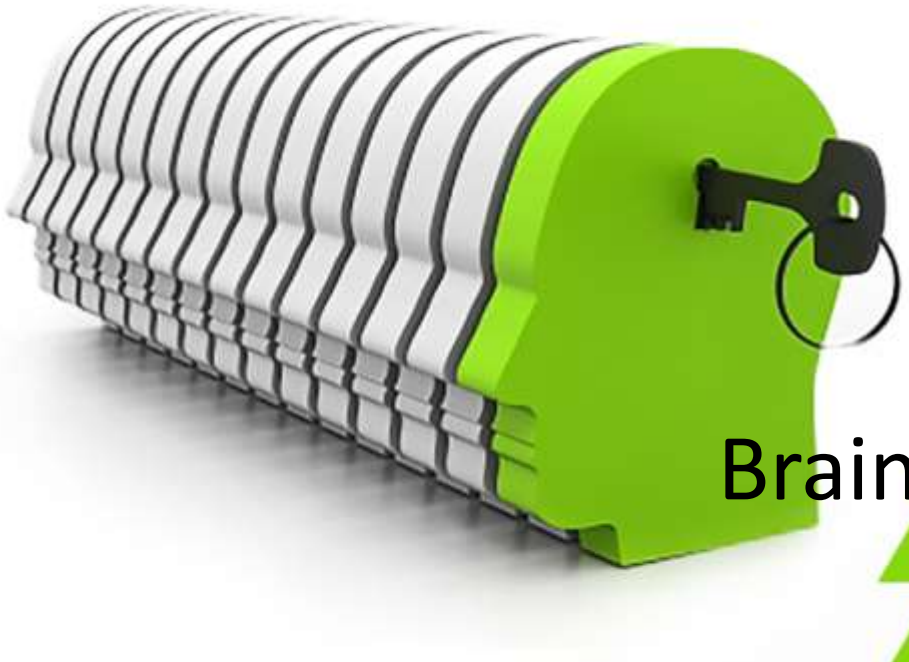
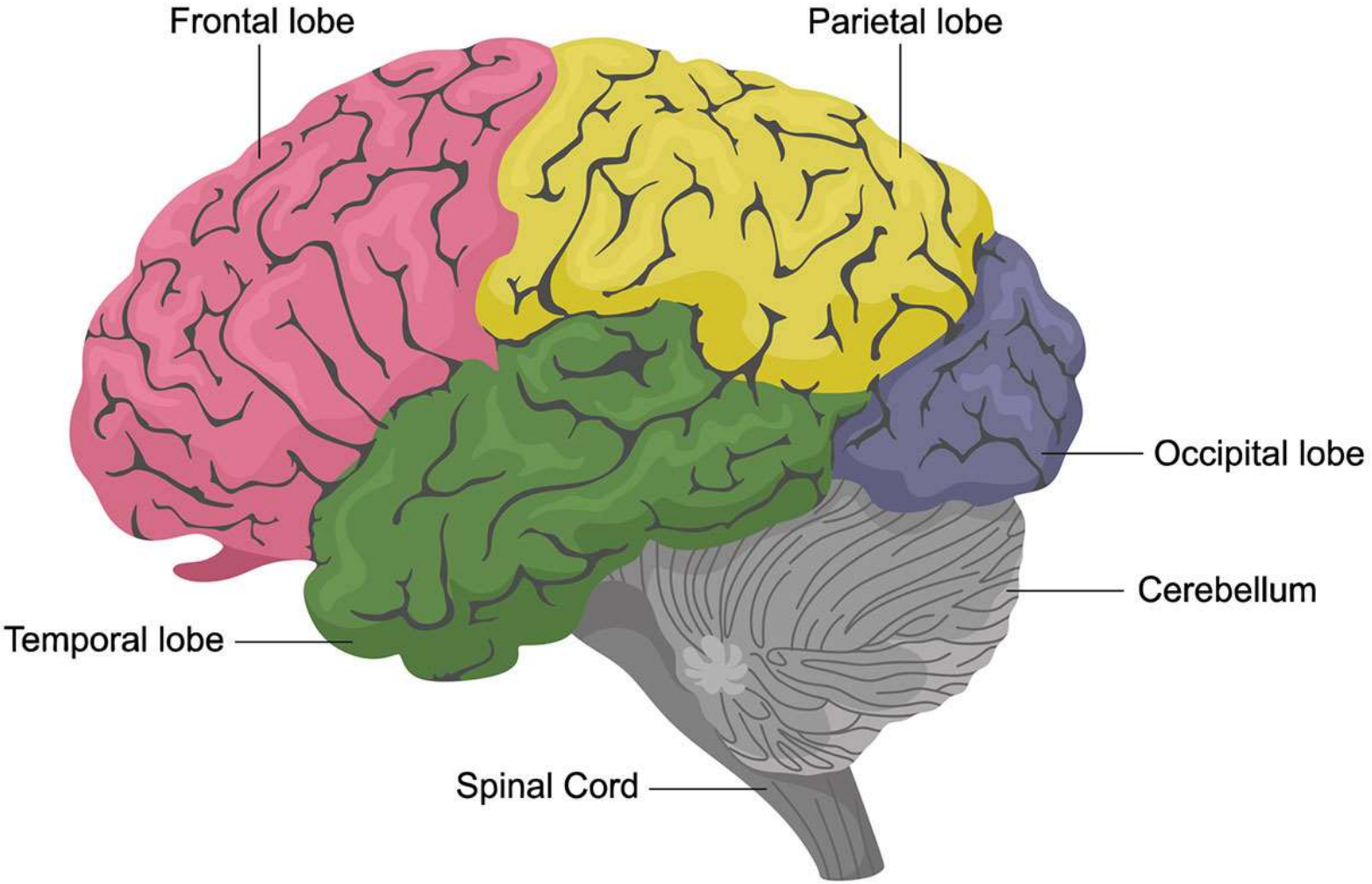


Brain tumors

Human Brain Anatomy



The annual incidence of tumors of the CNS ranges from 10 to 17 per 100,000 persons for intra-cranial tumors and 1 to 2 per 100,000 persons for intra-spinal tumors;

About half to three quarters are primary tumors, and the rest are metastatic.

Tumors of the CNS account for 20% of all cancers of childhood.

Tumors

GLIOMAS

astrocytomas,

oligodendrogliomas

ependymomas.

NEURONAL TUMORS

ganglioglioma

POORLY DIFFERENTIATED NEOPLASMS

medulloblastoma

Atypical Teratoid/Rhabdoid Tumor

OTHER PARENCHYMAL TUMORS

Primary CNS Lymphoma

Germ Cell Tumors

MENINGIOMAS

Glial tumors

Astrocytoma

The two major categories of astrocytic tumors are infiltrating astrocytomas and non-infiltrating neoplasms, of which the most common are the pilocytic astrocytomas.

These tumor types have characteristic histologic features, distribution within the brain, age groups typically affected, and clinical course.

Diffuse Astrocytoma

- grossly a poorly defined, gray, infiltrative tumor that expands and distorts the invaded brain.

- range in size from a few centimeters to enormous lesions that replace an entire hemisphere.

- cut surface is either firm or soft and gelatinous; cystic degeneration may be seen.

- may appear well demarcated from the surrounding brain tissue, but infiltration beyond the outer margins is always present.

Diffuse Astrocytoma. Microscopic features

-mild to moderate increase in glial cellularity,

- variable nuclear pleomorphism,

-intervening feltwork of fine, GFAP-positive astrocytic processes that give the background a fibrillary appearance.

Anaplastic Astrocytoma

-show regions that are more densely cellular and have greater nuclear pleomorphism;

- mitotic figures are often observed.

- term gemistocytic astrocytoma is used for tumors in which the predominant neoplastic astrocyte shows a brightly eosinophilic cell body from which emanate abundant, stout processes.

Diffuse astrocytoma, grade II

Recognition of secondary structures of Scherer aids in morphological diagnosis and distinction from reactive gliosis.

Reactive gliosis → uniformly distributed astrocytes that show regular spacing within the tissue and abundant processes, demonstrated by GFAP immunohistochemistry

Diffuse astrocytoma → irregularly distributed, tend to form cell clusters, and have much more variable cytoplasm and cell processes than reactive astrocytes.
Individual tumor cells often appear as isolated nuclei and tend to aggregate around neurons (perinuronal "satellitosis"), blood vessels or beneath the pia → called **secondary structures of Scherer**

Pilocytic astrocytoma - children and **cerebellum → classic biphasic appearance** with cellular areas alternating with hypocellular, microcystic areas, **hyalinized vessels,** rarely glomeruloid vessels, **infarct like necrosis**, **degenerative nuclear atypia**, brightly eosinophilic, corkscrew-shaped **Rosenthal fibers** (inset) and **PAS+ve eosinophilic granular bodies** (arrow) **no IDH mutation, instead have activating mutation in BRAF,** FGFR1 and PTPN11 genes.

Glioblastoma (glioblastoma multiforme)

Grossly some areas are firm and white, others are soft and yellow due to necrosis, and yet others show regions of cystic degeneration and hemorrhage.

The histologic appearance of glioblastoma is similar to anaplastic astrocytoma with the additional features of necrosis and vascular or endothelial cell proliferation.

Necrosis in glioblastoma often occurs in a serpentine pattern in areas of hypercellularity. Tumor cells collect along the edges of the necrotic regions, producing a histologic pattern referred to as pseudo-palisading.

Outline of gliomas, glioneuronal and neuronal tumors

1. Adult-type diffuse gliomas
Astrocytoma, IDH-mutant
Oligodendroglioma, IDH-mutant and 1p/19q codeleted
Glioblastoma, IDH-wild type
2. Pediatric-type diffuse gliomas
Pediatric-type low-grade gliomas
Pediatric-type high-grade gliomas
3. Circumscribed astrocytomas
Pilocytic astrocytoma
Others
4. Glioneuronal and neuronal tumors
Ganglioglioma
Others
5. Ependymal tumors

Pediatric type diffuse gliomas: Overview

Oligodendroglioma

These tumors constitute 5% to 15% of gliomas and are most common in the fourth and fifth decades. Patients may have had several years of neurologic complaints, often including seizures. The lesions are found mostly in the cerebral hemispheres, with a predilection for white matter.

Oligodendroglioma

Morphology.

On gross examination, oligodendrogliomas are well-circumscribed, gelatinous, gray masses, often with cysts, focal hemorrhage, and calcification. On microscopic examination, the tumors are composed of sheets of regular cells with spherical nuclei containing finely granular chromatin (similar to normal oligodendrocytes) surrounded by a clear halo of cytoplasm.

Oligodendroglioma, grade II → perinuclear halo, chicken wire vasculature, calcification

Anaplastic oligodendroglioma, grade III → increased cellularity, nuclear atypia, increased mitosis (> 6 per 10 HPF), necrosis may be present

Ependymoma

Ependymomas, most often arise next to the ependyma-lined ventricular system, including the oft-obliterated central canal of the spinal cord. In the first two decades of life they typically occur near the fourth ventricle and constitute 5% to 10% of the primary brain tumor.

Ependymoma

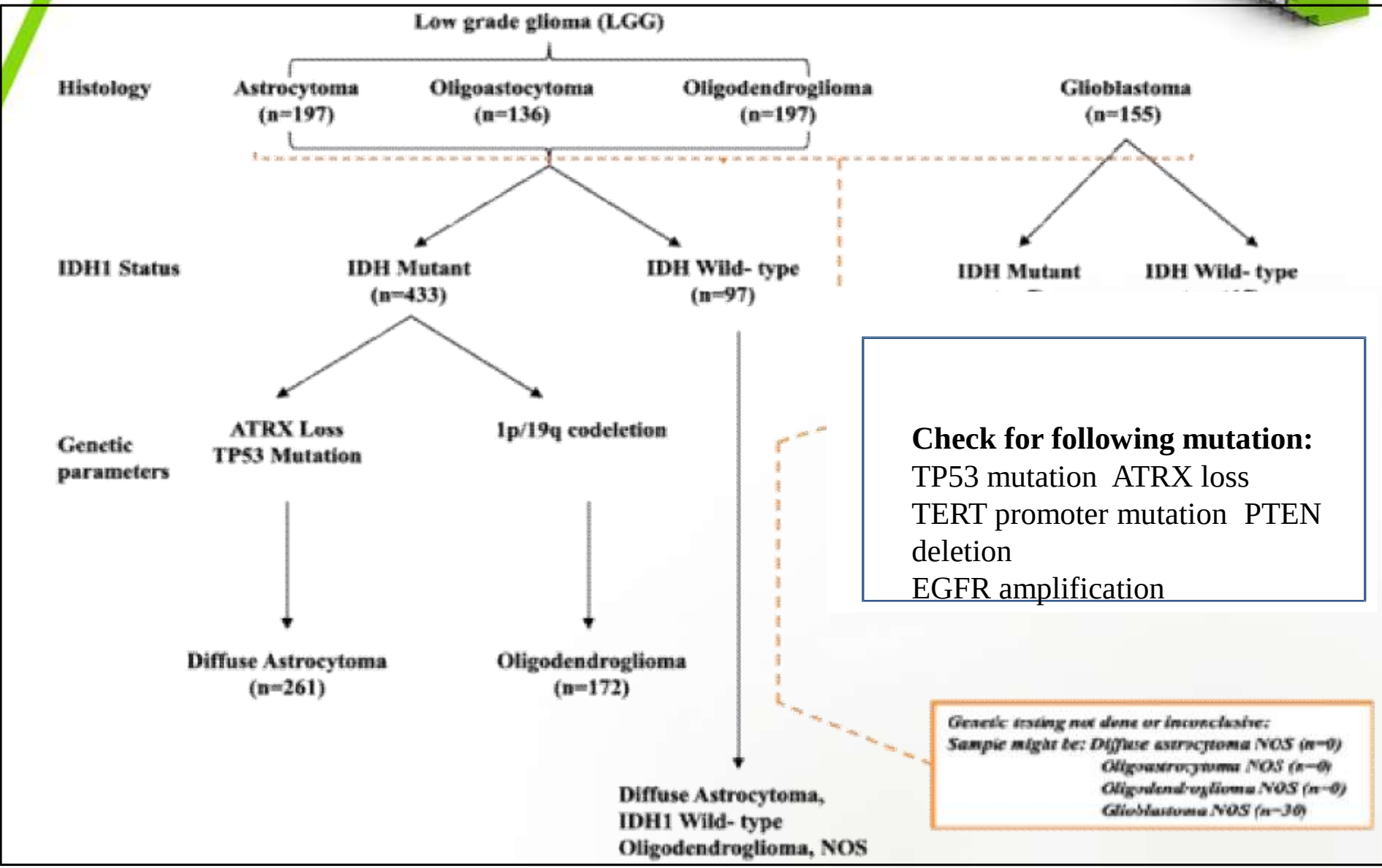
In the fourth ventricle, ependymomas are typically solid or papillary masses extending from the floor of the ventricle. Although ependymomas are moderately well demarcated from adjacent brain, the proximity of vital pontine and medullary nuclei usually makes complete extirpation impossible. In the intra-spinal tumors this sharp demarcation sometimes makes total removal feasible.

Gangliogliomas

Most commonly found in the temporal lobe and often have a cystic component.

The glial component of these lesions usually resembles a low-grade astrocytoma, lacking mitotic activity and necrosis.

IHC & molecular diagnostic algorithm in glial tumors



Embryonal tumors

Medulloblastoma

In children, medulloblastomas are located in the midline of the cerebellum, but lateral locations are more often found in adults.

Rapid growth may occlude the flow of CSF, leading to hydrocephalus.

The tumor is often well circumscribed, gray, and friable, and may be seen extending to the surface of the cerebellar folia and involving the leptomeninges.

Meningioma

MENINGIOMAS

Meningiomas are predominantly benign tumors of adults, usually attached to the dura, that arise from the meningothelial cell of the arachnoid.

Meningiomas may be found along any of the external surfaces of the brain as well as within the ventricular system, where they arise from the stromal arachnoid cells of the choroid plexus.

MENINGIOMAS

Meningiomas are usually rounded masses with well-defined dural bases that compress underlying brain but are easily separated from it. Extension into the overlying bone may be present.

The surface of the mass is usually encapsulated with thin, fibrous tissue and may have a bosselated or polypoid appearance.

The lesions range from firm and fibrous to finely gritty, or they may contain numerous calcified **psammoma bodies**.

CNS Lymphomas

- Primary central nervous system lymphoma (PCNSL) is defined as **lymphoma arising in the brain, spinal cord, or leptomeninges without prior or concurrent tumor outside the central nervous system (CNS)**.

- The patients with PCNSL may be immunocompetent or have immunocompromised status. **Immunocompetent patients** are **older** with a **slight male predominance**. PCNSL makes up 1.5% to 3% of primary brain malignancies and about 1% of non-Hodgkin lymphomas in this group. **Immunocompromised patients** include **HIV/AIDS** (most common), **transplant recipients**, and **congenital immunodeficiency disorders**. The patients are **younger** with a **striking male predominance**. The presentation depends upon the site of the tumor and includes motor disturbances, seizures, signs of increased intracranial pressure, and personality changes.

Morphology

- The lesions are usually **supratentorial**. Involvement of cerebellum and spinal cord is rare. The lesions are **solitary or multiple** and **poorly circumscribed** with hemorrhage and necrosis. There may be diffuse meningeal involvement or diffuse subependymal periventricular spread. There is **diffuse proliferation of large atypical lymphoid cells** with **perivascular growth pattern**. The vast majority of the cases, especially in immunocompromised patients, are **diffuse large B-cell lymphomas (DLBCL) composed of centroblasts, immunoblasts**.

METASTATIC TUMORS

Metastatic lesions, mostly carcinomas, account for approximately a quarter to half of intra-cranial tumors.

The five most common primary sites are lung, breast, skin (melanoma), kidney, and gastrointestinal tract, accounting for about 80% of all metastases.

Some rare tumors (e.g., choriocarcinoma) have a high likelihood of metastasizing to the brain, whereas some more common tumors (e.g., prostatic carcinoma) almost never grow in the brain, even when they are metastatic to adjacent bone and dura.

The meninges are also a frequent site of involvement by metastatic disease. Metastases to the epidural or subdural space can cause spinal cord compression, which requires emergency treatment.