Pediatric intracranial tumor classification

Pediatric intracranial tumors are classified based on their histological characteristics, molecular features, and location within the central nervous system (CNS). The **World Health Organization (WHO) Classification of CNS Tumors (5th edition, 2021)** provides a framework for understanding these tumors.

1. Classification by Histology and Molecular Features Pediatric brain tumors differ significantly from adult brain tumors in their genetic alterations, prognosis, and response to treatment. Below is an overview of major categories:

A. Embryonal Tumors Highly malignant tumors that arise from primitive neuroectodermal cells: - **Medulloblastoma** (most common malignant pediatric brain tumor)

1. **Molecular Subgroups**:
    1. WNT-activated (best prognosis)
    2. SHH-activated (TP53-wildtype or mutant)
    3. Group 3 (MYC amplification, poor prognosis)
    4. Group 4 (intermediate prognosis)

- **Atypical Teratoid/Rhabdoid Tumor (ATRT)**

1. **SMARCB1 (INI1) or SMARCA4 mutations**
2. Highly aggressive, poor prognosis

- **CNS Neuroblastoma, FOXR2-activated** - **CNS Ewing Sarcoma Family Tumors** - **CNS High-Grade Neuroepithelial Tumor (HGNET) with BCOR alteration** - **CNS High-Grade Neuroepithelial Tumor (HGNET) with MN1 alteration**

B. Gliomas - **Low-Grade Gliomas (LGGs)**

1. **Pilocytic Astrocytoma (WHO grade 1)**
    1. BRAF fusion or mutation (e.g., BRAF V600E)
2. **Diffuse Astrocytoma, MYB- or MYBL1-altered (WHO grade 1)**
3. **Pleomorphic Xanthoastrocytoma (PXA, WHO grade 2)**
    1. BRAF V600E mutation

- **High-Grade Gliomas (HGGs)**

1. **Diffuse Midline Glioma, H3 K27-altered**
    1. Poor prognosis, pontine location common (DIPG)
2. **Pediatric-type High-Grade Glioma, H3 G34-mutant**
3. **Pediatric-type High-Grade Glioma, IDH-wildtype and H3-wildtype**

C. Ependymomas - **Supratentorial Ependymoma, ZFTA fusion-positive** - **Supratentorial Ependymoma, YAP1 fusion-positive** - **Posterior Fossa Ependymoma (Group A and Group B)** - **Spinal Ependymomas, MYCN-amplified**

D. Germ Cell Tumors - **Germinoma (most common)** - **Mixed Germ Cell Tumors** - **Teratomas (mature, immature, or with malignant transformation)** - **Yolk Sac Tumor** - **Embryonal Carcinoma** - **Choriocarcinoma**

E. Choroid Plexus Tumors - **Choroid Plexus Papilloma (WHO grade 1)** - **Atypical Choroid Plexus Papilloma (WHO grade 2)** - **Choroid Plexus Carcinoma (WHO grade 3, TP53 mutations common)**

F. Meningeal Tumors - **Meningioma (rare in children, but aggressive subtypes exist)**

G. Craniopharyngiomas - **Adamantinomatous Craniopharyngioma** (CTNNB1 mutations, WNT signaling) - **Papillary Craniopharyngioma** (BRAF V600E mutation, rare in children)

2. Classification by Location - **Supratentorial Tumors**: Gliomas, embryonal tumors, ependymomas, craniopharyngiomas, germ cell tumors - **Infratentorial Tumors**: Medulloblastomas, ependymomas, pilocytic astrocytomas - **Midline Tumors**: Diffuse midline gliomas, germ cell tumors, craniopharyngiomas - **Spinal Tumors**: Ependymomas, astrocytomas, metastatic tumors

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They are classified into supratentorial tumor and Pediatric posterior fossa tumor. They could also be classified according to the age of diagnosis into congenital brain tumors (CBT) (diagnosed antenatally in the first 60 days of life), tumors of infancy (younger than 1 year of age), and older children.

The common pediatric brain tumors are gliomas (cerebellum, brainstem, and optic nerve), pineal tumors, craniopharyngiomas, teratomas, granulomas, and primitive neuroectodermal tumors (primarily medulloblastoma).

Meningiomas: 1.5% of meningiomas occur in childhood and adolescence (usually between 10 and 20 years), comprising 0.4–4.6% of intracranial tumors.

Many molecular and genetic characteristics have been elucidated in the WHO CNS 5. Molecular diagnostics and classification are essential for accurately categorizing pediatric brain tumors, and the significance of molecular and genetic information will continue to grow [1)].

1)
Kanemura Y. [Classification and Diagnostics of Pediatric Brain Tumors]. No Shinkei Geka. 2023 Sep;51(5):778-788. Japanese. doi: 10.11477/mf.1436204819. PMID: 37743329.