiasmatic, chiasmatic, and post-chiasmatic

- The MDC provides a more detailed anatomical description based on the images obtained by modern-day MRI.
  - Not currently in widespread usage

Problems in the Literature: The Importance of Histology

- Tumors grouped together regardless of histology
  - Outcomes in low and high-grade astrocytomas compared within the same studies

- Multiple studies include tumors in which no histologic diagnosis was confirmed
  - Diagnosis made by imaging characteristics alone

- Majority of studies include sporadic and NF-1 tumors together
  - Is there a difference in the natural history?
  - Tumors associated with NF-1 are considered to behave less aggressively
    - But, are we diagnosing these tumors at an earlier stage secondary to screening?
Surgical Intervention
Hoyt and Baghdassarian (1969): Setting the Surgical “Standard”

- 36 patients with presumed optic pathway gliomas
  - Histologic verification in only 21 of the 36
  - Remainder of diagnoses based on tomographic pneumoencephalography and clinical presentation
  - Tumors located at multiple points along optic pathway
  - Includes both adult and pediatric tumors
Hoyt and Baghdassarian: Conclusions

- Optic gliomas are “congenital, non-neoplastic, hamartomatous, and self-limiting”

- Neuroradiological imaging permits accurate diagnosis, eliminating the need for histological diagnosis

- Neither transcranial operations or radiation prolong life

- Neurosurgical intervention limited to:
  - Recurrent increases in intracranial pressure
  - The relief of severe proptosis in a blind eye

- Partial resection is “no sin”
Why discuss this paper?

- Repeatedly referenced throughout the literature
- Describes the fundamentals of the primary treatment algorithm over the next two to three decades
- Not until the early 1980s do we see literature that challenges this study

- All patients underwent tumor biopsy via pterional or transcallosal approach
  - If low-grade astrocytoma, then limited resection and decompression of the ventricular system and/or chiasm
  - No attempt at gross total resection

- Younger children
  - Actinomycin D and vincristine

- Older children
  - Radiation

- At time of progression
  - Treated with modality not yet utilized
  - Radical resection if progression despite chemotherapy and radiation

Sutton, et al
Toronto’s The Hospital for Sick Children 1976-1991

- Retrospective analysis of 88 children with biopsy-proven low-grade astrocytomas

- Tumor resection of 50% or more
  - Recurrence rate of 24% (versus 42.9% for < 50% resection)
  - All patients with greater than a 50% resection survived

- Conclusion
  - Resection should be considered in all patients at the time of presentation and recurrence
The Early 1990s

- A shift to more aggressive attempts at resection
  - Improvement in modern imaging
  - Advancements in surgical technology

- Resection categories

<table>
<thead>
<tr>
<th>Resection Category</th>
<th>Percentage of Tumor Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>&lt; 25%</td>
</tr>
<tr>
<td>Partial Resection</td>
<td>25-50%</td>
</tr>
<tr>
<td>Subtotal Resection</td>
<td>50-99%</td>
</tr>
<tr>
<td>Total Resection</td>
<td>100%</td>
</tr>
</tbody>
</table>
Established Indications for Surgery

- All patients require a biopsy for histological diagnosis
- Tumor debulking for the treatment of obstructive hydrocephalus
- Significant tumor progression associated with worsening symptoms
Proponents of cytoreductive surgery
- Literature to support arrest of growth or regression after radical subtotal resection

Low grade astrocytomas in other anatomic locations
- Cerebellum: GTR → PFS approaches 100%
- Supratentorial: GTR → PFS 50-95%

Optic Pathway Gliomas
- Radical Resection → prolonged PFS in ~ 2/3 of patients (Hoffman ‘93, Wisoff ‘90)
Radical Resection

- But, what about the risks?
  - Further compromise in vision, endocrine dysfunction, stroke
  - Are the surgical risks acceptable considering the true natural history has never been defined?

- Advances in chemotherapy and radiation
  - Are the available adjuvant therapies effective enough to justify limited resection and medical therapy?
Chemotherapy and Radiation
Chemotherapy

- Attempt to delay or eliminate need for radiation
- Trial results difficult to compare due to variability in:
  - Indication to begin treatment
  - Classification of response to treatment
  - Evaluation of time to response
- Multiple small studies of single agents in recurrent OCHGs
  - Show limited rates of tumor regression
  - Higher rates of disease stabilization
  - Etoposide (VP16) as example
    - 27% regression rate
    - 54% disease stabilization
Chemotherapy

- Front-Line: Vincristine and Carboplatin
  - Highest progression free survival
  - Well-tolerated

- Problems with chemotherapeutic regimens
  - Carboplatin allergy
  - Concerns for leukemia with multiple agents
    - Lomustine (CCNU), Procarbazine, Cyclophosphamide, or Etoposide
  - High frequency hearing loss with CPPD

Lafay-Cousin et al., Cancer 2008;112:892
## Larger Multi-Agent Studies

<table>
<thead>
<tr>
<th>Drugs (Author)</th>
<th>N</th>
<th>CR+PR</th>
<th>Dz Stable Rate</th>
<th>PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCR/AMD (Packer ‘88)</td>
<td>24 OPG</td>
<td>12.5%</td>
<td>96%</td>
<td>50% (3yr)</td>
</tr>
<tr>
<td>VCR/Carbo (Packer ‘97)</td>
<td>78 LGG, 58 OPG</td>
<td>33.3%</td>
<td>94%</td>
<td>68% (3yr)</td>
</tr>
<tr>
<td>TPCDV (Prados ‘97)</td>
<td>42 LGG, 33 OPG</td>
<td>36%</td>
<td>96%</td>
<td>45% (3yr)</td>
</tr>
<tr>
<td>CPPD/VP (Massamino ‘02)</td>
<td>34 LGG, 29 OPG</td>
<td>35%</td>
<td>100%</td>
<td>73% (3yr)</td>
</tr>
<tr>
<td>Proc/Carbo, VP/CPPD, Vcr/Cpm (Laithier ‘03)</td>
<td>85 OPG</td>
<td>42%</td>
<td>87%</td>
<td>52% (3yr), 34% (5yr)</td>
</tr>
<tr>
<td>VCR/Carbo (SIOP-LGG1)</td>
<td>204 LGG, 61 OPG</td>
<td>50%</td>
<td>84%</td>
<td>48% (5yr), 39% OPG</td>
</tr>
<tr>
<td>VCR/Carbo (COG, Ater ‘06)</td>
<td>130 OPG +NF1</td>
<td>66%</td>
<td>5yr</td>
<td></td>
</tr>
</tbody>
</table>

VP = Etoposide/ Carbo = Carboplatin/ VCR = Vincristine/ TPCDV = 6-Thioguanine, Procarbazine, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), Vincristine (TPCV)/ CPPD = Cyclophosphamide/ AMD = AMD 3100
Recent Chemotherapeutic Protocols

- **Temozolomide (Temodar)**
  - Gururangan ’07: N=30, 54% disease stabilization, 5yr PFS = 30%
  - Nicholson ’07: N=21, 57% disease stabilization

- **Vinblastine**
  - N=51, 24% partial response or complete remission, 74% disease stabilization (34/46)
  - Some with initial minor progression, then response

Lafay-Cousin et al., Cancer 2005;103:2636
Future Potential Regimens

- **Target angiogenesis**
  - Vascular prolif in PA, increased VEGF
  - Avastin/CPT11
    - Adult Phase II in Recurrent HGG: 63% resp rate
    - Open trial for HGG in PBTC
    - Packer et al.: 10 Recurrent LGG. 1CR, 5 PR
    - Thalidomide, Celebrex, Fenofibrate, Oral VP16

- **Target molecular abnormalities**
  - Activity in H-ras mutants not K-ras defective pathways (more common in NF1)
  - mTOR inhibitor - RAD001
  - Multi-institutional trial for Rec-LGG in non-NF1 pts
  - NF consortium considering for Rec-OPG

- CXCR4 G-protein coupled receptor pathway inhibitors – AMD3100, Rolipram (increases cAMP)
Toronto’s The Hospital for Sick Children 1976-1991: Radiotherapy

- Data is unclear
  - Radiation used for surgically challenging tumors, tumors in which lesser resection was achieved, and in larger tumors as adjuvant therapy

- Radiation did not necessarily prevent recurrence
  - 42.4% rate of recurrence with radiation as part of initial intervention
  - 34.5% rate of recurrence with surgery as only initial intervention

- Radiation therapy is associated with a significant morbidity
Radiotherapy

- **Significant toxicity**
  - Vision worse in 7-14%
  - Endocrine dysfunction: Panhypopituitarism, GH deficiency
  - Cerebrovascular Disease
    - Moya Moya in 3/5 (60%) NF+, 2/23 (9%) NF- (Kestle ’93)
    - Vascular disease in 11/37 (30%) NF+, 2/32 (6%) NF- (Grill ’99)

- **Secondary tumors**

- **Neurocognitive Deficits**
  - Cappelli ’98: 18/51 (35%), 12 with mental retardation, all had received radiation
  - Lacaze ’03: Mean IQ 19 points lower in the patients receiving radiation
  - Sutton ’95: N=33
    - 43% in special education (all received RT, mean age 5.7 yrs, only 3 > 6yo)
    - 57% in regular school (4 no RT) (12 RT, mean age 11yrs, 4 were 5-8yo)
<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Median F/U (yr)</th>
<th>TD (Gy)</th>
<th>Resp. (CR+PR)</th>
<th>PFS</th>
<th>VA Improved</th>
<th>VA Stable</th>
<th>VA Worse</th>
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</thead>
<tbody>
<tr>
<td>Horwich ‘85</td>
<td>29</td>
<td>10</td>
<td>45-50</td>
<td></td>
<td>90% (10yr)</td>
<td>43% (10)</td>
<td>48% (11)</td>
<td>9% (2)</td>
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<tr>
<td>Flickinger ‘88</td>
<td>25</td>
<td>10.2</td>
<td>38-56.9 (mean 47)</td>
<td>87% (5,10,15yr)</td>
<td>9% (2)</td>
<td>77% (17)</td>
<td>14% (3)</td>
<td></td>
</tr>
<tr>
<td>Pierce ‘90</td>
<td>24</td>
<td>6</td>
<td>45-56.6 (mean 54)</td>
<td>88% (6yr)</td>
<td>30% (7)</td>
<td>61% (14)</td>
<td>9% (2)</td>
<td></td>
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<tr>
<td>Bataini ‘91</td>
<td>57</td>
<td>7.5</td>
<td>40-60 (mean 52)</td>
<td>80% (10yr)</td>
<td>57% (25)</td>
<td>36% (16)</td>
<td>7% (3)</td>
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</tr>
<tr>
<td>Jenkin ‘93</td>
<td>38</td>
<td>50 (med)</td>
<td></td>
<td></td>
<td>73% (10yr)</td>
<td>13%</td>
<td></td>
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</tr>
<tr>
<td>Cappelli ‘98</td>
<td>54</td>
<td>7</td>
<td>45%</td>
<td></td>
<td>66% (10yr) (all 69)</td>
<td>33% (18)</td>
<td>54% (29)</td>
<td>13% (7)</td>
</tr>
<tr>
<td>Grabenbauer ‘00</td>
<td>25</td>
<td>9</td>
<td>45-60</td>
<td></td>
<td>69% (10yr)</td>
<td>36% (9)</td>
<td>52% (13)</td>
<td>12% (3)</td>
</tr>
</tbody>
</table>

- 45 - 60 Gy
- 10 yr PFS 65-90%
- Improvement in vision in 9-57%
Radiotherapy: Conclusions

- Radiation can be used as adjuvant therapy at the time of initial surgery if visual &/or motor function are compromised.

- Radiation can be used at the time of recurrence.
Radiotherapy: Recent Advances

- **Conformal**
- **Stereotactic**
- **Proton beam**

**Goals**
- May limit exposure to mesial temporal lobes
- Hypothalamus and vasculature probably still at risk
- Early response rates and PFS look similar

**Toxicity to be determined**

Debus et al., IJROBP 1999;44:243.
Saran et al., IJROBP 2002;53:43.
Marcus et al., IJROPB 2005;61:374.
Back to our three patients . . .
Patient #1

MRI on Presentation

What to do?

Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
- Orbitozygomatic craniotomy
- Intradural sectioning of optic nerve approximately 1 cm before the chiasm
- Sacrifice of ophthalmic artery
- Intra-orbital dissection of cranial nerves
- En bloc resection with clean margins
- Pathology: Juvenile pilocytic astrocytoma (WHO I)
Patient #2

MRI on Presentation

What to do?

Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
Operative/ Postoperative Course

- NF-1 work-up negative
- Right frontal craniotomy
  - Vessels encased in tumor
  - Multiple biopsies and tumor debulking
- Pathology: Grade II fibrillary astrocytoma
- Currently receiving weekly chemotherapy with vincristine and carboplatin (ten week course)
- Repeat MRI at twelve weeks
- Nystagmus resolving
Patient #3

MRI on Presentation

What to do?
Watch and repeat MRI?
Begin chemotherapy?
Stereotactic biopsy?
Open biopsy?
Limited resection?
Aggressive resection?
Operative/ Postoperative Course

- Orbitozygomatic craniotomy
- Infiltration of chiasm, encasement of vasculature
- Inferior, lateral, and posterior resection
- Frozen Section: Grade II Astrocytoma
- Final Pathology: Grade III Astrocytoma
- Severe intraoperative vasospasm with loss of global EEG on right hemisphere
Postoperative MRI
Enhanced with Gadolinium
Conclusions and The Study
Conclusions

- Low-grade OCHGs represent a distinct disease entity
  - A class of tumors defined by a specific anatomic location
    - Must be evaluated separately from other gliomas of the visual pathway (Cancer, Flickenger)
  - A class of tumors separate from those of a higher histological grade

- All patients require at least a biopsy for histological diagnosis
  - Associated with an extremely low morbidity and mortality rate

- The utility of radical surgical resection has yet to be proven in the literature
Conclusions

- **Adjuvant therapies**
  - **Chemotherapy**
    - Effective means of treatment while delaying radiation
    - Varying efficacy in the literature
    - New regimens actively being explored
  - **Radiotherapy**
    - Trends support stabilization/ possible improvement of vision and prevention of death secondary to tumor progression
    - Contraindicated in those children presenting under the age of 5 yo
The Proposed Study

- **Goal**
  - To define the extent of resection of OCHGs in children as an independent predictor of survival

- **Patient Population:** OCHGs seen by neurosurgery at CHOP between 1985-2005

- **Surgical Endpoints:** Extent of Resection, Complications

- **Functional Endpoints (Minimum follow up of three years):**
  - Progression free survival
  - Survival
  - Functional Vision
  - Endocrine Status
  - Neuropsychiatric parameters: Cognitive ability, Behavior, IQ
Independent Variables

- Pathology/ Histology
- Age at diagnosis: <1, 1-5, >5 yo
- Age at time of resection: <1, 1-5, >5 yo
- Extent of resection
- Prior chemotherapy or radiation
- Presentation with/ without existing endocrinopathy
- Visual status at presentation
Thank You

- Leslie N. Sutton, MD
  - Department of Neurosurgery
  - The Children’s Hospital of Philadelphia

- Phillip B. Storm, MD
  - Department of Neurosurgery
  - The Children’s Hospital of Philadelphia

- Jeffrey Greenfield, M.D., Ph.D.
  - Fellow, Department of Neurosurgery
  - The Children’s Hospital of Philadelphia

- Mike Fischer, M.D.
  - Department of Neuro-Oncology
  - The Children’s Hospital of Philadelphia