CENTRAL NERVOUS SYSTEM TUMORS(2)

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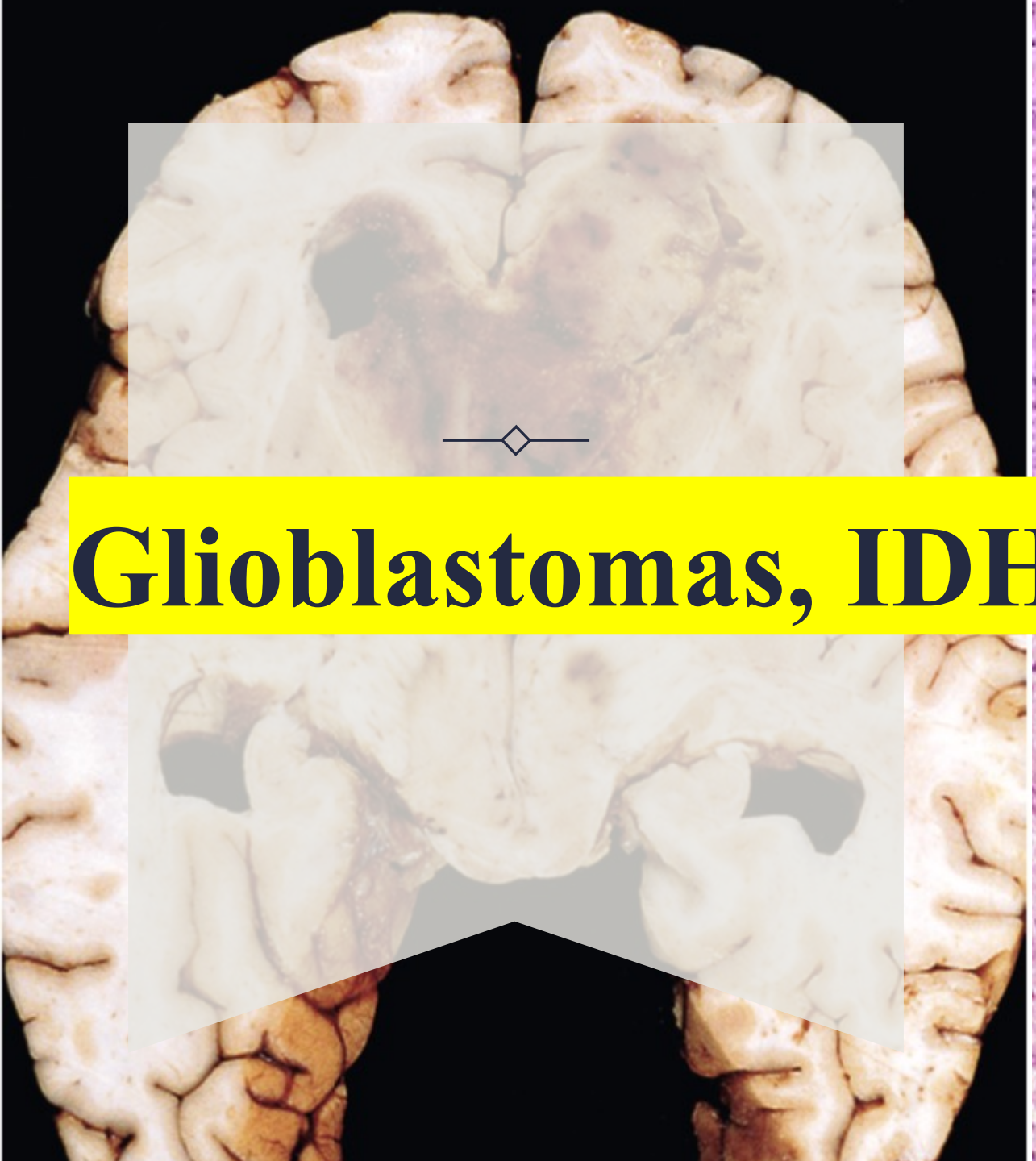
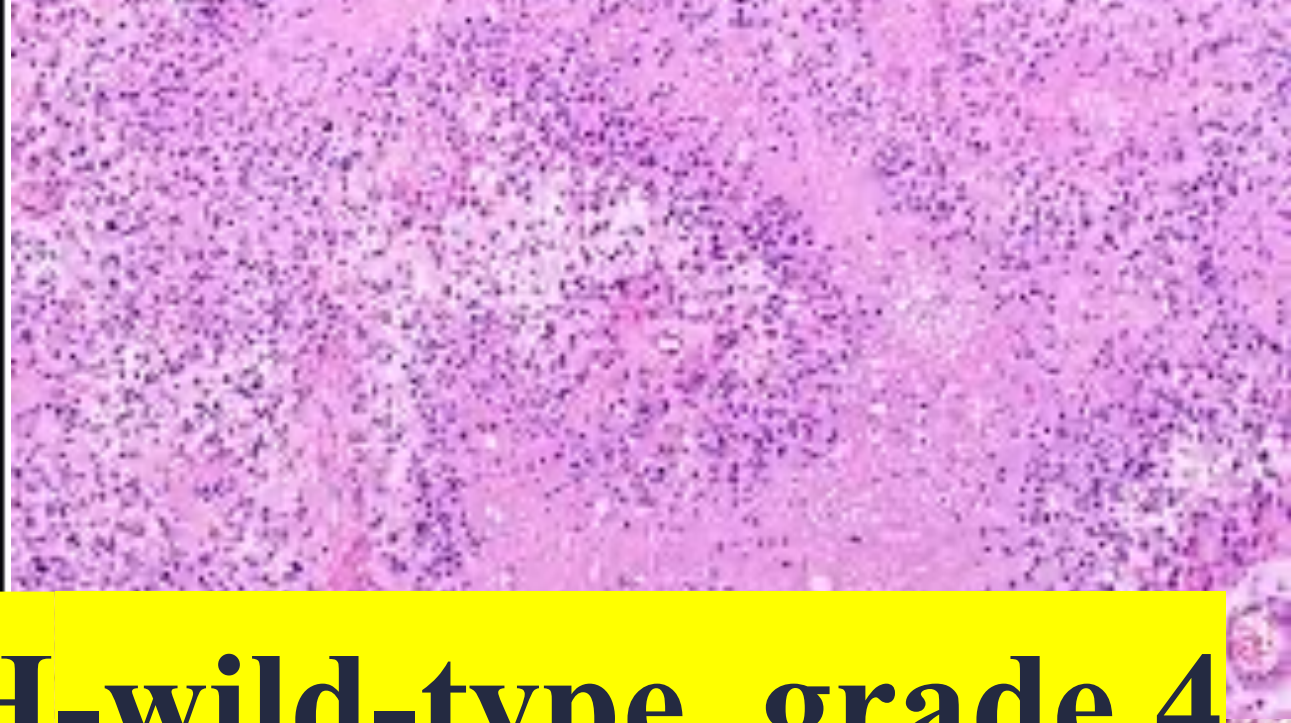
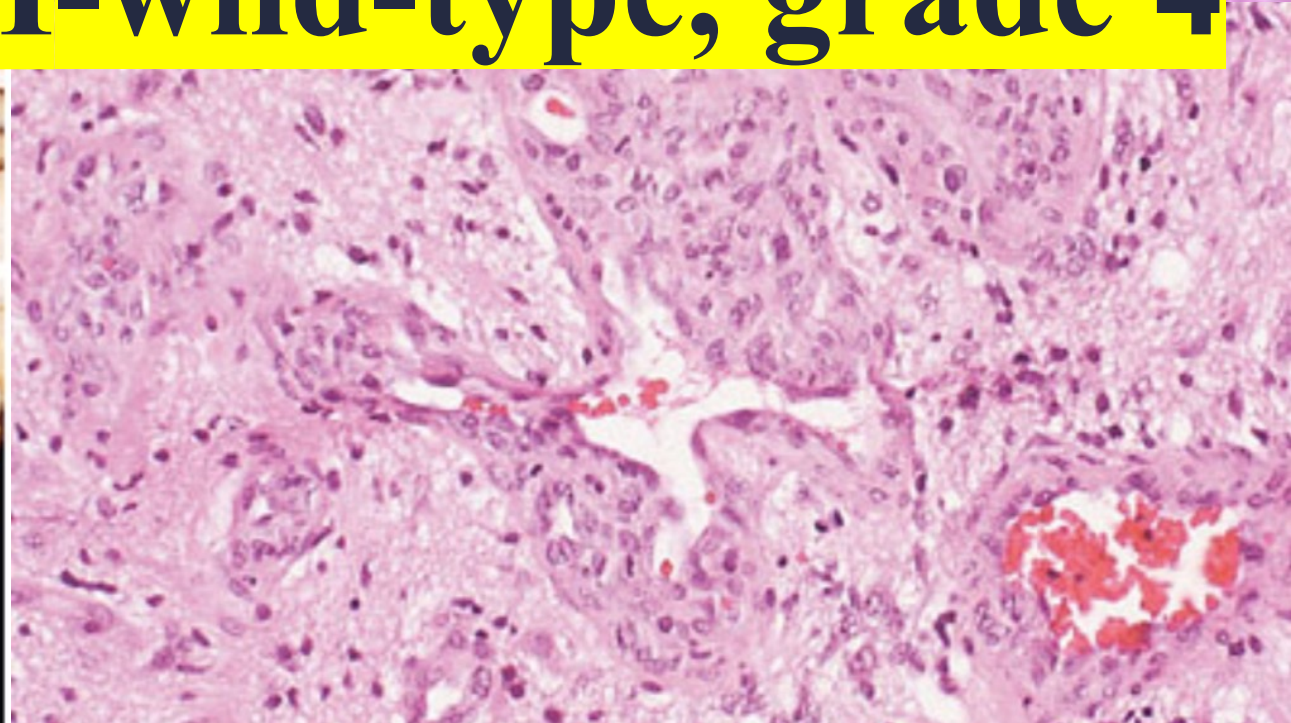




Glioblastomas, IDH-wild-type, grade 4



- **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 promotor mutation
- EGFR gene amplification
- combined gain of entire chromosome 7 and loss of entire chromosome 10 [+7 / -10]

Glioblastomas, IDH-wild-type:

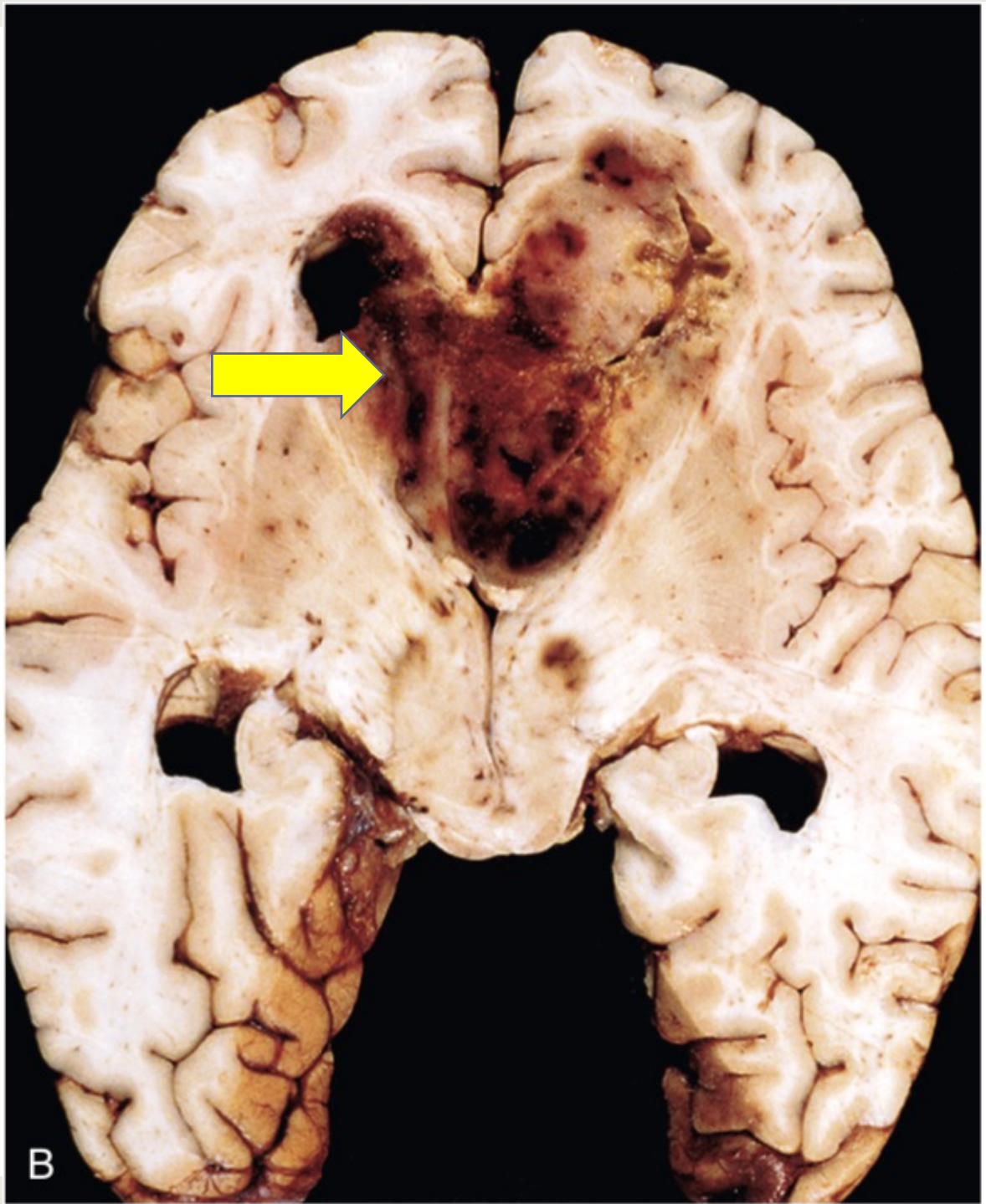
- The most common malignant glioma (50% of all primary malignant brain tumors in adults).
- Always grade 4 (no lower grade precursor)
- **Age:** 6th-8th decades of life
- **Site:** cerebral hemispheres (temporal , parietal, frontal lobes, basal ganglia and thalamus)
- **Radiology:** ring enhancing lesion

- **Clinically:**
  - rapid progression
  - Seizures, neurocognitive impairment, nausea, vomitting, and headache
  - Rapid infiltration of the corpus callosum with growth to the contralateral hemosphere 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:

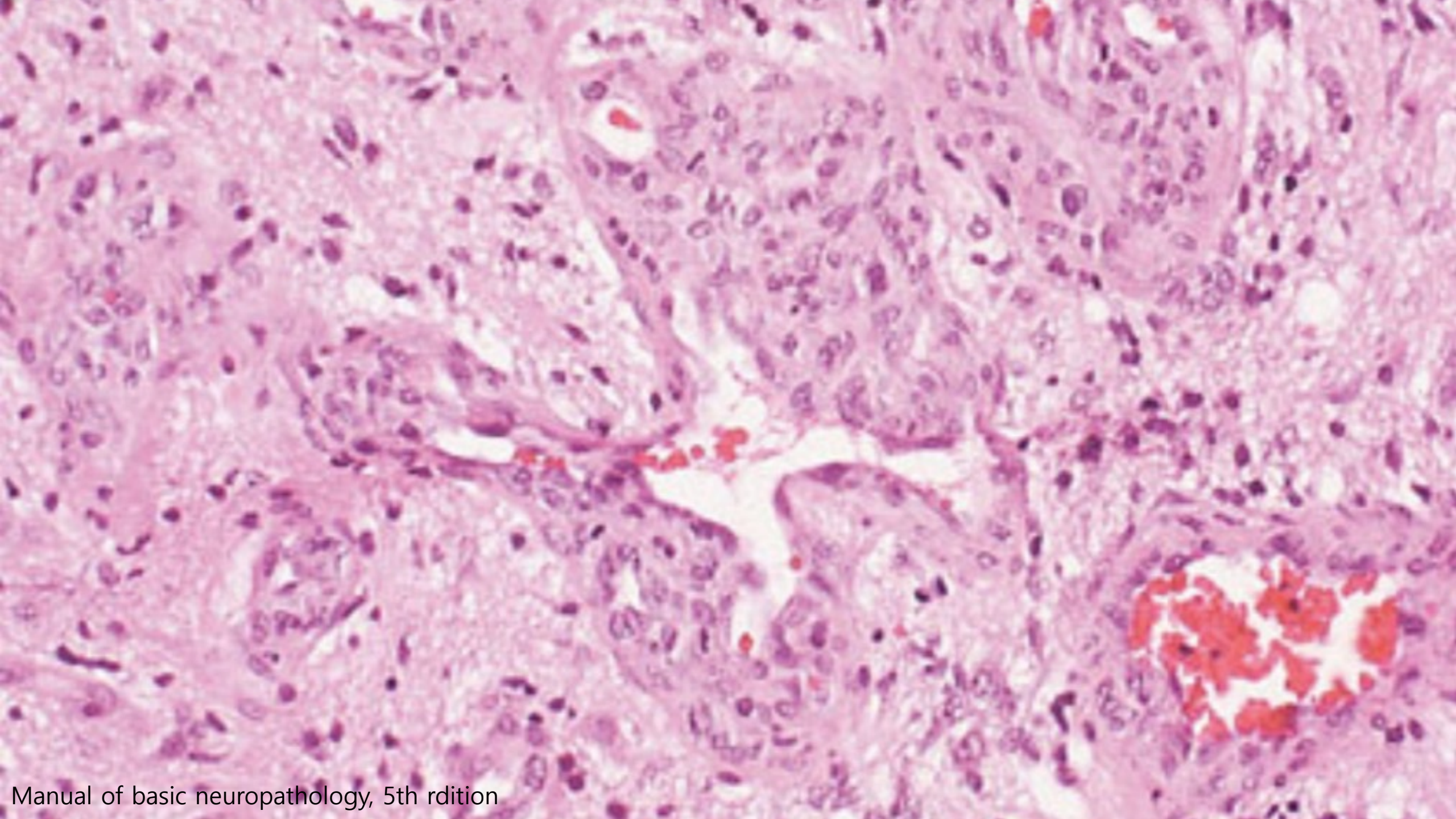
the presence of abnormal vessels with walls composed **2** ≥ layers of vascular wall cells.

or

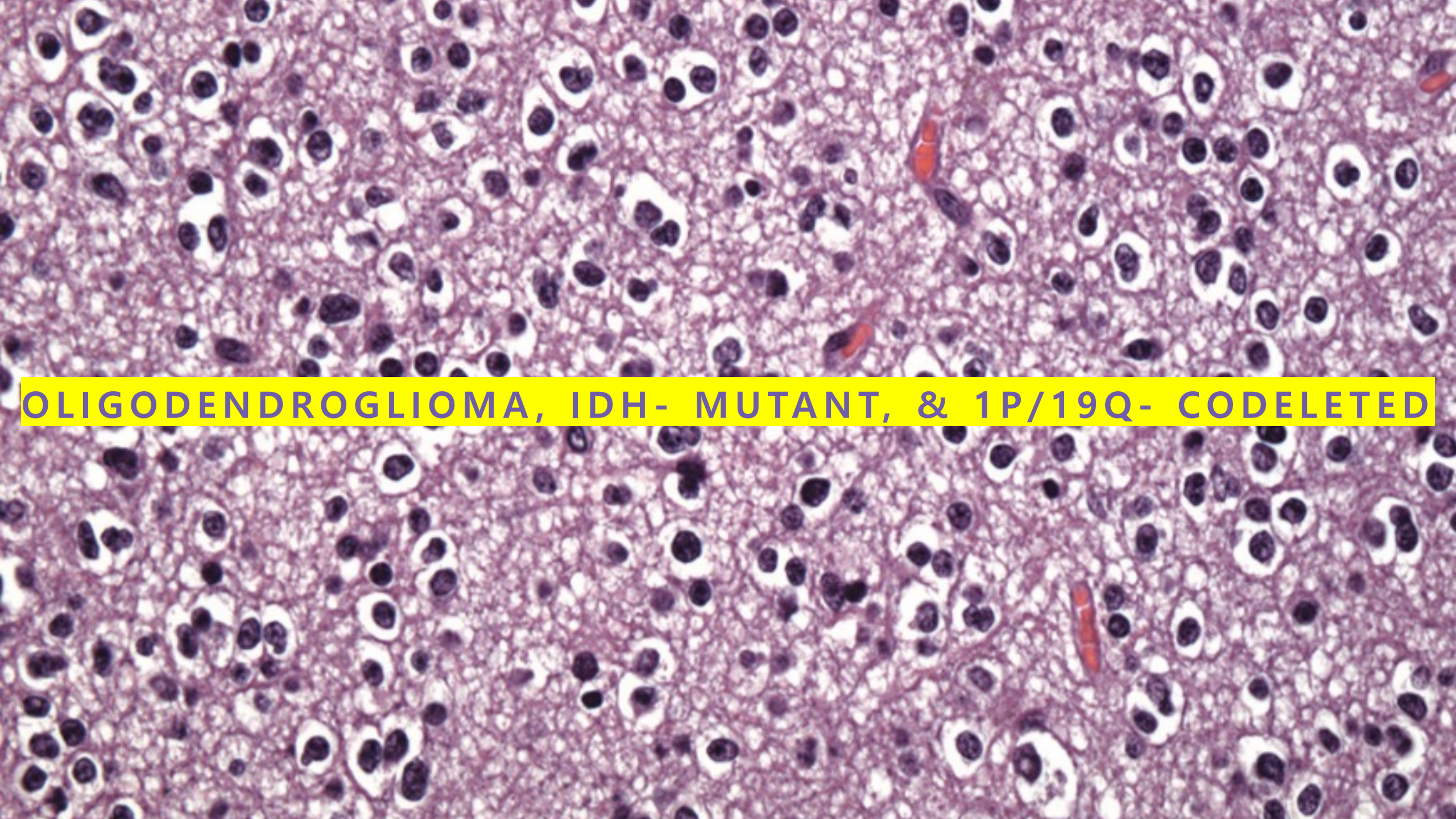
Molecular features

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:

- TERT promotor mutation
- EGFR gene amplification
- +7/-10 chromosome copy number changes



Manual of basic neuropathology, 5th rdition


OLIGODENDROGLIOMA, IDH- MUTANT, & 1P/19Q- CODELETED

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**

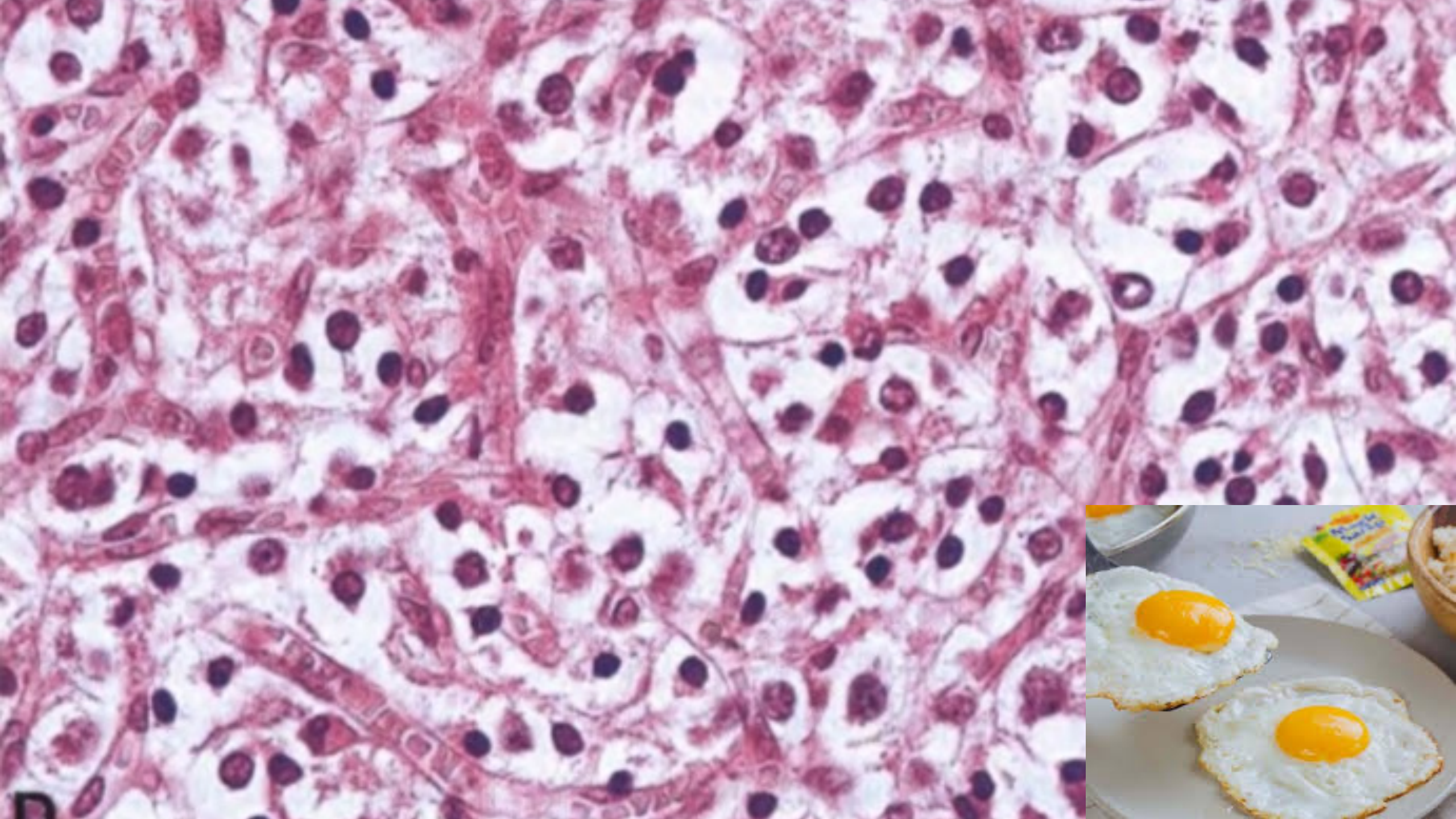
- **NO grade 1 OR 4 oligodendroglioma**

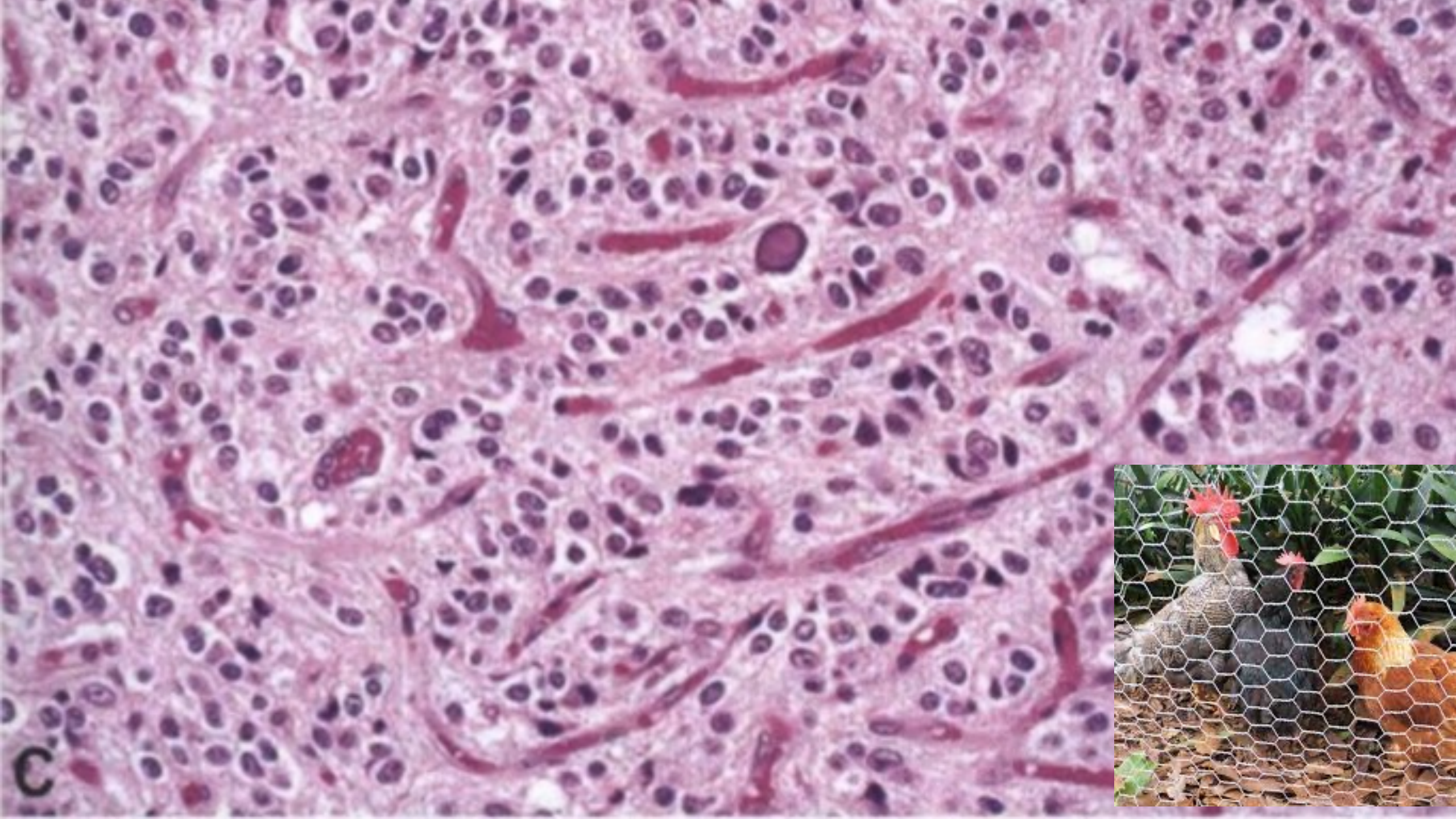
Marcoscopic:

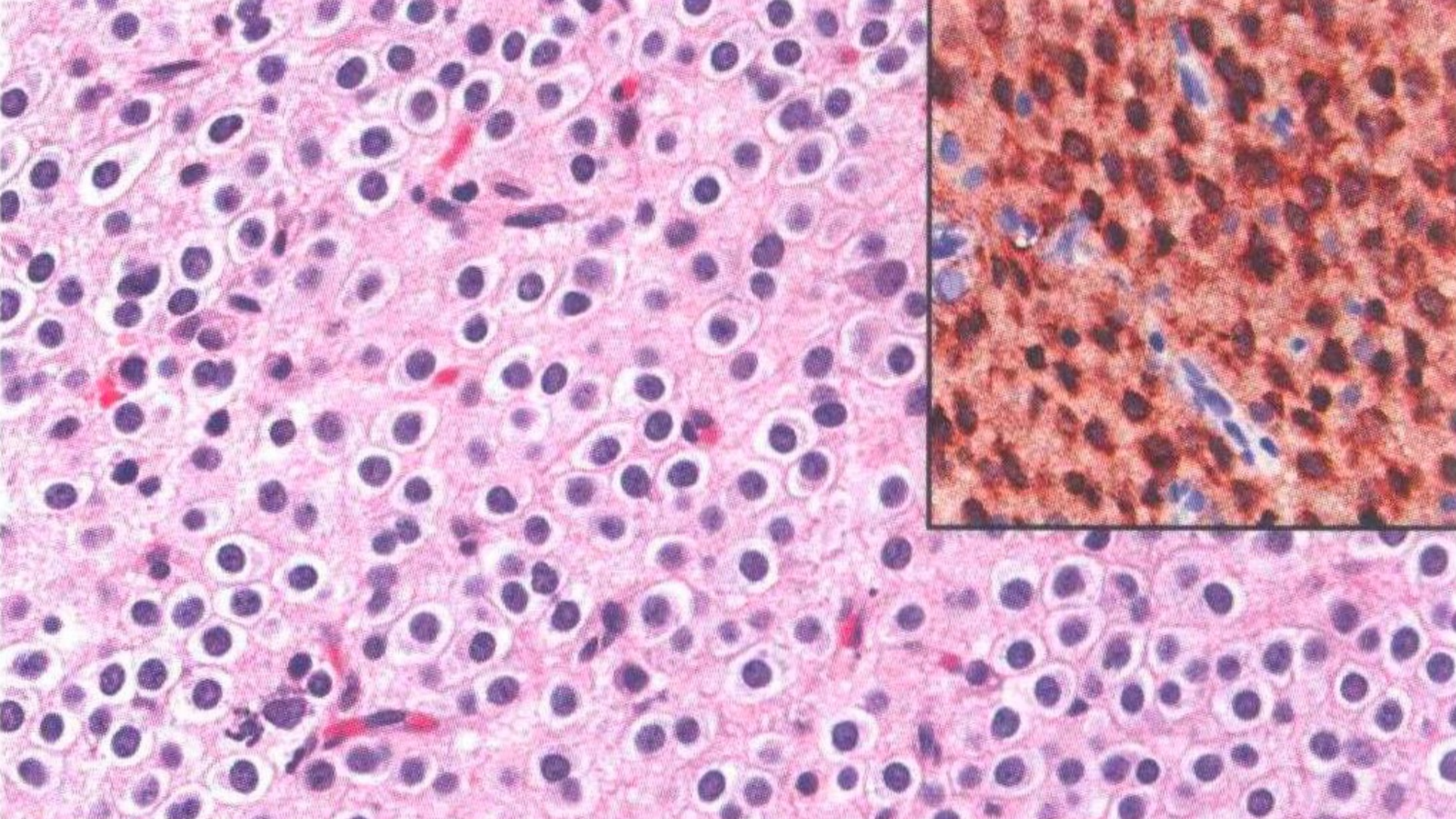
- infiltrative tumors with blurring of grey matter-white matter boundary.
- +/- gelatinous gray mass, cysts, focal hemorrhage, and calcification.

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

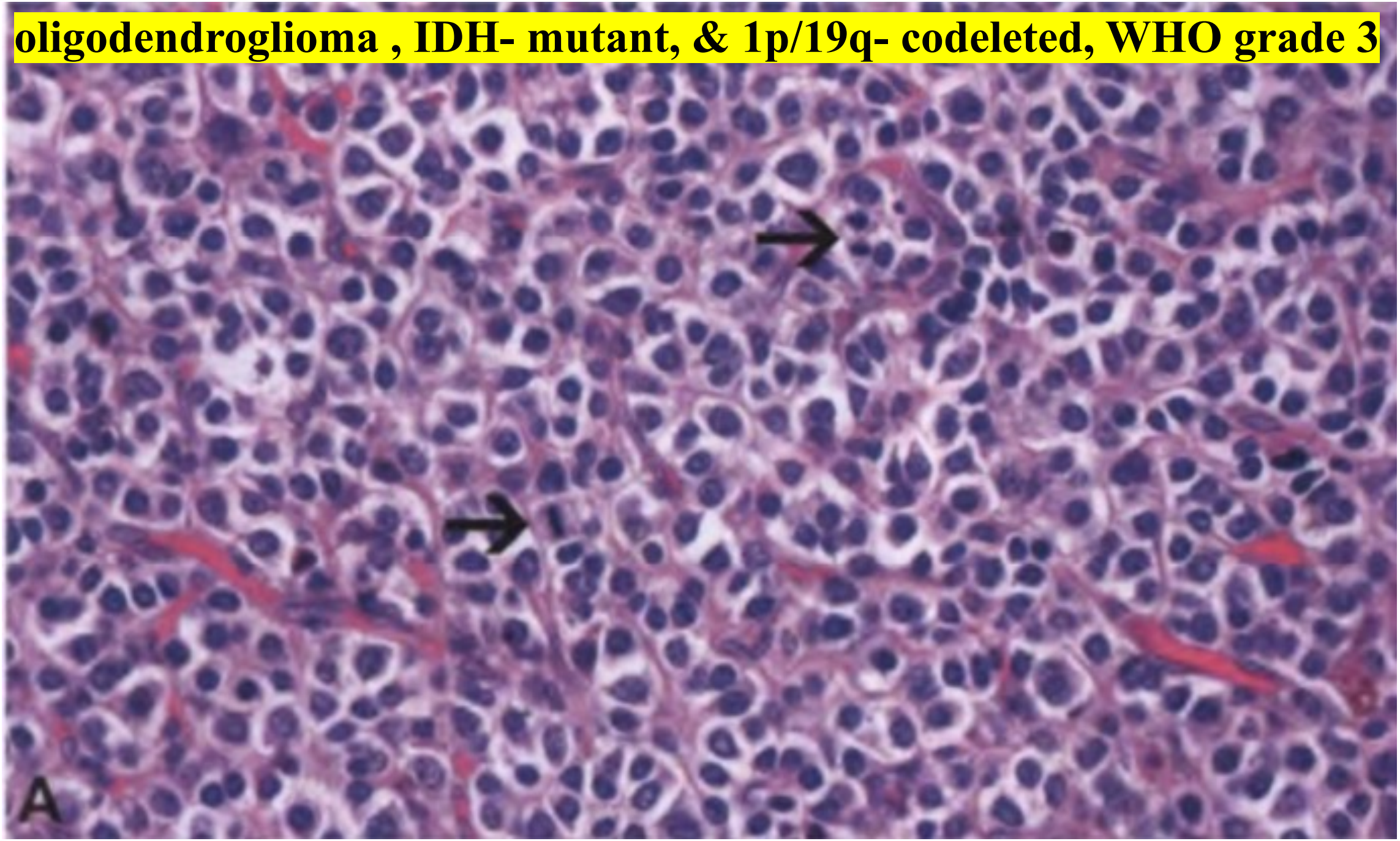






- Calcification up to 90% of cases.
- Mitotic activity usually is **absent or low (Ki67<5%)**
- **No** spontaneous necrosis
- **No** microvascular proliferation

oligodendroglioma , IDH- mutant, & 1p/19q- codeleted, WHO grade 3



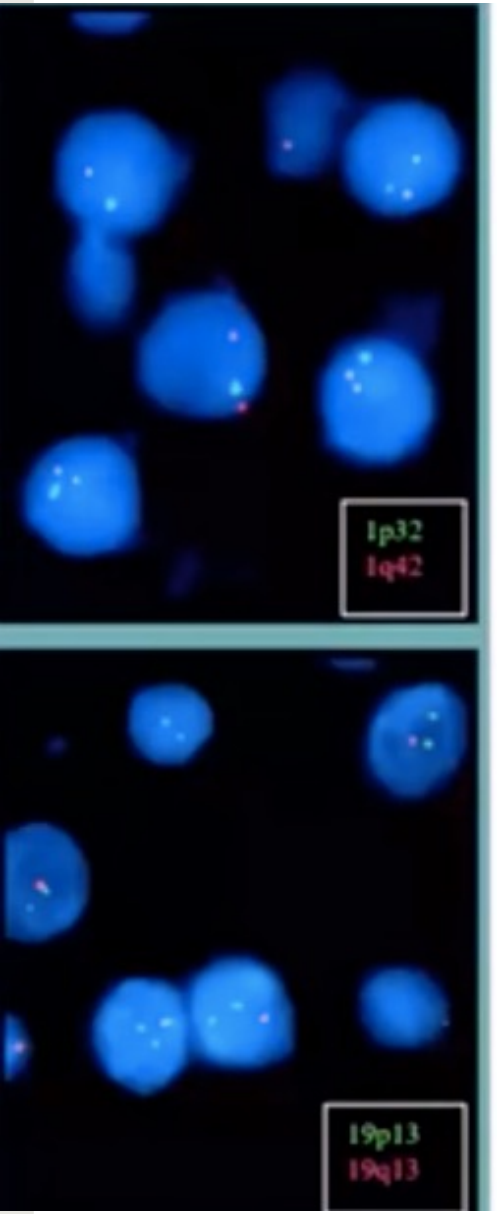
oligodendroglioma , IDH- mutant, & 1p/19q- codeleted WHO grade 3:

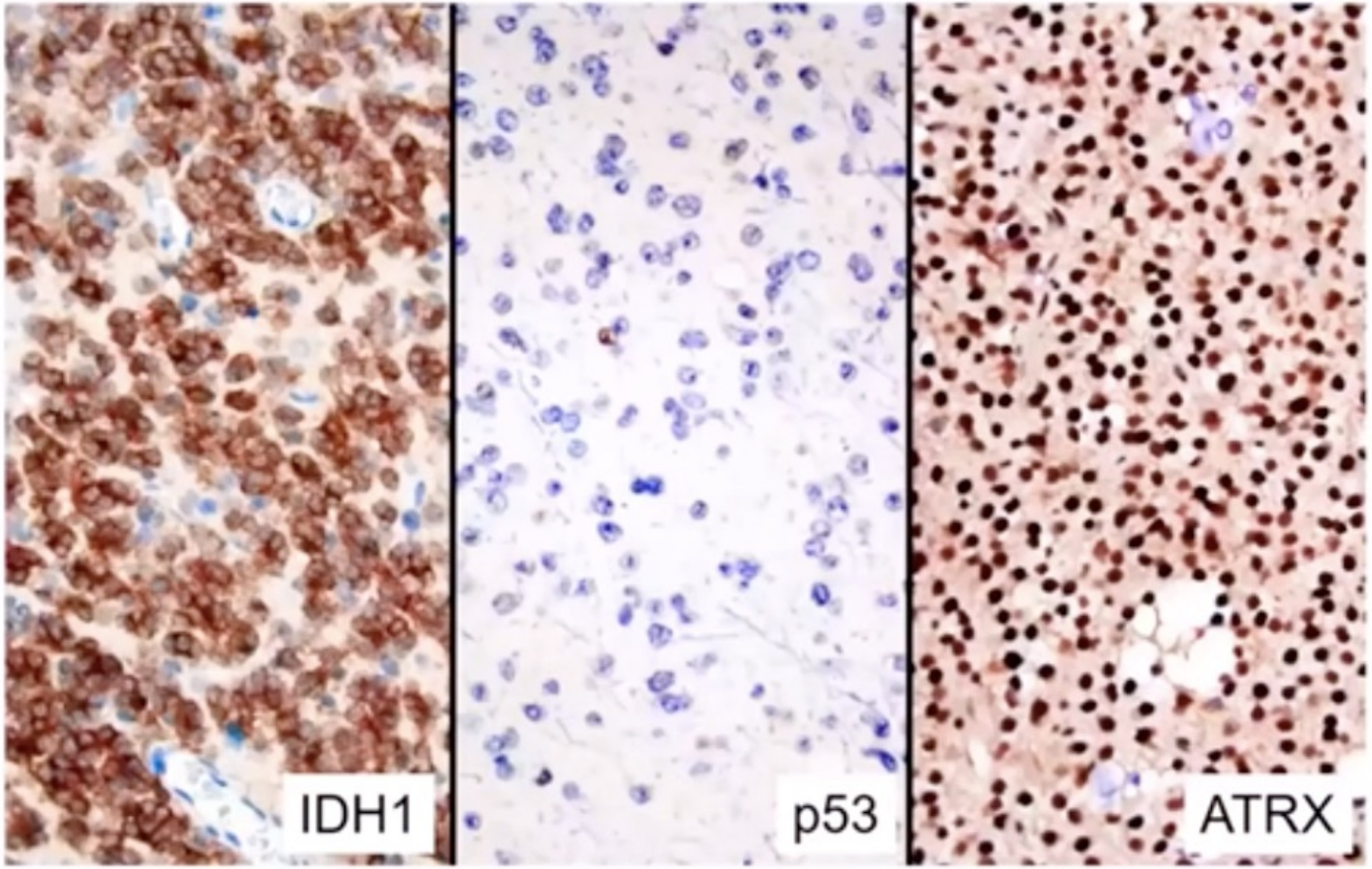
- Defined as: An IDH-mutant and 1p/19q-codeleted oligodendroglioma with focal or diffuse histological features of anaplasia (in particular, **pathological microvascular proliferation and/or brisk mitotic activity with or without necrosis**).

IDHm 1p/19q-codel Oligodendrogliomas, grades 2-3

Essential diagnostic criteria for **oligodendroglioma, IDH-mutant and 1p/19q-codeleted, WHO grade 2**
A diffuse glioma
WITH
an IDH1 codon 132 or IDH2 codon 172 missense mutation*
AND
combined whole arm deletions of 1p and 19q
AND
absence of histological features of anaplasia

Essential diagnostic criteria for **oligodendroglioma, IDH-mutant and 1p/19q-codeleted, WHO grade 3**
A diffuse glioma
WITH
an IDH1 codon 132 or IDH2 codon 172 missense mutation*
AND
combined whole arm deletions of 1p and 19q
AND
histological features of anaplasia, including brisk mitotic activity and/or pathological microvascular proliferation with or without necrosis AND/OR homozygous *CDKN2A* deletion**





UPDATE

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

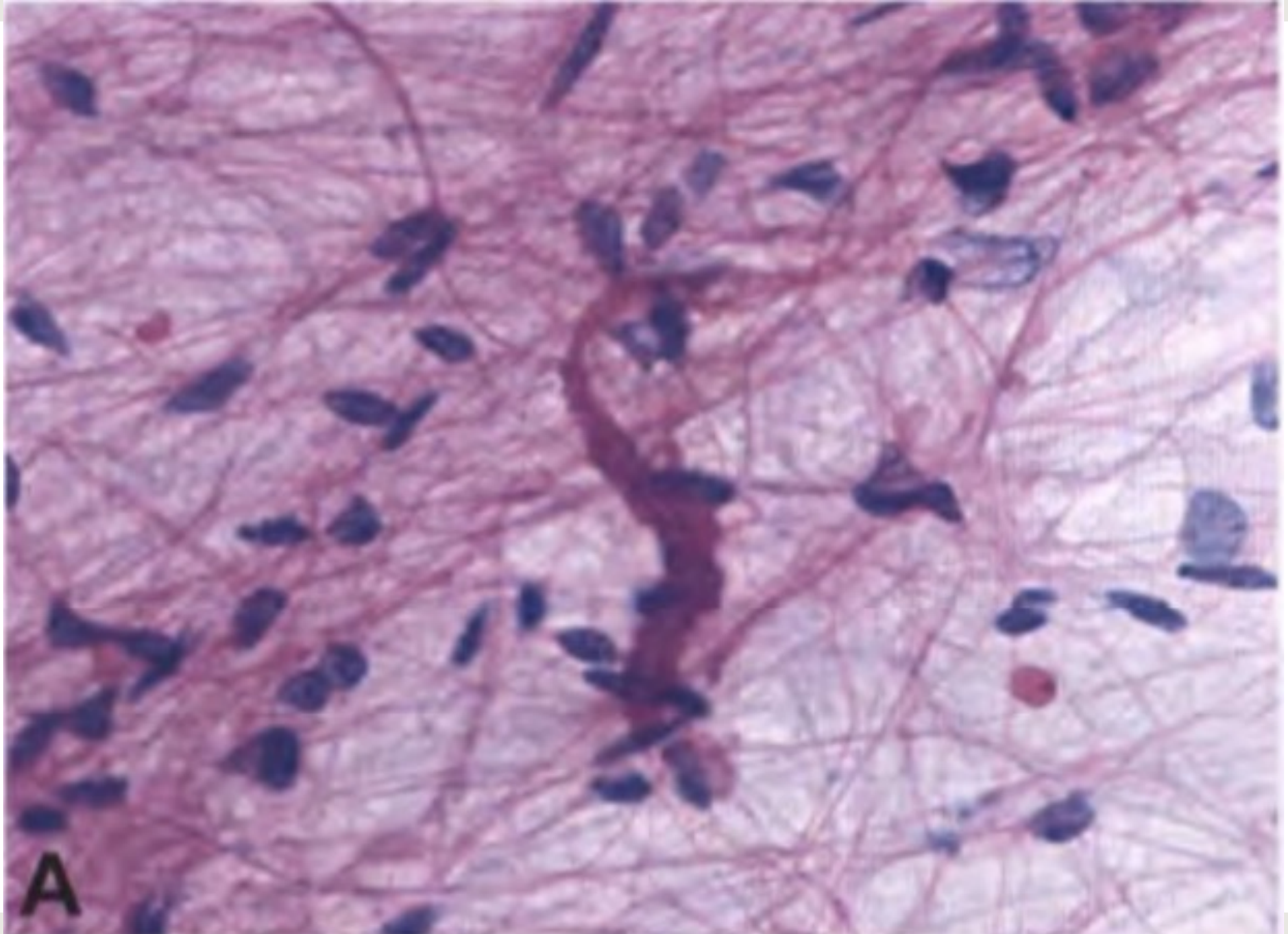
- **Treatment:** Well circumscribed tumor curable with complete resection

- **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
- eosinophilic granular bodies
- microcysts are often present
- necrosis and mitoses are rare.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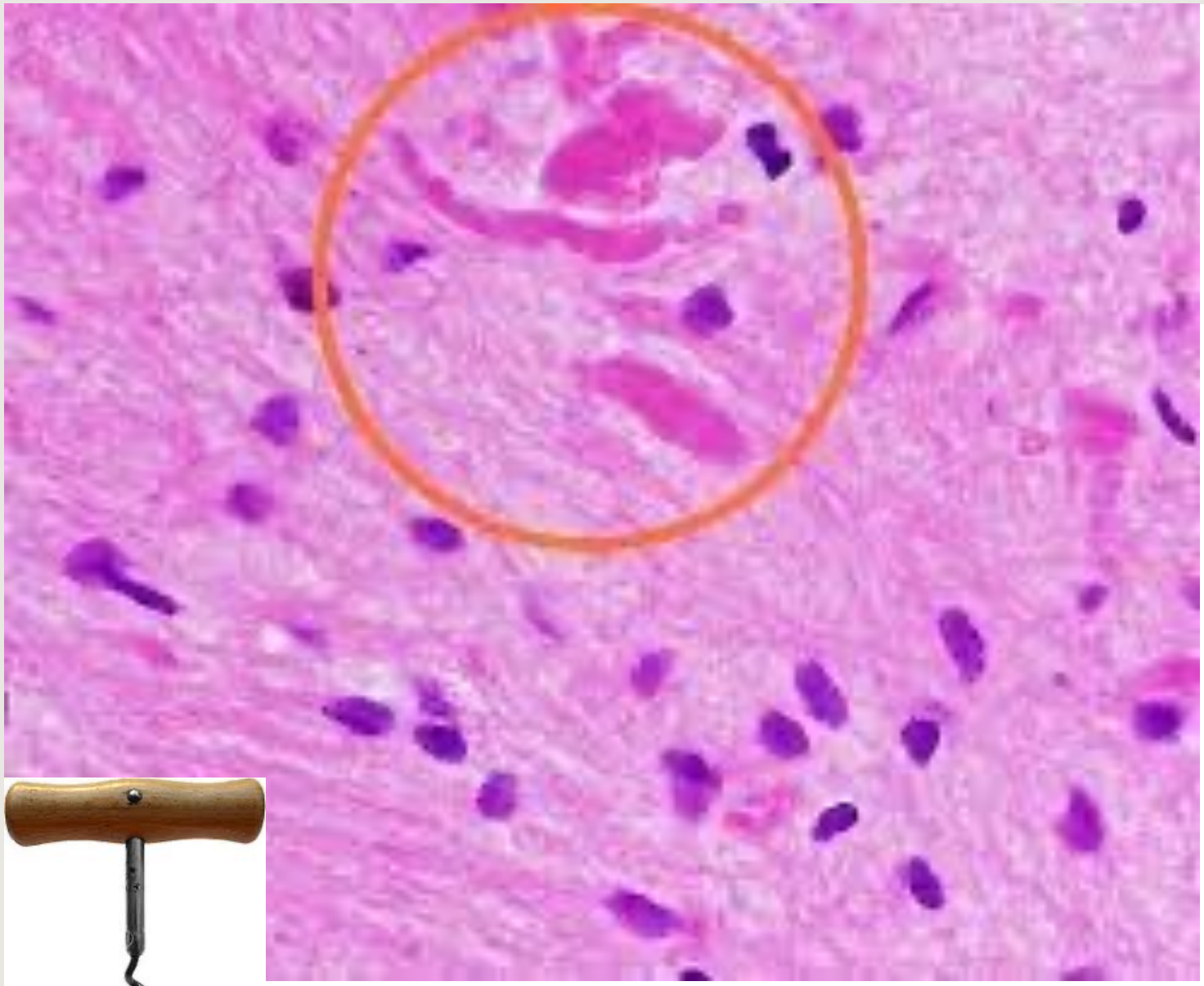
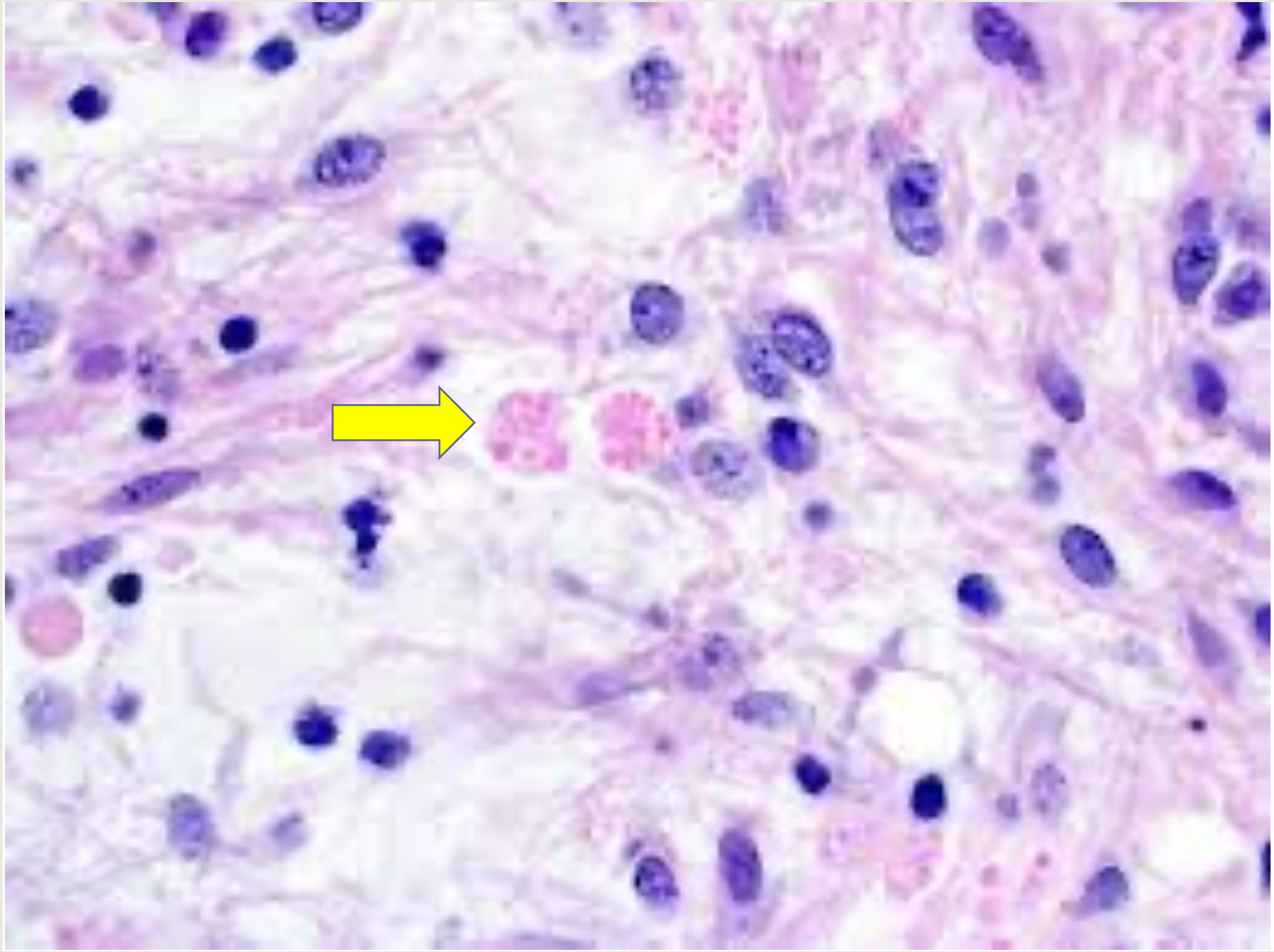


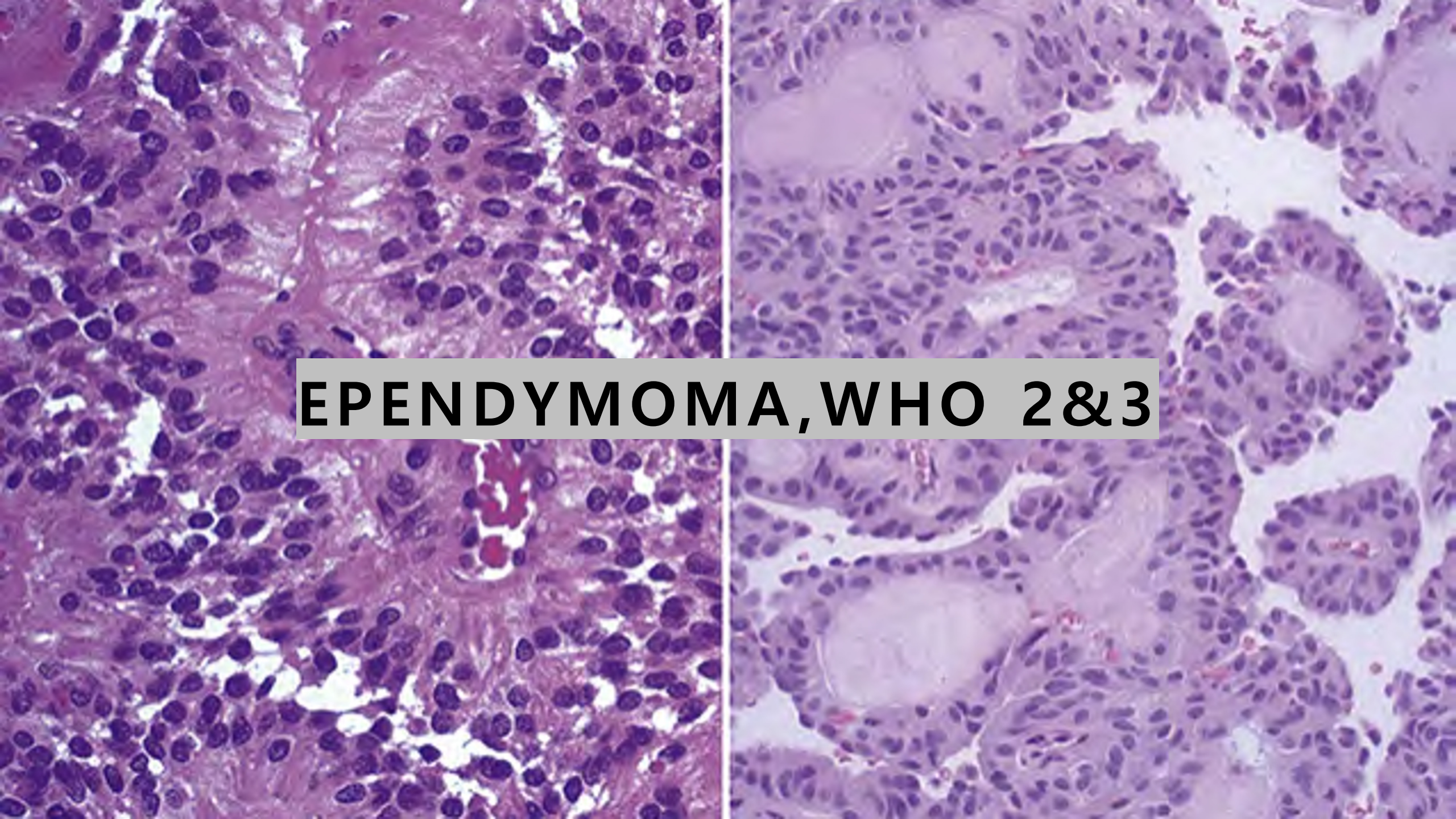
Rosenthal fibers

- 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.


EPENDYMOMA,WHO 2&3

Ependymoma:

- **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 spinal 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 examination.

Ependymoma WHO grade 2, Morphology:

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

- Ependymal rosettes: diagnostic hallmark of ependymoma (25%)

- perivascular pseudorosettes: not specific for ependymoma (seen in glioblastoma and medulloblastoma)

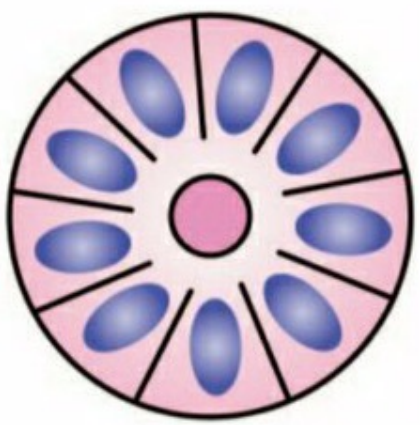
Ependymal rosettes:

- tumor cells arranged around central canal or lumen that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen.

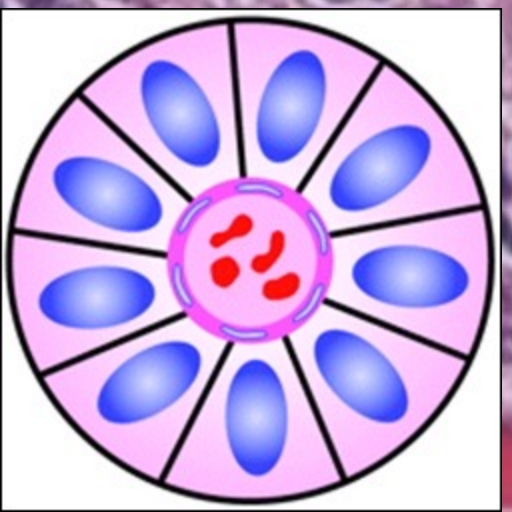
Perivascular pseudorosettes:

- 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.

Ependymal rosettes



perivascular pseudorosettes

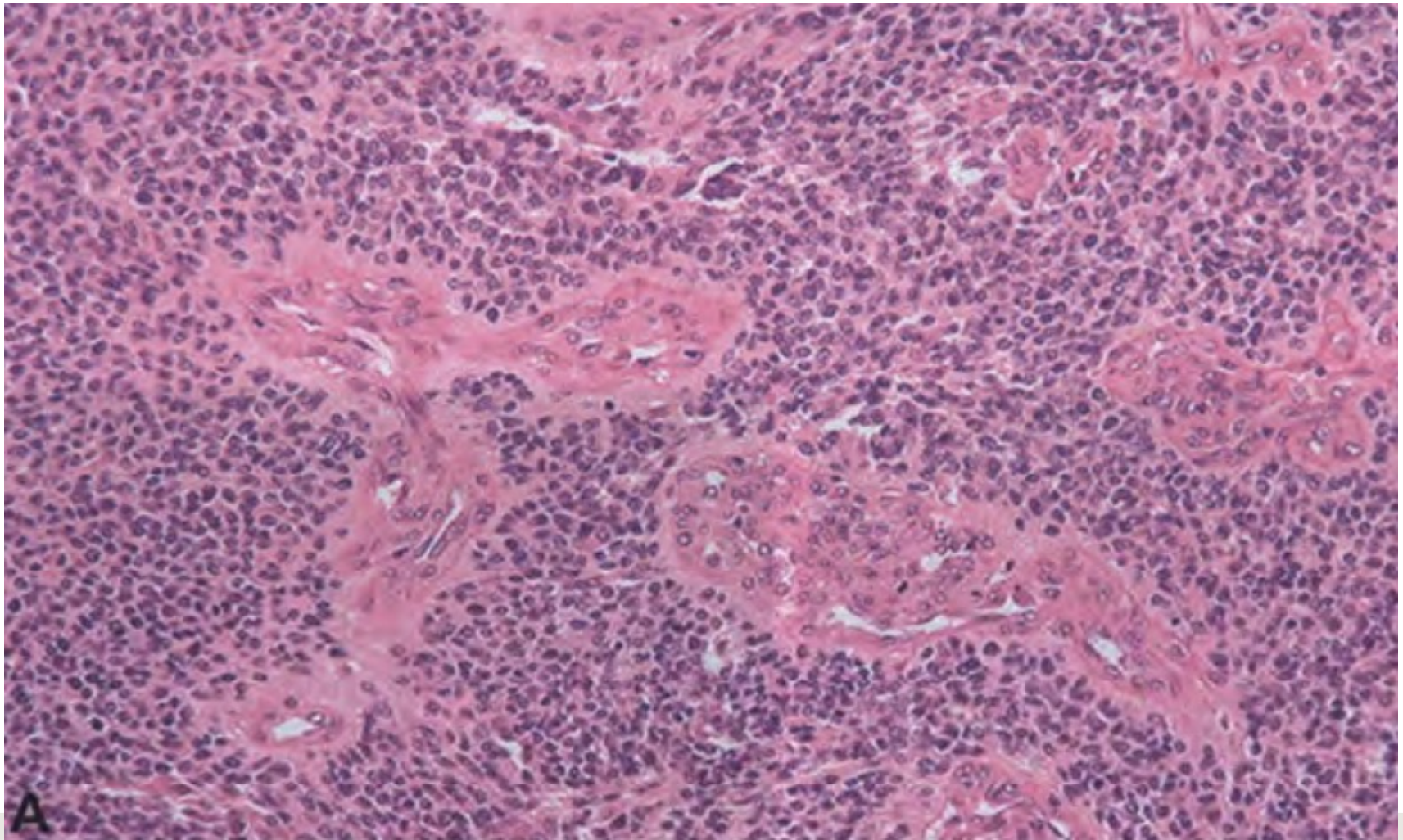


Ependymomas

		Age	Sex	WHO grade	Molecular Features	Outcome
Supratentorial	ST-SE		♂ ♂ ♂ ♀	1	*Balanced genome*	
Supratentorial	ST-~~ZFTA~~		♂ ♂ ♀		~~ZFTA~~ *fusions* *Chromothripsis* *CDKN2A/B loss*	
Supratentorial	ST-YAP1		♂ ♀ ♀ ♀		*YAP1 fusions*	
Infratentorial	PF-SE		♂ ♂ ♂ ♀	1	*Balanced genome*	
Infratentorial	PFA		♂ ♂ ♀		*EZHIP mutations* *H3K27M mutations* *Chr. 1q gain*	
Infratentorial	PFB		♂ ♀		*Chromosomal instability*	
Spinal	SP-SE		♂ ♀	1	*Chr. 6q deletion*	
Spinal	SP-EP		♂ ♂ ♀	2 / 3	*NF2 mutations*	
Spinal	SP-MP		♂ ♀	2	*Chromosomal instability*	
Spinal	SP-MYCN		♂ ♀		*MYCN amplification (Chr. 2p)*	

UPDATE

- **ependymomas, WHO grade 3:**
- Show less evident ependymal differentiation.
- brisk mitotic rates, and microvascular proliferation carry more prognostic impact than necrosis and atypia.




thank you