Aerospace Medical Certification

A Retrospective Review of Intracranial Neoplasms from 2006-2011

Presented to: Aerospace Medical Association Annual Scientific Meeting

By: Marvin Jackson, MD

Date: May 13, 2013
Disclosure Information

84th AsMA Annual Scientific Meeting

Marvin Jackson, MD MS

I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in my presentation.
Overview

FAA experience

Classification and grading

Dilemmas

Clinical experience and models

Emerging tools
<table>
<thead>
<tr>
<th>Disease/Condition</th>
<th>Class</th>
<th>Evaluation Data</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head Trauma associated with:</td>
<td>All</td>
<td>Submit all pertinent medical records, current status report, to include pre-hospital and emergency department records, operative reports, neurosurgical evaluation, name and dosage of medication(s) and side effects</td>
<td>Requires FAA Decision</td>
</tr>
<tr>
<td>Epidural or Subdural Hematoma;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal Neurologic Deficit;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed Skull Fracture;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unconsciousness or disorientation of more than 1 hour following injury</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig. 4.5  Survival from malignant CNS tumors in Victoria 1982–1991. Source: Victorian Cancer Registry 1993. Note: * = anaplastic or well differentiated; ** = presence of tumor ascertained on clinical and/or radiologic data only.
CRANIAL, DURAL & EXTRADURAL TUMORS
Cranial, Dural & Extradural Tumors

5 year retrospective review
53 tumors
Age range: 37-65 yr.
Lesion side: Left > Right
Duration of Symptoms: 1.35 yr

Histopathology

<table>
<thead>
<tr>
<th></th>
<th>Certification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Class</td>
</tr>
<tr>
<td>Meningioma</td>
<td>1</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>2</td>
</tr>
<tr>
<td>Varied locations</td>
<td>3</td>
</tr>
<tr>
<td>All supratentorial</td>
<td>Total</td>
</tr>
</tbody>
</table>
INTRADURAL TUMOR
Intradural Tumors

5 year retrospective review
33 intradural tumors
Gender: 30M, 3F
Median age at diagnosis: 32.8 yr.
  Issued: 35.4 yr.
  Denied: 30.7 yr.
Duration of symptoms: 4.85 yr.
  Issued: 3.77 yr.
  Denied: 5.75 yr.
Extremely varied pathology

<table>
<thead>
<tr>
<th>Certification</th>
<th>Issuance</th>
<th>Non-issuance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>19</td>
</tr>
</tbody>
</table>
Intradural Tumors: Neuropathology

**Intraparenchymal**
- Ganglioglioma
- Cavernoma
- Inflammatory lesion
- Venous Angioma

**Skull Base**
- Prolactinoma
- Pituitary apoplexy
- Vestibular Schwannoma
- Trigeminal Schwannoma

**Ventricular**
- Colloid Cyst
- Pinealoma/Pineocytoma
- Hemangioblastoma
- Ependymoma
<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Location</th>
<th>Denial Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade Glioma</td>
<td>Right posterior, medial thalamus</td>
<td>Seizures &gt; Trileptal</td>
</tr>
<tr>
<td>Germinoma</td>
<td>Pineal Region</td>
<td>Residual parinauds</td>
</tr>
<tr>
<td>Glioma, low grade, diffuse</td>
<td>Dorsal Pons</td>
<td>2 yr. wait post XRT</td>
</tr>
<tr>
<td>benign</td>
<td>3rd ventricle</td>
<td>Alcohol Dep, cyclothymia</td>
</tr>
<tr>
<td>Retention Cyst</td>
<td>Anterior temporal</td>
<td>Complex partial seizures</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>Left parietal-occipital</td>
<td>Lost to follow up</td>
</tr>
<tr>
<td>Neurodegenerative Cyst</td>
<td>Right Parietal</td>
<td>Seizures</td>
</tr>
<tr>
<td>Recurrent Anaplastic Oligodendroglioma, grade III</td>
<td>Left frontal</td>
<td>Seizure prophylaxis &gt; Trileptal</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>Right Frontal</td>
<td>FTP</td>
</tr>
<tr>
<td>Low grade Glioma</td>
<td>Tectum</td>
<td>FTP</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>Sella</td>
<td>Renal Stones</td>
</tr>
<tr>
<td></td>
<td>Failed to provide</td>
<td>FTP</td>
</tr>
<tr>
<td>Anaplastic Astrocytoma</td>
<td>Right Frontal</td>
<td>Cognitive deficit</td>
</tr>
<tr>
<td>DNET</td>
<td>Medial temporal</td>
<td>Absence Seizures</td>
</tr>
<tr>
<td>Glioma</td>
<td>Right Frontal</td>
<td>FTP</td>
</tr>
<tr>
<td>Ganglioglioma</td>
<td>Frontal</td>
<td>Seizures, ADD &gt; adderall</td>
</tr>
<tr>
<td>Metastatic Spindle Cell Carcinoma</td>
<td>Frontal</td>
<td>Seizure prophylaxis &gt; Keppra</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>Right Parietal</td>
<td>Poor Prognosis</td>
</tr>
<tr>
<td>Venous Angioma</td>
<td>Frontal</td>
<td>Ongoing Seizures</td>
</tr>
</tbody>
</table>
Dilemma

80% present with a single seizure

1-3rd decade

Intact neurological exam
## Low Grade Gliomas

### WHO Grade I
- Juvenile Pilocytic Astrocytoma
- Subependymal Giant Cell Astrocytoma
- Myxopapillary Ependymoma
- Subependymoma
- Dysembryoplastic Neuroepithelial Tumor
- Ganglioglioma
- Choroid Plexus Papilloma

### WHO Grade II
- Diffuse Astrocytoma
- Oligodendroglioma
- Oligoastrocytoma
- Pleomorphic astrocytoma
- Pilomyxoid Astrocytoma
- Ependymoma
- Central Neurocytoma

---

*World Health Organization*
Astrocytoma
  Diffuse Astrocytoma
  JPA
  SEGA
  PXA
  Pilomyxoid Astrocytoma

Oligodendrogliomas
  Oligodendroglioma

Mixed Gliomas
  Oligoastrocytoma

Glioma with Ependymal Differentiation
  Ependymoma
  Myxopapillary Ependymoma
  Subependymoma

Others
  DNET
  Ganglioglioma
  Choroid Plexus Papilloma
  Central Neurocytoma
# Low Grade Glioma: Survival

<table>
<thead>
<tr>
<th>Grade Level</th>
<th>Median Age at Diagnosis</th>
<th>2 yr. Survival (%)</th>
<th>5 yr. Survival (%)</th>
<th>10 yr. Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JPA Grade I</td>
<td>17</td>
<td>97</td>
<td>94</td>
<td>91</td>
</tr>
<tr>
<td>Astrocytoma Grade II</td>
<td>40</td>
<td>61</td>
<td>47</td>
<td>35</td>
</tr>
<tr>
<td>Oligodendrogloma Grade II</td>
<td>32</td>
<td>90</td>
<td>79</td>
<td>64</td>
</tr>
<tr>
<td>Mixed Glioma Grade II</td>
<td>35</td>
<td>75</td>
<td>57</td>
<td>46</td>
</tr>
</tbody>
</table>

2010 Central Brain Tumor Registry of the US
Low Grade Gliomas: Aeromedical Issues

- **80% present with seizures**
  - Kindling: 1 year of untreated seizures → multiple foci

- **Histologic Upgrading** (malignant transformation)
  - 50-75% of WHO grade I/II become grade III/IV
  - 7-8 years
  - Indolent Course?
    - Growth rate differences between transformers vs non-transformers

- **Routine MRI imaging can be misleading**
  - Sampling error on biopsy
  - MR-SPECT, DWI, (18)F-FET-PET → physiologic information
Low Grade Gliomas: Prognostic Scoring

Location relative to eloquent cortex

Karfosky Performance Scale ≤ 80

Age > 50

Tumor Size: 4cm or 65cm³
The Future: Biomarkers

Best indicators of Progression  Free  Survival
1p/19q loss of heterozygosity
IDH 1 & 2 mutations
Oligodendroglioma> mixed> astrocytoma
Extent of resection: Gross total > sub-total
Maximum tumor size < 4cm (UCSF)
5cm (Mayo Clinic)
6cm (Pigatelli)

<table>
<thead>
<tr>
<th>Finding</th>
<th>Astrocytoma, %</th>
<th>Oligoastrocytoma, %</th>
<th>Oligodendroglioma, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1p/19q Codeletion(^a)</td>
<td>7</td>
<td>45</td>
<td>69</td>
</tr>
<tr>
<td>p53 Mutation(^a)</td>
<td>53</td>
<td>44</td>
<td>13</td>
</tr>
<tr>
<td>MGMT hypermethylation(^a)</td>
<td>30–50</td>
<td>Data lacking</td>
<td>85</td>
</tr>
</tbody>
</table>

\(^a\) Please see the review by Schiff et al. [9] for a more comprehensive analysis of molecular findings

The FAA Response

Grade I/II issuance contingent upon:

- Genetic and Biomarker profile that is favorable
- Gross total resection
- Seizure free and weaned from anticonvulsants
- Normal neuropsychological evaluation following
  - Regional radiotherapy
  - Chemotherapy
    - Temozolamide
- Ten (10) year interval from the last intervention to certification
Thank You