Brain Tumours-Treatment options and outcomes

Mr. Yagnesh Vellore FRACS
Neurosurgeon and Spine Surgeon
WHO Classification

- Neuroepithelial tissue
- Cranial and paraspinal nerves
- Meninges
- Lymphomas and haematopoietic
- Germ cell
- Sellar region
- Metastatic
Primary brain tumours

• Incidence 24.6/100000 adults in US

• One third malignant

• Less in children but more malignant

• Ranked 19th in incidence for cancer in Australia, but 4th in person years lost to 75
### Adults (11/12)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supratentorial</td>
<td>80-85%</td>
</tr>
<tr>
<td>Gliomas</td>
<td>50%</td>
</tr>
<tr>
<td>Meningiomas</td>
<td>15%</td>
</tr>
<tr>
<td>Metastases</td>
<td>15%</td>
</tr>
<tr>
<td>Pituitary</td>
<td>8%</td>
</tr>
<tr>
<td>Acoustic neuroma</td>
<td>8%</td>
</tr>
</tbody>
</table>

### Children (1/12)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infratentorial</td>
<td>60%</td>
</tr>
<tr>
<td>Pilocytic astrocytomas</td>
<td>27%</td>
</tr>
<tr>
<td>Medulloblastomas</td>
<td>27%</td>
</tr>
<tr>
<td>Brain stem gliomas</td>
<td>28%</td>
</tr>
<tr>
<td>Ependymoma</td>
<td></td>
</tr>
</tbody>
</table>
Presentation

• Raised ICP
• Progressive neurological deficit e.g. motor weakness
• Headache
• Seizure
• Mental state change
• TIA like sx
• Endocrinopathies
Aetiology

- Familial syndromes eg NF 1 optic glioma
- Genetics eg. p53 loss in glioblastoma
- Radiation eg. meningioma, Glioblastoma
- Immunosuppression eg. Lymphoma
- Weak evidence: trauma & meningioma
- Unproven: power lines/mobile phones
Glioma

- Half of brain tumours are gliomas
- 2/3 are high grade astrocytomas (ie GBM)
- Types
  - Astrocytomas
  - Oligodendroglial tumours
  - Mixed gliomas
  - Ependymomal tumours
  - Choroid plexus tumours
  - Glial tumours of uncertain origin
Astrocytoma

- WHO grade I: Pilocytic astrocytoma
- WHO grade II: Diffuse astrocytoma
- WHO grade III: Anaplastic astrocytoma
- WHO grade IV: Glioblastoma multiforme
  - Diffusely infiltrating astrocytomas = WHO grade II, III & IV
Pilocytic astrocytoma

- Children, young adult
- 1/3 PCA have NF1
- Preferred sites:
  - Optic nerve
  - Chiasmal/hypothalamic
  - Thalamus/basal ganglia
  - Cerebellar hemisphere
  - Brainstem
  - Spinal cord
Pilocytic astrocytoma

- Occasionally seed the neuraxis
- Surgical cure if total removal
- Better prognosis: 10 yr survival 94%
- May recur later in life
- May undergo malignant degeneration?RTX
- RTX for inoperable recurrence
- Chemo preferred over RTX in children
Difusely infiltrating astrocytoma

• >60% primary brain tumours

• Adults

• Cerebral hemisphere
Diffusely infiltrating astrocytoma

Diffuse astrocytoma (DA)

Anaplastic astrocytoma (AA)

Glioblastoma (GBM)

Increasing degrees of malignancy
# Diffusely infiltrating astrocytoma

<table>
<thead>
<tr>
<th>WHO designation</th>
<th>DA</th>
<th>AA</th>
<th>GBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO grading</td>
<td>II</td>
<td>III</td>
<td>IV</td>
</tr>
<tr>
<td>Mean age</td>
<td>34</td>
<td>41</td>
<td>53</td>
</tr>
<tr>
<td>% of astrocytomas</td>
<td>10-15%</td>
<td>35-40%</td>
<td>50-60%</td>
</tr>
<tr>
<td>Incidence</td>
<td>1.4/million/yr</td>
<td></td>
<td>2-3/100,000/yr</td>
</tr>
<tr>
<td>Clinical</td>
<td>Seizures</td>
<td>Deficits</td>
<td>Increased ICP</td>
</tr>
<tr>
<td></td>
<td>Subtle deficits</td>
<td>Seizures</td>
<td>Deficits</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased ICP</td>
</tr>
<tr>
<td>Imaging</td>
<td>CT: low density</td>
<td>complex enhancement</td>
<td>ring enhancement</td>
</tr>
<tr>
<td>Median survival (optimal Rx)</td>
<td>7-10 years</td>
<td>3 years</td>
<td>12-14 months</td>
</tr>
</tbody>
</table>
LGG

- WHO 2 astrocytoma
- Oligodendroglioma
- Oligoastrocytoma
- 15% of all primary brain tumours
- Younger age
- Seizures in 80%
- Predilection for insula and supplementary motor area
Management of LGG

• Controversial
• Options:
  – Serial exams & imaging investigations
  – Surgery
    • Biopsy
    • Partial resection
    • Total resection
  – Radiotherapy (early vs late)
  – Chemotherapy
• Diffuse vs focal
• Extent of resection
• 1p19q status (oligo)
AA/GBM (HGG)

- Older age
- Mental state changes more common
- Poor prognosis
Treatment of HGG

• Issues:
  – Age (70)
  – Histology
  – Karnofsky score (70)
  – Location: deep/lobar
  – Patient’s wishes
  – Presenting features

• Good evidence for extent of resection

• Stupp protocol: concurrent temozolamide + RTX
Treatment (AA & GBM)

- Biopsy versus cytoreductive surgery
  - NOT cure
  - Aim: prolong quality survival

<table>
<thead>
<tr>
<th>Options</th>
<th>Median survival (months)</th>
</tr>
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<tbody>
<tr>
<td>Biopsy</td>
<td>3-4</td>
</tr>
<tr>
<td>Resection</td>
<td>6</td>
</tr>
<tr>
<td>Biopsy + RadioRx</td>
<td>6-8</td>
</tr>
<tr>
<td>Resection + RadioRx</td>
<td>9-10</td>
</tr>
<tr>
<td>Resection + RTx + chemo</td>
<td>15-18</td>
</tr>
</tbody>
</table>
Newer Technologies

• Functional MRI
• DTI fibre tracking
• 5-ALA assisted resection
Meningioma

- 14-19% primary brain tumour
- Extrinsic
- Origin: arachnoid cap cells
- Peak age 45
- F>M=1.8:1
- Excellent prognosis
Meningioma

- Mostly benign, slow growing (WHO grade I)

- Greater likelihood of recurrence and aggressive behaviour
  - Atypical meningioma (WHO grade II)
  - Anaplastic meningioma (WHO grade III)
Sites

- Convexity
- Parafalcine/parasagittal
- Olfactory groove
- Sphenoidal ridge
- Parasellar
- Optic sheath
- Tentorium cerebelli
- CPA
- Intraventricular
- Foramen magnum
- Spinal
CT/MRI

- Well-circumscribed, extrinsic, durally-based
- Homogenous enhancement
- Dural tail
- +/- oedema
- +/- hyperostosis
- +/- calcification
- Occa en-plaque
Management

• Surgery
  – Aim for complete removal of tumour and its dural origin
  – Simpson grading
  – Sinus involvement

• Radiotherapy:
  – Unhelpful
  – For grade III meningioma

• 5 year survival 92%
Pituitary adenoma

- 10% intracranial tumours
- Anterior lobe of pituitary gland
- Usually benign
- 20-40s
- M=F
- MEN
- Microadenoma, <1cm
- Macroadenoma, ≥ 1cm
Classification (Histology)

- **Histology**
  - Chromophobe, acidophil, basophil
- **Endocrine function**
  - Endocrine-active tumours
    - Prolactinoma
    - ACTH-secreting tumours
    - GH-secreting tumours
    - Thyrotropin-secreting tumours
    - Gonadotropin-secreting tumours
  - Endocrine-inactive tumours
    - Null-cell adenoma
    - Oncocytoma
    - others
Presentation

• Endocrinological disturbance: over or underproduction of hormones

• Mass effect (more common with non-functioning tumours):
  optic chiasm
  3rd ventricle (hydrocephalus)
  cavernous sinus (cranial nerves)

• Apoplexy

• CSF rhinorrhea

• Headache

• incidental
Clinical- Local mass effect

- Headache
- Visual field defects
  - Sup temp quadrant anopia
  - Bitemporal hemianopia
- Cavernous sinus compression
  - CNIII, IV, V1, V2, VI palsies
  - Proptosis, chemosis
  - ICA encasement
- Vertical extension
  - Hydrocephalus
  - Hypothalamic compression
- Inferior extension
  - CSF rhinorrhea
Evaluation: Hx & O/E

- Signs/symptoms of endocrine hyperfunction

**prolactin**: amenorrhea, nipple discharge, impotence

**thyroid**: heat intolerance, anxiety, palpitations

**GH**: acromegaly/gigantism

**cortisol**: hyperpigmentation, Cushing’s syndrome
Evaluation: Hx & O/E

- Endocrine deficits (in order of likelihood):
  
  **GH**: growth delay, metabolic syndrome

  **LH/FSH**: hypogonadism, amenorrhea, low libido, infertility

  **Thyroid**: myxedema, cold intolerance, weight gain

  **ACTH**: orthostatic hypotension, easy fatigability

  **DI**: almost never seen pre-operatively
Pituitary apoplexy

• Acute H/A
• Rapid progressive visual loss
• Extraocular nerve palsies
• Acute pituitary insufficiency
• Mx:
  – Steroid
  – Urgent decompression
Endocrine screening

- 8am cortisol & 24 hr urine free cortisol
- Free T4, TSH
- PRL
- FSH, LH, sex steroids
- IGF-1
- Fasting BSL
Imaging

- MRI
- CT (stereotaxis)
Treatment

- If prolactinoma, medical treatment with bromocriptine, cabergolide
- Operative approaches:
  - Transsphenoidal
  - Craniotomy
- (Radiotherapy)
When to operate: hormonally inactive macroadenomas

• Apoplexy: rapid visual/neurological deterioration: an emergency

• Tumours causing mass effect: visual field deficit / panhypopituitarism

• Tumours elevating chiasm even without signs/symptoms

• To obtain tissue in questionable cases

• Nelson’s syndrome (hyperpigmentation, raised ACTH, progression of pituitary tumour after bilateral adrenalectomies)
Outcomes

• Generally good, especially

• Endocrinological cure in 25% PRL and 20% GH tumours

• ACTH tumour: 85% cure for microadenomas

• Recurrence rate: 12%