An Introduction to Brain Tumours and Neuroanatomy

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Key Learning Objectives

• Be able to describe the common clinical presentations of intra-cranial tumours.

• Describe the most common primary brain tumours, their relevant neuroanatomy and their prognoses.

• List the common tumours (from outside the brain) which metastasise to the brain
Tumours affecting the CNS

• EXTRINSIC
  – Primary tumours arise from bone, meninges (dura), nerve.
  – May be metastatic from malignancy elsewhere

• INTRINSIC
  – Primary tumours arise from cells normally comprising the brain or spinal cord
CNS Neural Cell Types (gives rise to intrinsic CNS tumours)

- Neurons
- Glia
  - Astrocytes
  - Oligodendrocytes
In cancer, one brain cell becomes faulty (sufficient number of mutations) and grows out of control to produce a tumour.
Not as rare as you think.....

• Increasing incidence – 10 000 primary tumours per year in UK

• 5000 people per year die in the UK

• Second commonest group of tumours after leukaemias in children, leading cause of death

• Sixth commonest group of tumours in adult

• 10.7% of cancer deaths under 45yrs

• 13% of patients dying from cancer have CNS involvement
- Most common solid tumour in children

- Leukaemias 32%
- Brain & spinal tumours 30%
- Sympathetic nervous system 11%
- Soft-tissue sarcomas 10%
- Lymphomas 5%
- Bone tumours 4%
- Renal tumours 3%
- Carcinoma & melanoma 1%
- Hepatic tumours 1%
- Gonadal & germ cell tumours 1%
- Retinoblastoma 1%
- Other & unspecified 0%

(Cancer Research UK)
Figure 2.1: Average annual number of deaths in children previously diagnosed with cancer, 0-14 years, GB 1996-2005

- Brain & CNS tumours: 32%
- Leukaemias: 30%
- SNS tumours: 11%
- Soft tissue sarcomas: 9%
- Lymphomas: 5%
- Bone tumours: 5%
- Renal tumours: 4%
- Hepatic tumours: 1%
- Gonadal & germ cell tumours: 1%
- Carcinomas & Melanomas: 1%
- Retinoblastomas: 1%
- Other & unspecified cancers: 1%

Average number of cases per year
Overall 5-year survival for adult brain cancer is also poor.
But the general trend for all cancers is increased survival
Aetiology

- **Unknown despite considerable research effort**
- Links to mobile phone usage scientifically unproven as yet.
- Childhood Irradiation
- Genetic Factors
  - NF1 and NF2 genes, Von Hippel Lindau syndrome

Childhood brain cancer – a developmental biology disorder
Adult brain cancer – multi-step progression, acquisition of mutations
Fallacy of causation

“The most dangerous job in the United Kingdom is not, as expected, bomb disposal expert, steeplejack, or Formula One racing driver but.....

 ..........having a role in one of the United Kingdom's most well known soap operas.”

Death rates of characters in soap operas on British television: is a government health warning required? BMJ 1997
Clinical Symptoms - extrinsic

- Extrinsic tumours compress underlying brain or spinal cord – focal neurological signs

- Extrinsic brain tumours cause symptoms of raised intracranial pressure
Clinical Symptoms - intrinsic

- Infiltration of brain or spinal cord
- Focal neurology depending on site of involvement
- Intrinsic brain tumours cause brain swelling and lead to symptoms of raised intracranial pressure
Helping to diagnose childhood brain tumours earlier

**Babies**
- Persistent/recurrent vomiting
- Balance/co-ordination/walking problems
- Abnormal eye movements or suspected loss of vision
- Behaviour change, particularly lethargy
- Fits or seizures (not with a fever)
- Abnormal head position such as wry neck, head tilt or stiff neck
- Increasing head circumference (crossing centiles)

If your child has one of these, see your doctor, if two or more, ask for an 'urgent referral'.

**Children**
- Persistent/recurrent headache
- Persistent/recurrent vomiting
- Balance/co-ordination/walking problems
- Abnormal eye movements
- Blurred or double vision/loss of vision
- Behaviour change
- Fits or seizures
- Abnormal head position such as wry neck, head tilt or stiff neck

If your child has one of these, see your doctor, if two or more, ask for an 'urgent referral'.

**Teens**
- Persistent/recurrent headache
- Persistent/recurrent vomiting
- Balance/co-ordination/walking problems
- Abnormal eye movements
- Blurred or double vision/loss of vision
- Behaviour change
- Fits or seizures
- Delayed or arrested puberty

If you or your child has one of these, see your doctor, if two or more, ask for an 'urgent referral'.

https://www.headsmart.org.uk/
Clinical Presentation

- **Low grade tumours** – brain can accommodate growth and slow pressure rise, so more likely to present with seizures or focal neurology

- **High grade tumours** – brain struggles with rapid pressure rise; more likely to present with pressure symptoms
Common Brain Tumours

• Secondary = metastases

• Primary –
  • Astrocytoma / Glioma – High and low grade
  • Meningioma

• Rarer – Ependymoma, Medulloblastoma/PNET, Choroid Plexus tumours Pineal
Metastases

• The most common type of brain tumour

• Most likely to come from breast, lung, bone, melanoma or renal. Others can spread to the brain but rarely

• Can be single or multiple tumours

• Treatment options are palliation, surgery, stereotactic radiosurgery or whole brain radiotherapy
Metastases

~30% of brain tumours

Spherical masses often at grey-white junction or in cerebellum (hindbrain).

Often multiple

Lung  60%
Breast  15%
Kidney  10%

Untreated median survival is only 1-2 months.
Primary Brain Tumours

High Grade Astrocytoma
Low Grade Astrocytoma
Meningioma
Tumour nomenclature & WHO grading

- **Histogenesis** – what is the cell of origin

- **Malignancy grade** – pleomorphism, mitoses, microvascular proliferation, necrosis

- **Grade 1**: low grade – curative with surgery
- **Grade 2**: astrocytoma (low grade)
- **Grade 3**: anaplastic astrocytoma
- **Grade 4**: high grade – death within one year of diagnosis
# Histological grading of Astrocytomas

<table>
<thead>
<tr>
<th>Grade of Glioma</th>
<th>Name</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pilocytic Astrocytoma</td>
<td>Low proliferation, -children / young adults</td>
</tr>
<tr>
<td>2</td>
<td>Diffuse Astrocytoma</td>
<td>Low cellularity, minimal atypia – young adults</td>
</tr>
<tr>
<td>3</td>
<td>Anaplastic Astrocytoma</td>
<td>Anaplasia, mitotic activity – 30 to 60 years</td>
</tr>
<tr>
<td>4</td>
<td>Glioblastoma multiforme (GBM)</td>
<td>Microvascular proliferation, necrosis – 50-70 years</td>
</tr>
</tbody>
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No predictive biomarker for progression. Difficult to communicate to patient.
Low grade diffuse Astrocytoma (Grade 2)

Fig. 1.7 Age distribution of low-grade diffuse astrocytomas, based on biopsies of 190 patients treated at the University Hospital, Zurich.

May be long history, seizures, relatively well, younger age group
Anaplastic Astrocytoma (Grade 3)

May be more unwell, shorter history, slightly older. Some will have progressed from known Grade 2 tumour.
Malignant Glioma – Glioblastoma (Grade 4)

Usually short history (<3 months) especially of headache and personality change
Prognosis

Relative survival by WHO grade and tumour type for Brain tumours diagnosed 2005-2009 in residents of the East of England Region.

- Grade I cerebral meningioma Relative survival rate
- Grade I cerebral glioma Relative survival rate
- Grade II cerebral glioma Relative survival rate
- Grade III cerebral glioma Relative survival rate
- Grade IV cerebral glioma Relative survival rate

Percent relative survival

Time in months from diagnosis
Glioblastoma multiforme (GBM) prognosis remains dismal

GBM is a WHO Grade IV astrocytoma (glial).

Most prevalent and aggressive malignant brain tumour.

Incidence 2-3 per 100,00 in Europe/N.America.

Median survival
~ 14.6 months
Treatment - Glioblastoma

• Radical surgery & steroids (dexamethasone)

• Radiotherapy – 60Gy in 30 fractions

• Chemotherapy – Temozolomide (some patients respond)
History

Bennett AH, Godlee RJ

“Excision of a tumour from the brain”

Lancet 1884
Surgery for Brain Tumours

Nothing at all

Biopsy

Debulking

Macroscopic Resection

Resection with margins

Unfit, elderly, risky eloquent areas

Small deep lesions, eloquent areas

To control intra-cranial pressure symptoms from larger tumours, cytoreduction
Image Guidance - StealthStation

CT / MRI scans of patients uploaded to StealthStation.

Fix patient’s head and register position of head (Pixar technology)

Neurosurgeon can decide where to remove fragment of skull and where to locate tumour using real-time feedback.

PROBLEMS – brain size and position shifts leading to inaccuracies
Fluorescence (5ALA)- guided surgery
Improving diagnosis (MRI), treatment, prognostic markers, palliative care / survivorship, basic and translational science e.g. molecular biology
Genomic era (1972-2003)
Post-Genomics Era – will soon cost just £100 to sequence your genome!
Chemotherapy tailored to the sub-type of glioblastoma
No objective response in any phase II clinical trial
Cancer as a process of evolution – implications for therapy

Genetic Mutations

- Unique
- Shared
- Common
- Unique

[Image of a tree with genetic mutations labeled]
Thank you

Any questions?

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