Brain Tumor Learning Points

Second most common (20%) pediatric cancer (after Leukemia)

Most common solid tumor in children

Hereditary Neurocutaneous Syndromes:

a. NF-1
b. NF-2
c. Tuberous Sclerosis
a. Nevoid Basal Cell Carcinoma Syndrome

Hereditary Cancer Syndromes:

a. Von Hippel-Lindau Disease
b. Turcot's Syndrome
c. Li-Fraumeni Syndrome

	NF-1	NF-2
Prevalence	1:4000	1:50,000
Genetics	Chromosome 17, Autosomal dominant (50% New Mutations)	Chromosome 22, Autosomal dominant
Tumor	Neurofibromas, Café-au-lait spots	Acoustic Schwannomas, Meningiomas
Minor Tumors	Pilocytic Astrocytoma, Optic Nerve Glioma	Neurofibromas

Signs and Symptoms:

Headache
(Most common, least helpful; present at arising, relieved by vomiting, improved during the day).
Vomiting
(Frequently in the morning, relieves headache, no nausea or anorexia, hunger soon after).
Visual Difficulties
(Blurred vision common complaint in the young child; double vision common complaint in the older child; due to inability to deviate eye laterally-stretching/paresis of abducens).
Seizure
Neurological Deficit
Alteration in Consciousness
Academic Deterioration

Diagnostic Evaluation:

Either computed tomography (CT) or magnetic resonance imaging (MRI) should be performed with and without intravenous contrast. MRI is preferred since it provides superior resolution and multiplanar imaging capabilities. It avoids the “spray” artifact from the petrous ridge that may obscure CT images of the base of the brain. A repeat MRI should be done as soon as possible after surgery (within 72 hours) to evaluate residual disease. If not done within that period of time, it should be performed 2 weeks later. (When surgery related changes have stabilized).

For lesions with a high frequency of CSF dissemination, such as PNET, medulloblastoma, ependymoma and germ cell tumors, MRI of the whole spine should also be done. Lumbar CSF should be obtained in these tumors for cytology, and in germ cell tumors also for alpha-fetoprotein and beta-HCG. Because brain tumors rarely have disseminated extra-neurally at the time of diagnosis, a bone scan and a bone marrow biopsy are seldom indicated initially. (Unless required for a study). They are indicated for recurrent medulloblastoma.

A hearing test should be done in all patients with a brain tumor since either the tumor itself, or radiation therapy or some chemotherapeutic agents (like cisplatin and carboplatin) can cause hearing loss.

Diagnosis:

Histologic diagnosis is done on a resection or a biopsy specimen. When resection is not feasible, the neurosurgeon can do a stereotactic biopsy. Stereotactic biopsy is the precise (CT guided) introduction of a metal probe into the brain tumor and removal of a small piece of it.

Common Childhood Brain Tumors:

Low-grade astrocytoma 49%

Medulloblastoma 21%

High-grade glioma 15%

Ependymoma 9%

Germ Cell tumor 3%

Brainstem Glioma 3%

Grading of Astrocytoma

The grading of Astrocytoma is based on the specific combination of the following histological criteria: Nuclear atypia, mitotic activity, endothelial proliferation and necrosis. The more criteria present, the higher the grade.

GLIOMA	WHO GRADE
ASTROCYTOMA	
Pilocytic	I
Fibrillary	II
Anaplastic	III
Glioblastoma Multiforme	IV
OLIGODENDROGLIOMA	I
Anaplastic	II
EPENDYMOMA	I
Anaplastic	II

Treatment:

Surgery is the mainstay of treatment. Whenever possible the tumor should be removed or debulked surgically, either at diagnosis or after response to radiation or chemotherapy. Unfortunately, this is not possible in many cases because of the location of the tumor.

Radiation therapy involves aiming beams of x-rays or gamma rays at the tumor in exactly prescribed dose over a scheduled period of time. The radiation volume is calculated with the aid of a computer and using MRI and CT scan information. Conformal radiation therapy uses computers to create a 3-dimentional picture of the tumor so that multiple radiation beams can be shaped exactly (conform) to the contour of the treatment area. It spares normal tissue.

Radiosurgery is an even more precise technique. It uses a large number of narrow, highly focused beams of ionizing radiation. It can be given in one treatment using a high dose, or divided into daily fractions (so called fractionated radiosurgery). Radiosurgery is used for small tumors.

Because of the risks of radiotherapy to the developing brain there is a growing trend to defer radiation in young children (especially those below 3 years of age), by using chemotherapy as the initial treatment. In addition, on-going studies in older children with selected lesion, such as “standard risk” medulloblastoma and germinoma, use reduced doses of radiation in conjunction with chemotherapy to minimize radiation-induced neurotoxicity.

Chemotherapy can be given in conventional doses and schedules. It can also be given in high-dose with stem-cell support, either as an autologous stem cell transplant, or as consecutive high-dose chemotherapy with stem-cell support.

TYPE OF TUMOR	**5 YEAR SURVIVAL**
Medulloblastoma	
Local	90%
Metastatic	67%
Ependymoma	
Less than 3 years of age	22%
Older children	75%
Cerebelar Astrocytoma	
Pilocytic (resected)	90%-100%
Brain Stem Glioma	
Focal (midbrain, medulla)	
Completely resected	94%
Partially resected	52%
Cervicomedullary	70%
Diffuse (intrinsic, pontine)	< 20% 2 year survival

Late Effects

Many of the sequelae of treating childhood brain tumors manifest several years after diagnosis, which mandates long-term multidisciplinary follow-up.

Loss of IQ: Children younger than 7 years of age who receive whole brain radiation demonstrate progressive deterioration of intelligence. In one study the average loss of IQ was 27 points and all patients required special education.

Endocrine Deficiencies are extremely common in children who have been treated. Growth hormone deficiency is seen in the majority of children who have received whole brain radiation. Growth may also be stunted from irradiation of the spine. In addition patients may have thyroid and gonadal dysfunction.

Hearing Loss: Either the tumor itself, or radiation therapy or some chemotherapeutic agents (like cisplatin or carboplatin) can cause hearing loss, partial or complete.

Second malignancy is another concern in long term survivors. It ranges from 1% to 3% and may include secondary brain tumors (usually more malignant than the primary), sarcomas and hematological malignancies.

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