Brain Tumors: Where do they come from?

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Topics

- Characteristics and distribution of brain tumors
- Risk factors for brain tumors
- Promising avenues of research
Estimated new cases of cancer in US, 2010

<table>
<thead>
<tr>
<th>Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>28%</td>
<td>28%</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>15%</td>
<td>14%</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney and renal pelvis</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity and pharynx</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>16%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Source: American Cancer Society, 2010
Brain tumors

- In 2010, the estimated number of new cases of brain tumors will be 22,020 (11,980 men and 10,040 women)
- Brain tumors represent ~ 1.3% of all cancers (adults and children)
- Metastatic brain tumors are most common and occur in 10-15% of people with cancer
- Primary brain tumors generally do not metastasize to other parts of the body
- Breast, lung and melanoma are most common cancers to metastasize to the brain
- Brain tumors in children are different from those in adults
Glioblastoma 21%
Astrocytomas 10%
Ependymomas 2%
Oligodendrogliomas 4%
Embryonal, including Medulloblastoma 2%
Meningioma 29%
Pituitary 6%
Nerve sheath 8%
Craniopharyngioma 1%
Lymphoma 3%
All other 14%

Gliomas account for 42% of all brain tumors and 77% of malignant brain tumors

Source: CBTRUS, 2005
Distribution of brain tumors by age & grade

- **Grade III gliomas**
  - 40-49 years old: 40%
  - More than 60 years old: 60%

- **Grade IV gliomas**
  - 10%

- **High grade tumors**
  - 90%

**Legend**
- Grade III gliomas
- Grade IV gliomas
Distribution of brain tumors by ethnic group

- Incidence rates are higher in Caucasian populations than in other ethnic groups
- These differences have also been observed in children

Source: American Cancer Society, 2005
Global distribution of brain cancer

- Incidence rates more elevated in industrialized countries (could be due to underreporting or ethnic differences in susceptibility)

- Men have higher incidence rates than women (independently of ethnic group)

Source: GLOBOCAN 2002 database
Risk factors of brain cancer

Epidemiologic studies of the effect of:

- Radiation
- Lifestyle
- Occupational and environmental exposures
- Genetic factors
A scientific process that attempts to link the effects of factors such as lifestyle or exposure to toxic chemicals to disease.
Limitations of epidemiologic studies

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Epidemiologic studies of brain tumors

Variation in:
- Study designs
- Population characteristics
- Information sources
- Measurement
- Classification

Reliance on proxy and historic information

Environmental exposures:
- Suspect agents can cross blood brain barrier
Established risk factors

- High dose radiation
- Hereditary syndromes
- Man vs. woman
- White vs. African-American
- Increasing age
- Epilepsy, seizures, convulsions  
  (probably an early symptom)
- Exogenous hormones  
  (for meningioma)
Ionizing radiation

Therapeutic X rays are only environmental factor unequivocally associated with an increased risk of brain tumors

- Several studies: increase risk of brain cancer in children who received radiation for leukemia
- Atomic bomb survivors: dose-related excess of nervous system tumors
Probable risk factors

- Family history of brain tumors
- Mutagen sensitivity
- Allergies/asthma/elevated IgE
- Chickenpox/
  anti-varicella zoster virus IgG
Allergy & immunological conditions

- Reduced glioma risk has been attributed to allergy and allergic conditions
- Reduced risk for people who reported a history of infectious disease (colds, influenza)

Suggests an influence of immunological factors on development of gliomas, but molecular basis has not been elucidated.
Probably not risk factors

- Dental x-rays
- Head injury
- Residential power frequency EMF
- Prior cancers
- Filtered cigarette smoking
- Alcohol consumption
Case reports on occurrence of gliomas after a head injury at the same site

Plausible association since trauma induces a strong proliferative astrogliosis

Studies have found a weak but inconsistent association with adult and perinatal traumatic head injury and brain tumors

Brain tumors may be a factor in development of falls and subsequent head injury
Too few studies

- Cellular telephone use
- Diagnostic radiation (CT)
- Dietary intake
  - Calcium (high vs. low)
  - Cured foods
  - Antioxidants
  - NSAIDs drugs
- Genetic susceptibility factors
Cell phones

- Operate at radio frequencies, a form of EM energy
- Widespread use is just two decades old
- Decreasing levels of non-ionizing radiation with time and these levels vary across cell phone types
Cell phone use

- Most early studies provide no evidence for association
- Positive association with malignant brain tumors in a study in Sweden
- Studies in US, Germany, France, and Japan, did not find associations with glioma, meningioma or acoustic neuroma
- INTERPHONE study in 13 European countries showed no increase in glioma or meningioma with use of cell phones
Genetic factors

- Different forms of genes involved in the metabolism of chemical carcinogens may be associated with higher susceptibility to glioma.

- A study found that glioblastoma patients with mutations in either of two genes, IDH1 or IDH2, had a longer survival than patients whose tumors lacked either mutation.

- Another study identified up to 31 genes that, when containing certain mutations, set the stage for the development of gliomas.

- A third study showed that one particular gene, the ANXA7 gene, may make a good target for future treatments for glioblastomas.
Family history

- Familial cancer syndromes associated with tumors of nervous system:
  - Li-Fraumeni syndrome
  - Neurofibromatosis 1
  - Turcot syndrome

- Family members of glioma patients may be more susceptible to glioma development than general population

- Recent study found twice the risk of brain tumors in people with immediate relatives who had glioblastomas and four times the risk in those with relatives with astrocytomas
Occupational exposure

Studies have shown associations with exposure to:

- Vinyl chloride (glioblastomas)
- Arsenic, mercury, and petroleum products in men (gliomas)
- Polycyclic aromatic hydrocarbons
- Lead (gliomas)
Promising research avenues:

- Role of immune function
- Genetic components in families
- Metabolic and DNA-repair pathways
- Neurocarcinogen exposures
- Genes responsible for etiology and progression of brain tumors

Brain Tumor Epidemiology Consortium - open scientific forum to foster development of multicenter, international and inter-disciplinary collaborations that will lead to better understanding of etiology, outcomes, and prevention of brain tumors.
An ounce of prevention is worth a pound of cure

"Antioxidants! Antioxidants!..."