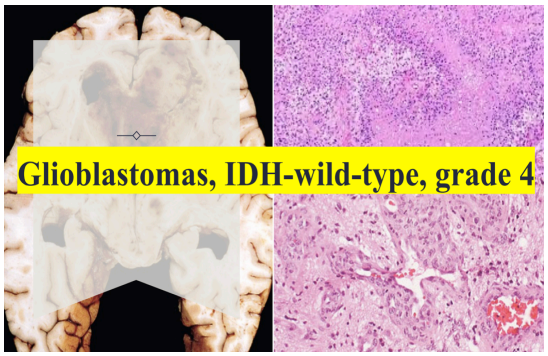
Rawan Mohammed

CNS Tumors 2:



Glioblastomas (IDH-Wild-Type, Grade 4)

-Definition:

-Diffuse glioma that is IDH-wildtype and **H3** wildtype and has one or more of the following histologic or genetic features:

-Microvascular proliferation
-**Necrosis**
-**TERT** promoter mutation
-**EGFR** gene amplification
-combined **gain** of entire **chromosome 7** and **loss** of entire **chromosome 10 [+7 /-10]**

-The **most common malignant glioma** (50% of all primary malignant brain tumors in adults).
-**Always grade 4** (no lower grade precursor)
-Age: 6th-8th decades of life
-Site: **cerebral hemispheres** (temporal , parietal, frontal lobes, basal ganglia and thalamus)
-Radiology: **ring enhancing lesion**

-Clinically:

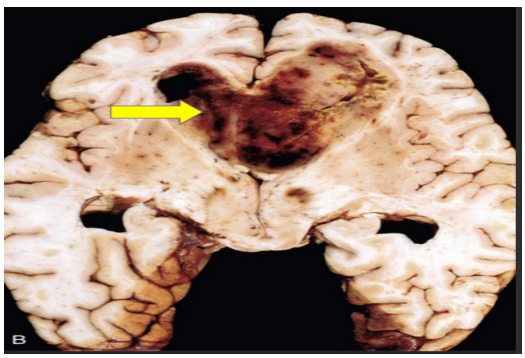
-rapid progression
-Seizures, neurocognitive impairment, neursea, vomiting, and headache
-Rapid infiltration of the corpus callosum with growth to the contralateral hemisphere leading to bilateral symmetrical lesion **(butterfly glioma)**

-Prognosis:

-**Very Poor** even with **resection**
-chemotherapy and radiotherapy the median survival is only about **15-18 months.**

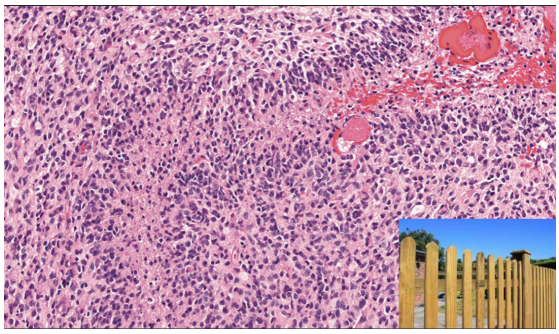
-Macroscopic:

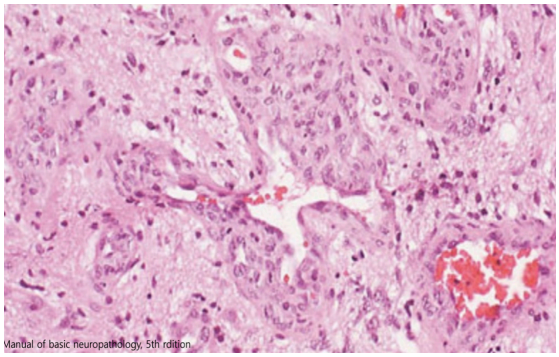
-variation in the gross appearance of the tumor from region to region is characteristic (was called **glioblastoma multiforme**)
-Some areas are firm and white, others are soft and yellow (due to tissue necrosis)



-others show regions of **cystic degeneration** and **hemorrhage**.

-Microscopic:

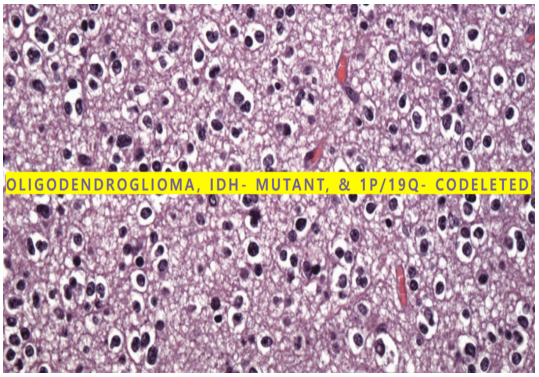




-Similar to **astrocytoma**
-IDH- mutant
-grade 4 with High cellularity
-Prominent nuclear atypia
-Brisk mitotic activity and
-Necrosis: **irregular** zones of necrosis surrounded by dense accumulations of tumor cells (**palisading necrosis**)
-OR…
-microvascular proliferation:
-the presence of abnormal vessels with walls composed of 2 **≥** layers of vascular wall cells.

-The presence of any of the following Molecular features (even in the absence of necrosis or microvascular proliferation) lead to the designation of glioblastoma, IDH wildtype, grade 4:
-The presence of **TERT** promoter mutation
-**EGFR** gene amplification
- **+7/-10 chromosome** copy number changes

Oligodendroglioma (IDH-MUTANT, & 1p/19q-Co-deleted)



-Definition:

-A diffusely infiltrating, slow-growing glioma with IDH1 or IDH2 mutation and codeletion of chromosomal arms **1p and 19q.**
-5-15% of gliomas
-Age at diagnosis: 40-50 yrs.

-Location:

-mostly in the cerebral hemispheres:
-mainly in the **frontal** or
-**temporal** lobes
-white matter.

-The combination of **surgery**, **chemotherapy**, and **radiotherapy** yields an average survival of:

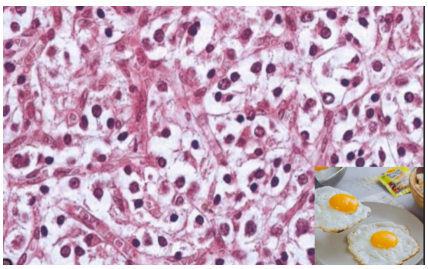
-**10-20** years for WHO grade **2**.
-**5-10** years for WHO grade **3**.

-Grade 3 is more aggressive than grade 2 oligodendroglioma
-When corrected for tumor grade, oligodendrogliomas (CNS WHO grade 2,3) Have best prognosis among diffuse glial tumors
-**NO grade 1 OR 4 oligodendroglioma**

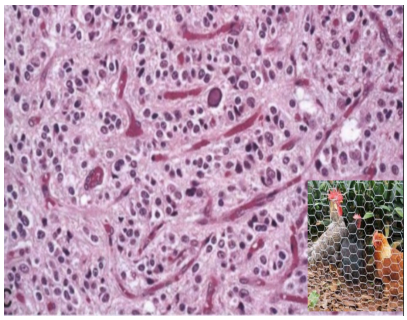
-Macroscopic

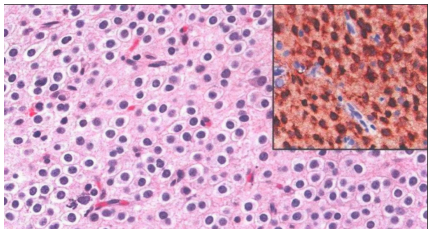
-infiltrative tumors with blurring of gray matter-white matter boundary.
- **+/- gelatinous gray mass**, **cysts**, focal hemorrhage, and **calcification**.

-Microscopic:



-sheets of regular uniform cells resembling oligodendrocytes
-spherical nuclei containing finely granular chromatin (salt and pepper)
-The nuclei are surrounded by a clear halo of cytoplasm → **fried-egg** appearance.
-delicate network of "**chicken-wire"**- like anastomosing capillaries
-Calcification up to **90%** of cases.
-Mitotic activity usually is absent or low (Ki67<5%)
-**No** spontaneous necrosis
-**No** microvascular proliferation

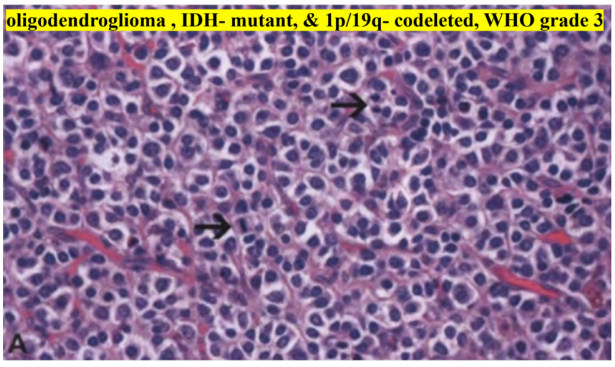


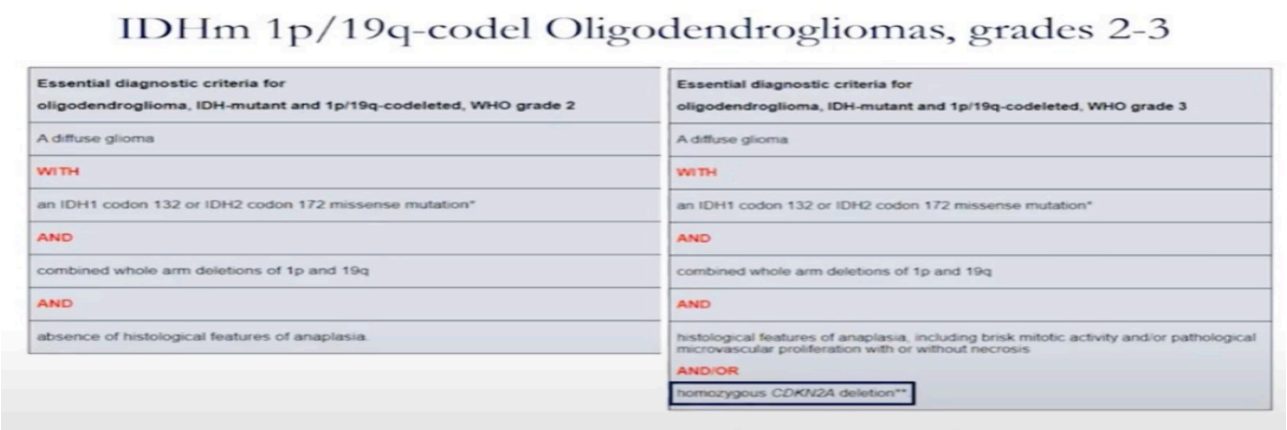


Oligodendroglioma (IDH-mutant & 1p/19q- Codeleted, Grade 3)

-Definition:

- An IDH-mutant and **1p/19q-codeleted** oligodendroglioma with focal or diffuse histological features of anaplasia (in particular, pathological microvascular proliferation and/or brisk mitotic activity **with or without necrosis**).





Circumscribed astrocytic gliomas

Pilocytic Astrocytoma, WHO grade 1

-Relatively **benign** tumor
-Age at presentation: **children and young adults.**

-Location:

-**cerebellum (especially in children)** > **Optic** nerve> Midline locations: Brainstem, optic chiasm/ hypothalamus, basal ganglia > Spinal cord> Cerebral hemispheres:
-**Rare in children** but happens in adults

-Clinically:

-mass effect,
-**Hydrocephalus**,
- **increased intracranial pressure**

-Treatment: Well circumscribed tumor curable with complete resection

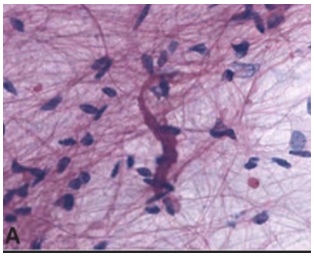
-Molecular profile:

-activating mutations or translocations involving the gene encoding the **BRAF** → resulting in activation of the **MAPK** signaling pathway.
-do **NOT** have mutations in IDH1 and IDH2, supporting their distinction from the adult type low-grade diffuse gliomas

-Macroscopic:

-well circumscribed (**discrete**) Cystic tumor
- +/- calcifications

-Macroscopic:

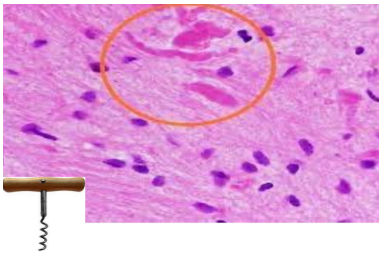


-bipolar cells with long, thin **GFAP** positive "hairlike" processes

-Rosenthal fibers:

-brightly eosinophilic corkscrew shaped structures within the astrocytic processes

-made of Can be physiologic (gliosis) or pathologic (PA) and Alexander disease

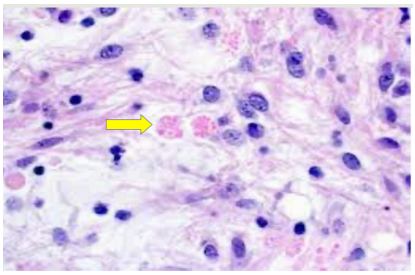


-eosinophilic granular bodies:

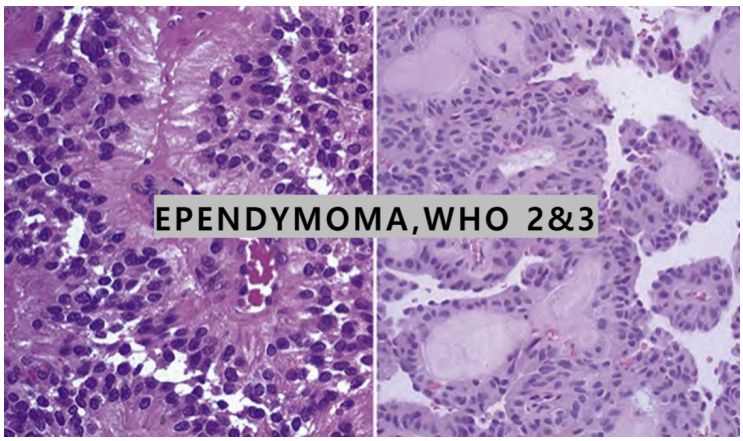
-rounded hyaline droplets in cytoplasm of astrocytes seen in **PA** and ganglion-cell tumors

-**microcysts** are often present

-necrosis and mitoses are **rare**.



Ependymoma (Grade 2 & 3)



-Definition:

-**glioma**, Mostly arise next to the ependyma- lined ventricular system, including the central canal of the spinal cord.

-Location:

-posterior fossa:

-near the **4th ventricle,**

accounting for 5-10% of tumors in the **first two decades** of life

-supratentorial

-Spinal: the **most common location in adults** and in patients with **NF2**

-Age:

-In the **first 2 decades** of life; near the **4th ventricle** (post. Fossa) accounting for 5-10% of primary brain tumors in this age group.

-In adults the spinal cord and supratentorial ependymomas occur with almost equal frequency

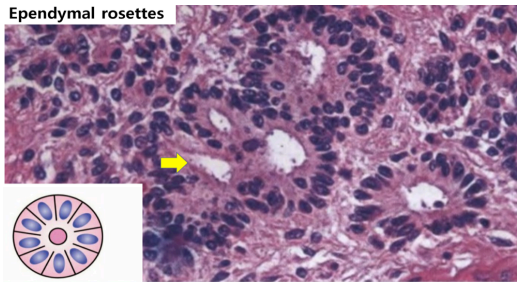
-The clinical outcome for completely resected **supratentorial** and s**pinal ependymomas** is better than for those in the **posterior fossa**

-Ependymoma, WHO grade 2, microscopic:

-**uniform small cells** with round to oval nuclei and granular chromatin in a fibrillary background
-**low** cellularity
-**low** mitotic count
-**No** necrosis or MVP
-**Cilia and microvilli** are seen on ultrastructural examinations

-Ependymoma WHO grade 2, Morphology:

-Tumor cells may form glandlike structures (rosettes) → Rosette formation:

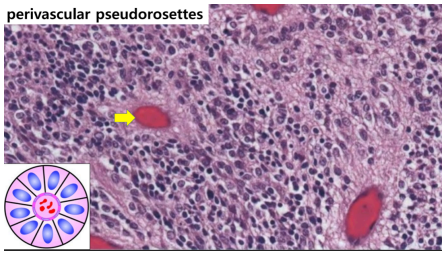


-Ependymal rosettes:

-**diagnostic hallmark** of ependymoma (25%)
- tumor cells arranged around a **central canal or lumen** that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen

- perivascular pseudorosettes:

-**not specific** for ependymoma (seen in **glioblastoma and medulloblastoma**)
-tumor cells radially arranged around vessels.
-Called "pseudo" because the central structure is not formed by the tumor itself, but instead represents a **native, non-neoplastic element**



Anaplastic ependymomas, WHO grade 3:

-Show **less evident ependymal differentiation**
-brisk mitotic rates, and microvascular proliferation carry more prognostic impact than necrosis and atypia.