Astrocytic Brain Tumors in Pediatric Neuropathology
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UAB/COA TASK FORCE LECTURE

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OBJECTIVES

• Discuss the prevalence of astrocytomas in children.

• Review the World Health Organization’s classification system for astrocytomas as well as the gross, radiologic and histopathologic features of these tumors.

• Discuss the biology of astrocytic tumors and malignant glioma invasion.
Gliomas

- Normal glia includes astrocytes, oligodendrocytes and ependyma.

Gliomas are analogously designated as astrocytomas, oligodendrogliomas and ependymomas, respectively.
## WHO GRADING SYSTEM FOR ASTROCYTIC TUMORS

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<th>GRADE</th>
<th>NAME</th>
<th>HISTOLOGIC FEATURES</th>
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<td>PILOCYTIC ASTROCYTOMA, SEGA, PXA</td>
<td>VARIABLE HISTOLOGY, LOW PROLIFERATIVE POTENTIAL</td>
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<td>II</td>
<td>DIFFUSE ASTROCYTOMA</td>
<td>LOW CELLULARITY, MINIMAL NUCLEAR ATYPIA, LOW PROLIFERATIVE INDEX</td>
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<td>III</td>
<td>ANAPLASTIC ASTROCYTOMA</td>
<td>ANAPLASIA, INCREASED CELLULARITY, MITOTIC ACTIVITY</td>
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<td>GLIOBLASTOMA MULTIFORME</td>
<td>MICROVASCULAR PROLIFERATION, NECROSIS</td>
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Astrocytomas in children

- Astrocytomas account for the majority of pediatric brain tumors.
- About 700 children are diagnosed with low-grade astrocytomas each year.
- In children, more than 80 percent of astrocytomas are low-grade; nearly 20 percent are high-grade.
Clinical symptoms and tumor location

- The most common location is in the cerebellum. Patients with cerebellar tumors have symptoms that include headache, vomiting, and unsteadiness in walking.
- Tumors in the cerebral hemispheres commonly cause seizures; occasionally there is weakness of the arms and legs.
- Tumors in the hypothalamus often cause visual problems, while thalamic tumors cause headaches and arm or leg weakness.
Pilocytic astrocytoma

- Relatively circumscribed, slow growing
- Children and young adults
- WHO grade I
Pilocytic astrocytoma

• Most common glioma in children

• 5-6% of all gliomas (0.37/100,000)

• 67% arise in the cerebellum
Frozen section
Take home

• Well circumscribed slow growing tumor
• Cyst with enhancing mural nodule
• Biphasic histology
• Vascular proliferation, atypia, necrosis
• WHO grade I
Subependymal giant cell astrocytoma (SEGA)
WHO grade I

- Benign or hamartomatous astrocytic and partially neuronal intraventricular tumor (lateral or third ventricle near foramen of Monro)
- Less than 1% of primary intracranial tumors
- Children and young adults
- Almost exclusively in setting of TS.
Pleomorphic xanthoastrocytoma
WHO grade II

• Specialized variant of astrocytoma with reticulin deposition and pleomorphism incongruent with proliferative activity.
• Less than 1% intracranial tumors with a predilection for the temporal lobe.
• Mostly children and young adults.
• 15-20% undergo malignant transformation (grade III).
Stem cells and tumor differentiation

(a) Neural stem cell

- Mature glial cell
- Tumour stem cell
- Genetic change A (TP53 mut)
- Genetic change B (1p^-/19q^-)

- ? Micro environment
- Astrocytoma
- Oligodendroglioma

(b) Neural stem cell

- Mature astrocyte
- Tumour stem cell
- Genetic change A (TP53 mut)
- Genetic change B (1p^-/19q^-)

- ? Micro environment
- Astrocytoma
- Oligodendroglioma

Glioma progression

Activation of growth signaling pathways

Inactivation of cell cycle control pathways
Diffuse astrocytoma
WHO grade II

• Diffuse astrocytoma comprises 40% of primary intracranial tumors (4/100,000).
• All ages
• Borders are ill defined with tumor foci that are grossly invisible.
• Tumor epicenter most often white matter or deep gray matter.
Diffuse astrocytoma
WHO grade II
Malignant glioma invasion

- Perivascular spread
- Subpial growth
- Pial surface
- Neuron cell body
- Perineuronal satellitosis
- Spread along white matter tracts

Proteases: MMP2, MMP9, uPA, cathepsin B

ECM: tenascin, vitronectin, fibronectin

EGFR
FAK
Integrins
Single tumour cell
Axons
Cerebral cortex
White matter

Necrosis/hypoxia and angiogenesis

Upregulation of migration-associated genes

Take home for astrocytomas in children

• Astrocytomas account for the majority of pediatric brain tumors.

• In children, more than 80 percent of astrocytomas are low-grade; nearly 20 percent are high-grade.

• Pilocytic astrocytoma is the most common glioma in children.
Thank you.