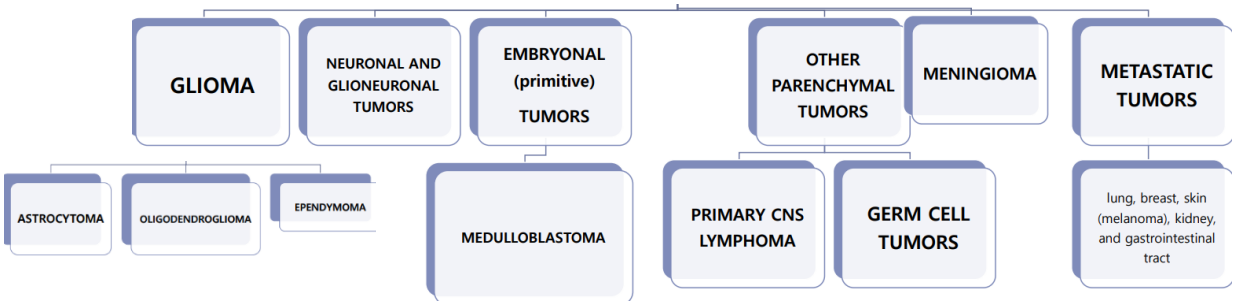
CNS tumors

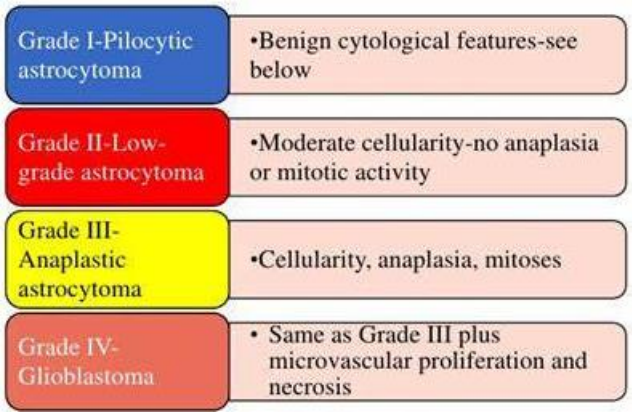


*25-50% are metastatic (usually from lung, breast, kidney,..)

*while metastasis is rare!

*any stage can be infiltrative even low grade ones

*so histologic grading of these tumors depends on 3: atypia and mitosis, microvascular proliferation, necrosis.it is graded into 4:



Now, we can classify it according to the age of patient that is usually affected:

	Children & pediatric	**Adults**
Astro	PCA pilocytic astrocytoma	GBM glioblastoma
Oligo		OGD oligodendroglioma
Ependy	Ependymoma	
Neurons	Medulloblastoma	
Meningo		Meningioma

Genetic mutations in GLIOMAS:

1.IDH (isocitrate dehydrogenase) function mutation MOST IMP

- Seen in astro and oligo (glial origin).
- Mutation affect IDH1 codon 132 (most common) or IDH2 codon 172.
- EFFECT: production of 2-hydroxyglutarate (oncometabolite) that causes DNA hypermethylation and put the cell in stem-like state→ self renewal and tumorgenesis.

2.deletion mutation in the whole short arm -p- of ch1 and the whole long arm –q- of ch19 = loss of 1p19q

- Diagnostic of oligo in the presence of IDH mutation → carry TERT promotor mutation that is important in telomerase stabilization, immortalization and proliferation.

3.ATRX and P53 loss of function mutation

- Both occur in astro in the presence of IDH mutation
- EFFECT: ATRX → alternative lengthening of telomeres

P53 → no tumor suppression = survival

ATRX is mutual exclusive with the activating promotor mutation of TERT (1p/19q codeletion) – they can`t both exist -- , so ATRX is kind of exclusive for astro while tert for oligo and both are IDH mutant.

Let`s start with gliomas (GFAP positive) : astrocytoma, oligodendroglioma and ependymoma.

ASTROCYTOMA classified into 2 major categories according to their infiltrative potential:

1-diifuse (infiltrating) astrocytoma (G 2-4)
2-circumscribed astrocytic gliomas: PCA, SEGA, PXA.

1- Diffuse (infiltrating) astrocytoma (G2-4)

Account for 80% of primary brain tumors in adults (40-60 yrs) , mostly affect cerebrum

• diffuse astrocytoma (grade 2), hypercellular, no atypia not malignant + fibrillary fine astrocytic processes background, mean survival is > 5 years.

• anaplastic astrocytoma (grade 3) ,mitotic figures, mean survival is 2-3 years

• Glioblastoma (grade 4) is called glioblastoma multiforme (GBM) due to various gross appearance of the tumor from region to region, palisading necrosis, MVP microvascular proliferation, mean survival is 15 months

*no G1 diffuse astrocytoma

2-Circumscribed astrocytic glioma (G1)

Pilocytic astrocytoma : children and young adults, mostly affect cerebellum

Have BRAF mutation but NO IDH mutation (bcz it`s not diffuse)

Rosenthal fibers which is eosinophilic corkscrew shaped structures within the astrocytic processes {NOT diagnostic}

Eosinophilic granular bodies which is rounded hyaline droplets is cytoplasm of astrocytes (seen in PA and ganglionic)

OLIGODENDROGLIOMA is diffusely infiltrating slow growing glioma with IDH and 1p19q codeletion, mostly affect cerebrum white matter (bcz they are the mylienating cells of CNS)

Graded into grade 2 (mean survival is 10-20 yrs) and 3(mean survival is 5-10 yrs) only!

better prognosis than astrocytoma of same grade (maybe bcz its slowهاي هبد مني)

Grade 2:

• sheets of regular uniform cells resembling oligodendrocytes

• round nuclei containing finely granular chromatin (salt and pepper)

• The nuclei are surrounded by a clear halo of cytoplasm à fried-egg appearance.

• delicate network of anastomosing capillaries “chicken-wire”

• Calcification in 90% of tumors.

• Mitotic activity usually is absent or low (Ki67<5%)

Grade 3: Anaplastic oligodend

Anaplasia = Microvascular proliferation with without necrosis

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EPENDYMOMA: circumscribed , and graded into 2 and 3 only (same as oligo but at the opposite they are circumscribed!)

Affect children in the posterior fossa (near 4th ventricle) + adults in spinal cord and supratentorial (away from ventricles)

G 2: uniform small cells with benign appearance , tumor cells may form 2 structure

1.ependymal rosette that is diagnostic but not sensitive

2.perivascular pseudorosette that is sensitive but not specific

G 3: less ependymal differentiation so less ependymal rosettes

Frequent mitotic figures and MVP

NEURONAL tumors : affect children mainly , low graded and most commonly present with seizures.

1• Central neurocytoma, WHO grade 2: neuronal tumor within and adjacent to the lateral ventricle(s) and/or the third ventricle

2• Gangliogliomas, WHO grade 1: glioneuronal tumor composed of a mixture of neoplastic ganglion and glial cells, most commonly in the temporal lobe.

3• Dysembryoplastic neuroepithelial tumor (DNT), WHO grade 1: glioneuronal tumor affecting the cerebral cortex most commonly in the superficial temporal lobe

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EMPRYONAL: Medulloblastoma, WHO grade 4:

• predominantly in children, mainly in cerebellum

• All are highly malignant, WHO grade 4 but well circumscribed !

• the prognosis for untreated patients is dismal but with total excision, chemotherapy, and irradiation

Bcz its radiosensitive 5-year survival rate may be as high as 75%

•have a tendency to spread to subarachnoid space and disseminate through CSF ☹

- ➔ Very cellular that is composed of sheets of small primitive cells blue (high N/C ratio) plus mitoses are abundant. They also often express neuronal marker such as synaptophysin.
- ➔ Homer-Wright rosettes: represent focal neuronal differentiation; NOT specific.

ONCOGENIC PATHWAYS of MEDULLOBLASTOMA:

Ø Wnt pathway activation: associated with gain of function mutations in the gene for β-catenin; have the most favorable prognosis of all the genetic subtypes.

Ø MYC overexpression: due to MYC amplification; these tumors have the poorest prognosis.

Ø Hedgehog pathway activation: associated with loss of function mutations in PTCH1 (a negative regulator of the Hedgehog); these tumors have an intermediate prognosis, but the concomitant presence of P53 mutation confers a very poor prognosis.

MENINGIOMA: adults (women>men)

• tumors that arise from meningothelial cells of the arachnoid matter and usually attached to the dura

• usually solitary, but multiple sites can be affected, rubbery, rounded, or bosselated dural masses that compress underlying brain that are mostly circumscribed ((separable)) from underlying brain, but some tumors are infiltrative.

• Location: intracranial, intraspinal or orbital attached to the dura.

• The most common cytogenetic abnormality is loss of chromosome 22, especially the long arm (22q). •The deletions include the region that harbors the NF2 neurofibromatosis 2 gene.

Grading -- > 1,2,3.

Meningiomas (WHO grade 1): well-defined dura-based masses that may compress the

brain but do not typically invade it +/- overlying bone extension.

- Epithelioid cells arranged in whorly (syncytial)pattern +/- psammoma bodies

- meningothelial (most common) clusters of epithelioid cells with fuzzy or indiscernible

(blurry) cell membranes

- Other patterns include fibroblastic, transitional, and psammomatous

ATYPICAL MENINGIOMAS, WHO grade 2

• recurrence and aggressive local growth (may require radiation & surgery)

1- 4 >mitoses/10 HPF; or
2- (3 out of 5): increased cellularity, small cells with high N/C ratio, prominent nucleoli, patternless growth, ornecrosis; or

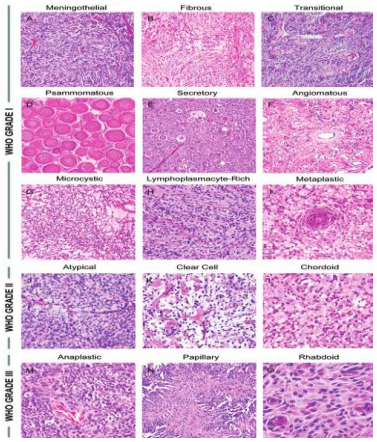
3- clear cell or chordoid subtypes of meningioma

ANAPLASTIC MENINGIOMA, WHO grade 3

• highly aggressive, resemble a high-grade sarcoma or carcinoma morphologically.

1- >20 mitoses/ 10HPF; or
2- Papillary; or rhabdoid meningioma.

extra pic to see how many types of meningiomas there are! ` byeee.



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