CENTRAL NERVOUS SYTEM TUMORS(3)

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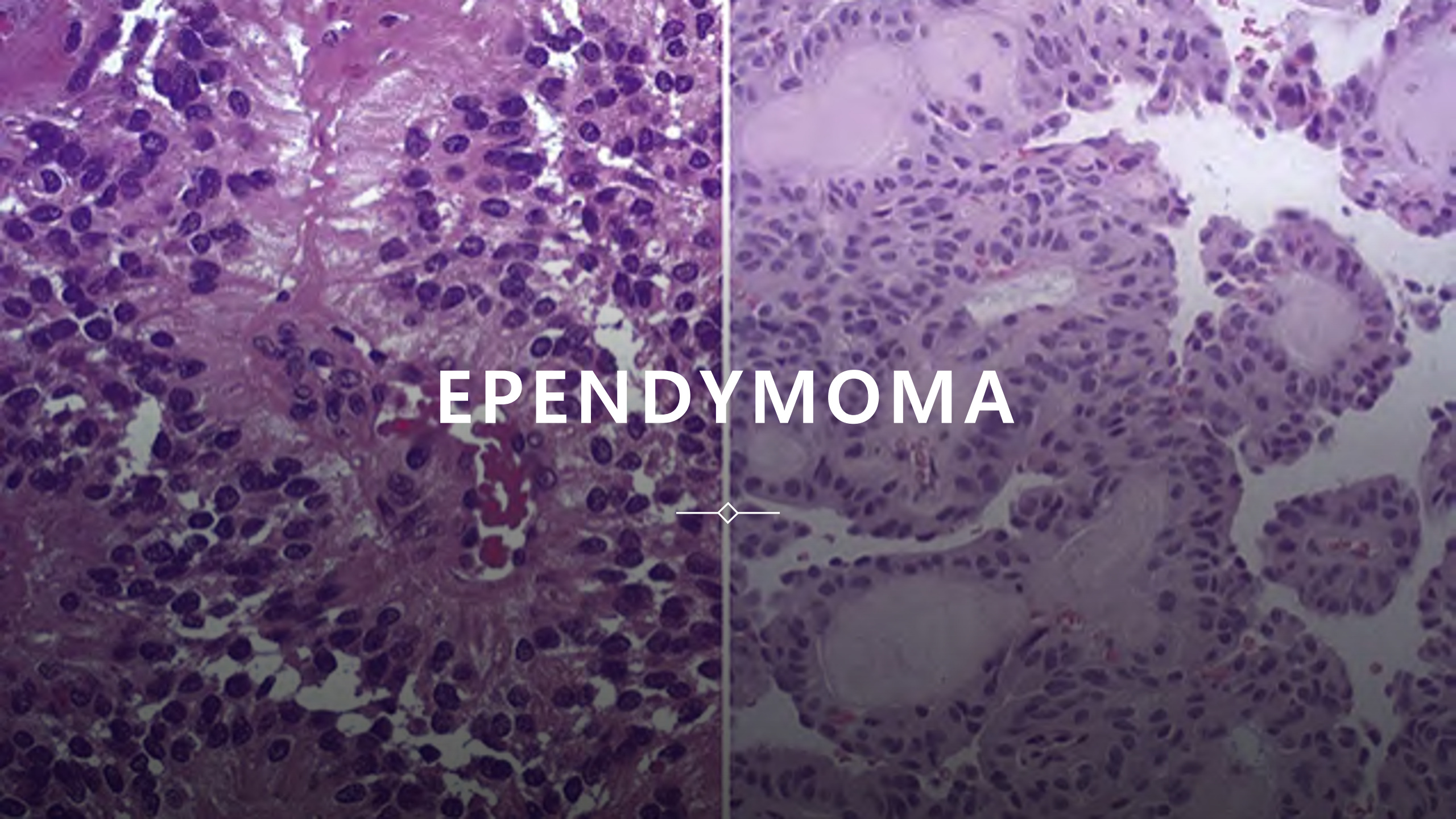


EPENDYMOMA

Ependymoma:

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

- **Location:**
  - **posterior fossa**
  - **supratentorial**
  - **spinal**

Ependymoma:

- **Age:**
  - In the first 2 decades of life; near **the 4th ventricle (post. Fossa)**
  - 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, macroscopic:

- solid and non-infiltrative mass.
- moderately well demarcated from adjacent brain
- the proximity to vital structures often makes complete removal impossible, except in the spinal cord
- in the spinal cord total resection is more feasible.

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)

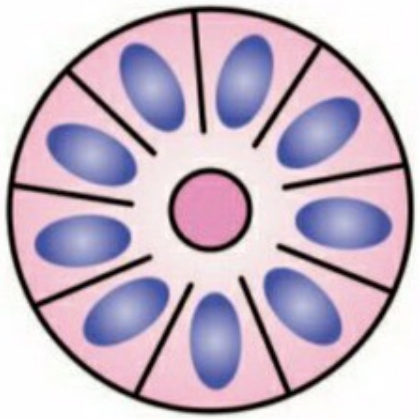
Ependymal rosettes:

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

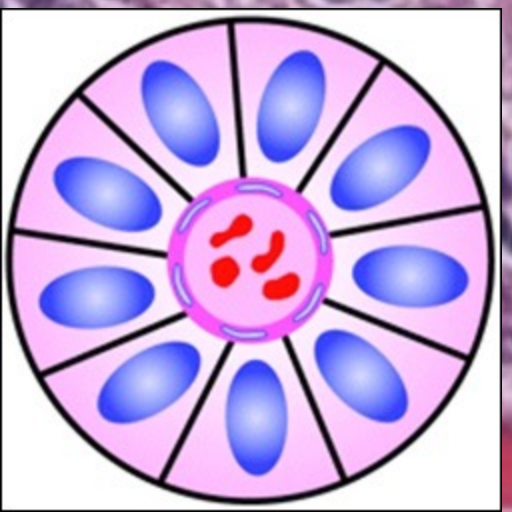
Perivascular pseudorosettes:

- 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.

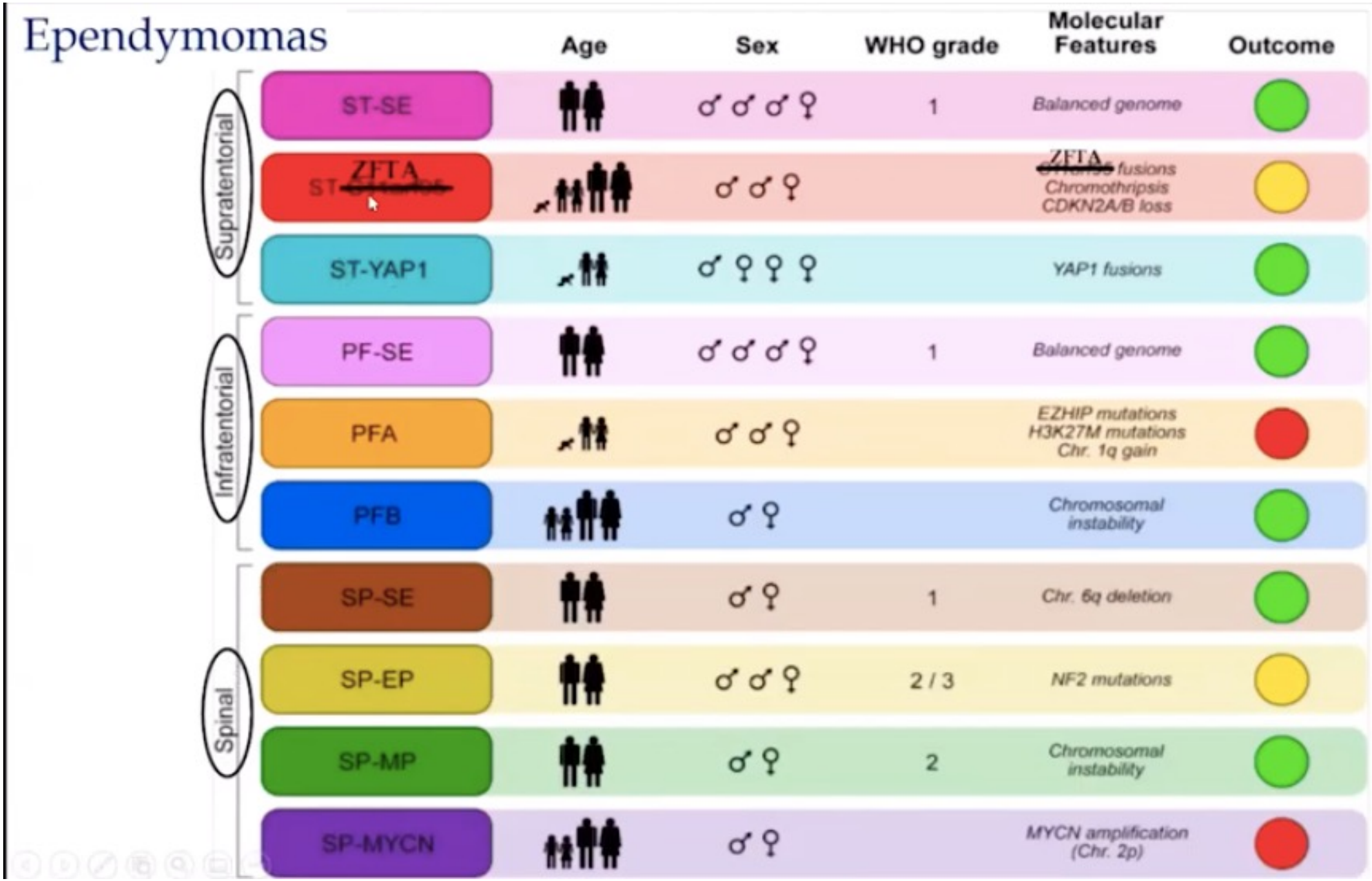
Ependymal rosettes



perivascular pseudorosettes

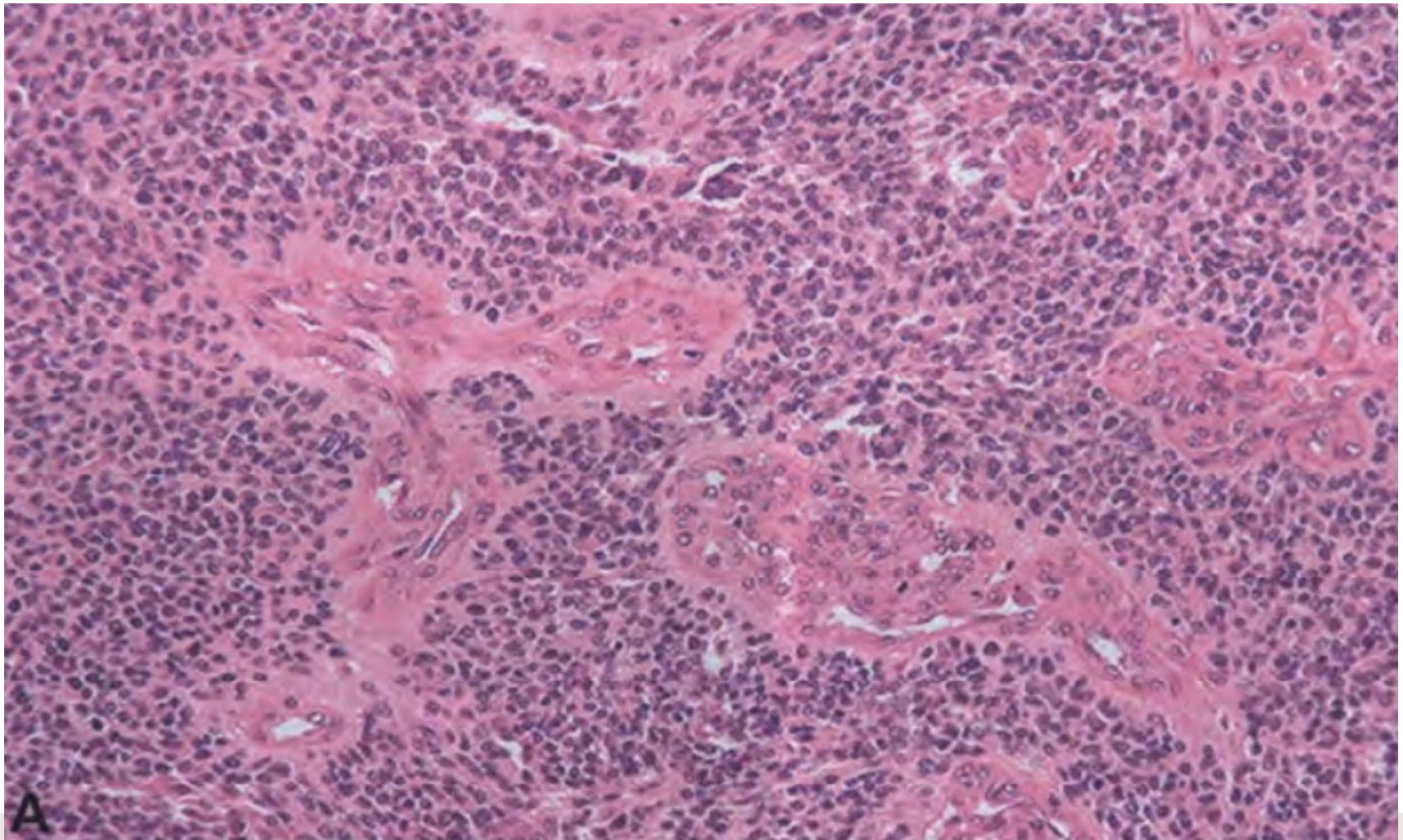


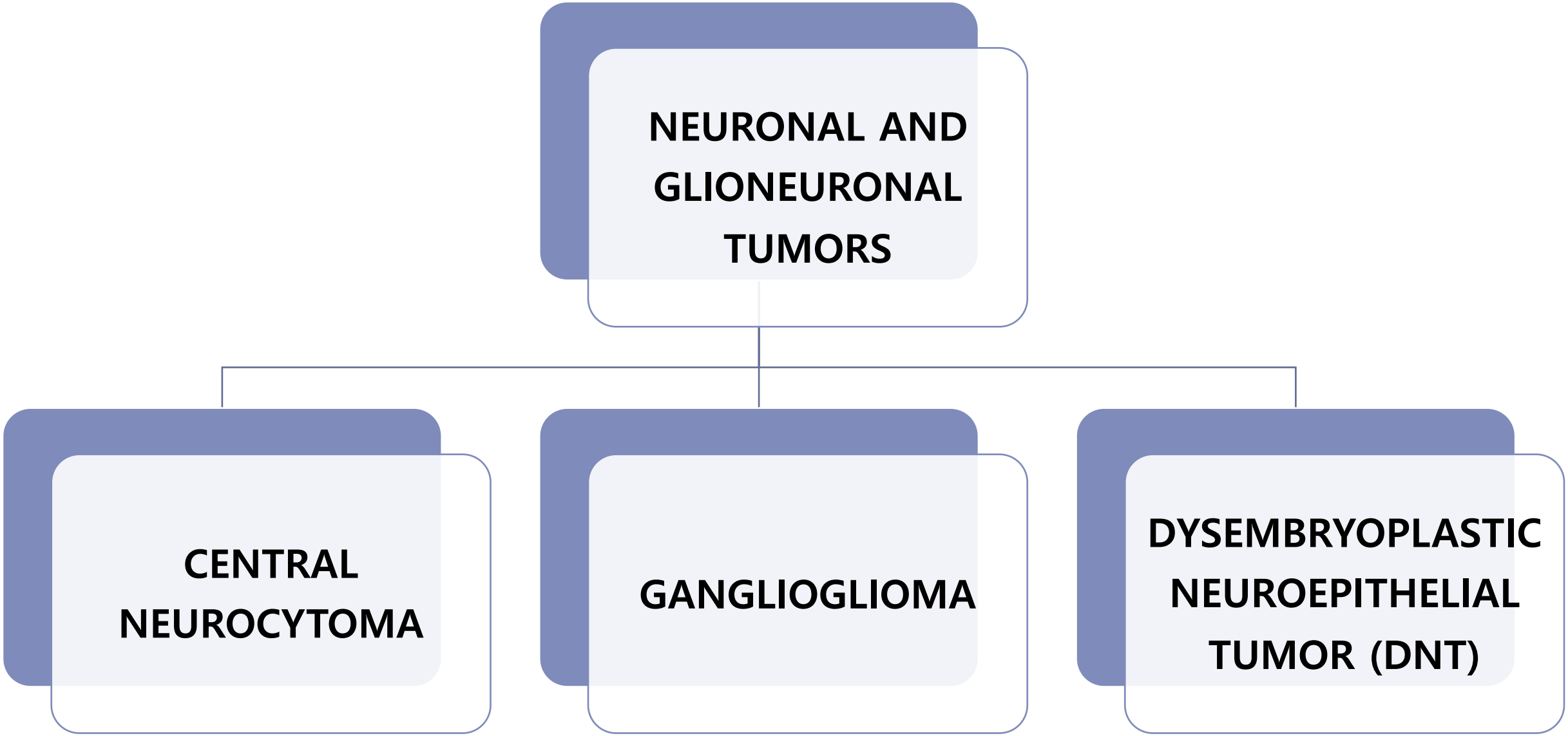
Ependymomas



UPDATE

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




NEURONAL AND GLIONEURONAL TUMORS
CENTRAL NEUROCYTOMA
GANGLIOGLIOMA
DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMOR (DNT)

Neuronal Tumors

- **less** frequent than gliomas
- composed of cells with **neuronal characteristics and express neuronal markers**, such as synaptophysin and neurofilaments.
- typically, **lower-grade** lesions
- often present with **seizures**.

- **Central neurocytoma, WHO grade 2: neuronal tumor** within and adjacent to the **lateral ventricle(s) and/or the third ventricle** affecting **young adults**

- **Gangliogliomas, WHO grade 1: glioneuronal tumor** affecting **children and young adults.** composed of a mixture of **neoplastic ganglion and glial cells**, most commonly in the **temporal lobe.**

- **Dysembryoplastic neuroepithelial tumor (DNT), WHO grade 1: glioneuronal tumor** affecting the cerebral cortex of **children and young adults** most commonly in the **superficial temporal lobe.**

Embryonal (Primitive) Neoplasms

- Primitive or undifferentiated small round cell tumor of neuroectodermal origin resembling normal progenitor cells in the developing CNS.

- The most common CNS embryonal tumor is **Medulloblastoma** accounting for 20% of pediatric brain tumors

Medulloblastoma, WHO grade 4:

- predominantly in **children**
- mainly in **cerebellum**
- **All are highly malignant, WHO grade 4**
- **radiosensitive**.
- the prognosis for untreated patients is **dismal**
- **5-year survival rate may be as high as 75% w**ith total excision, chemotherapy, and irradiation

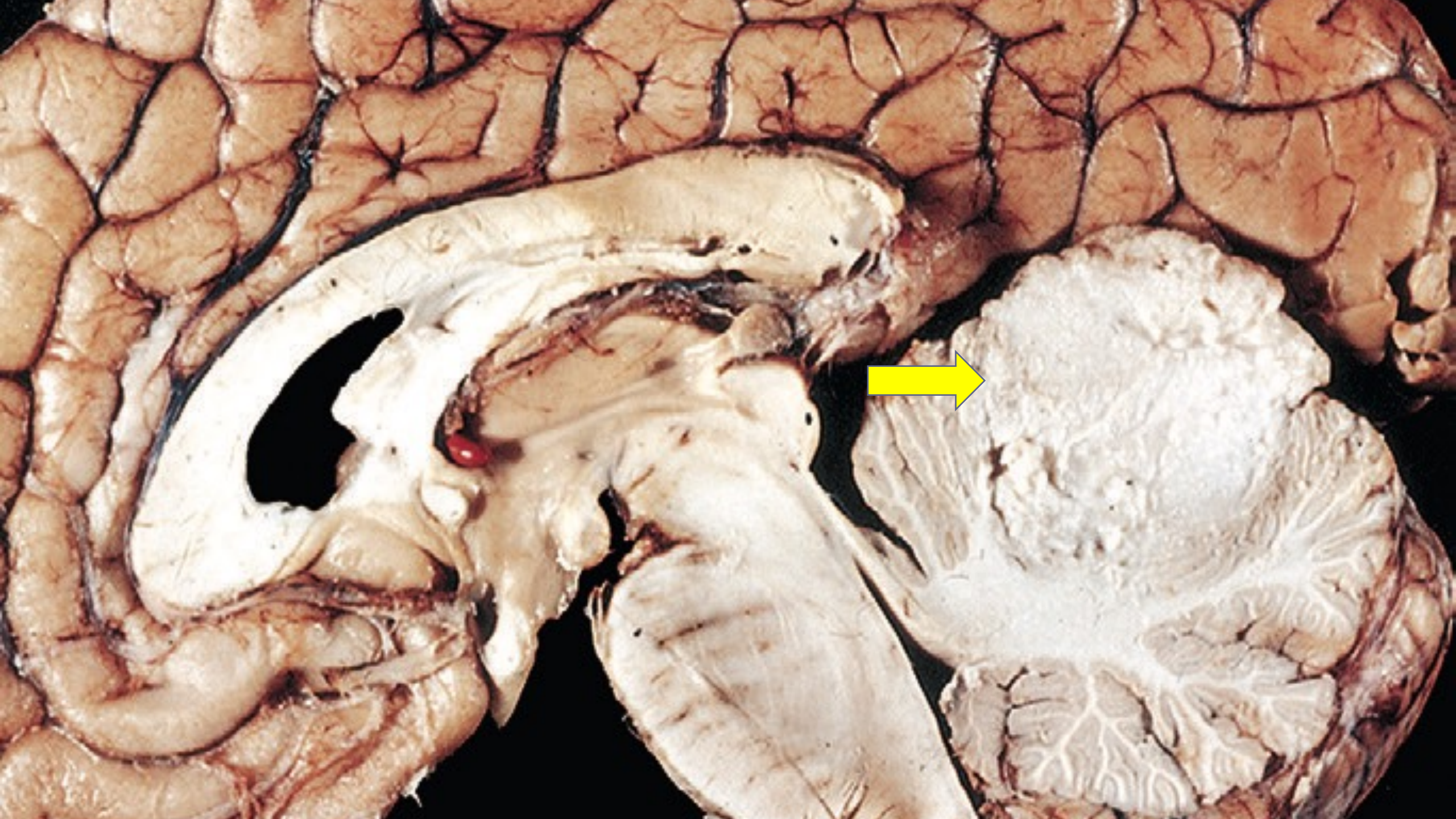
Macroscopic:

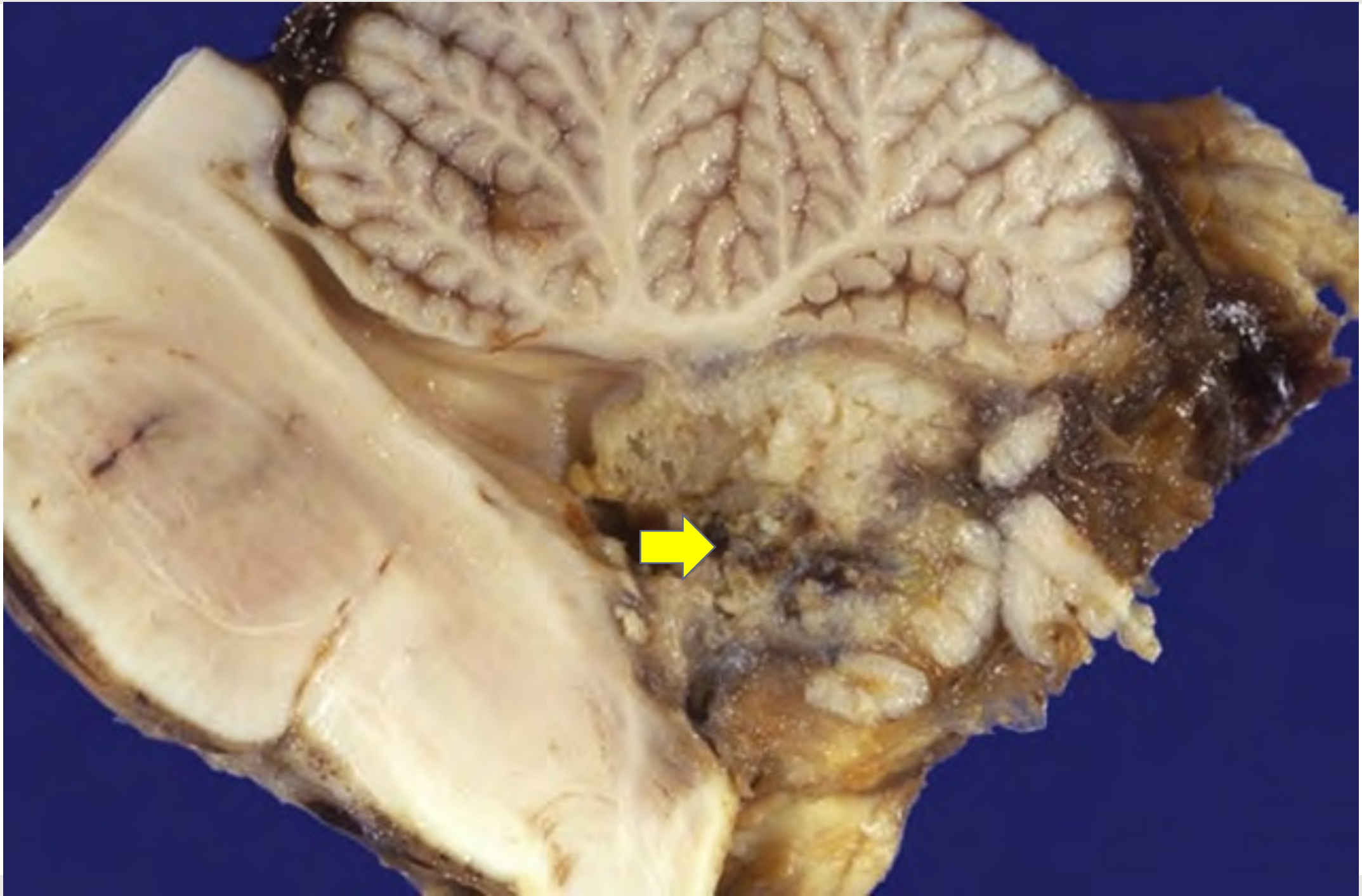
- well circumscribed (often)

- may extend to the cerebellar surface and involve the Leptomeninges

- **common complication:**
  - Medulloblastomas have tendency to spread to the subarachnoid space
    → Dissemination through the CSF

- +/- Small foci of necrosis, but extensive necrosis is rare.





Morphology:

- Very Cellular

- sheets of small primitive cells (“small blue”), Each cell with little cytoplasm and hyperchromatic elongated or crescent-shaped nuclei

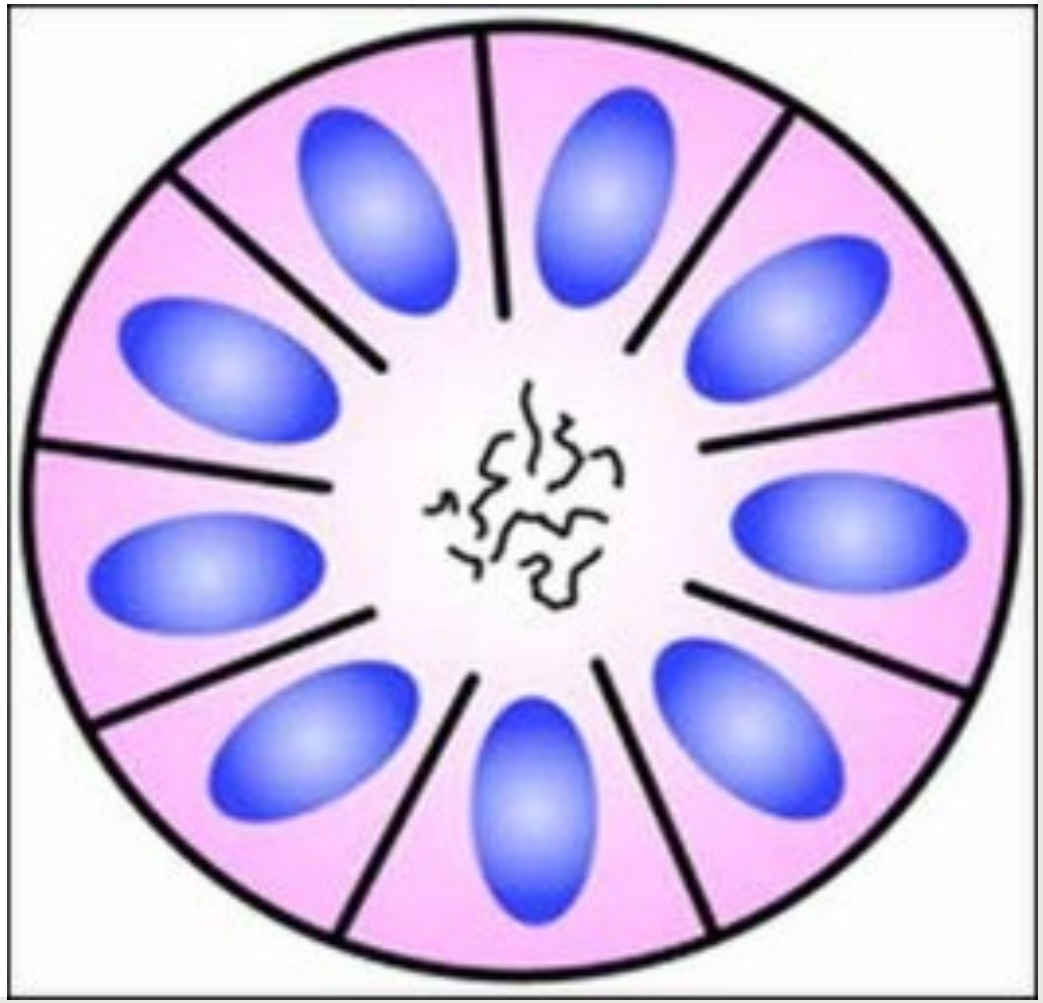
  - mitoses are abundant.

  - often express neuronal markers such as synaptophysin

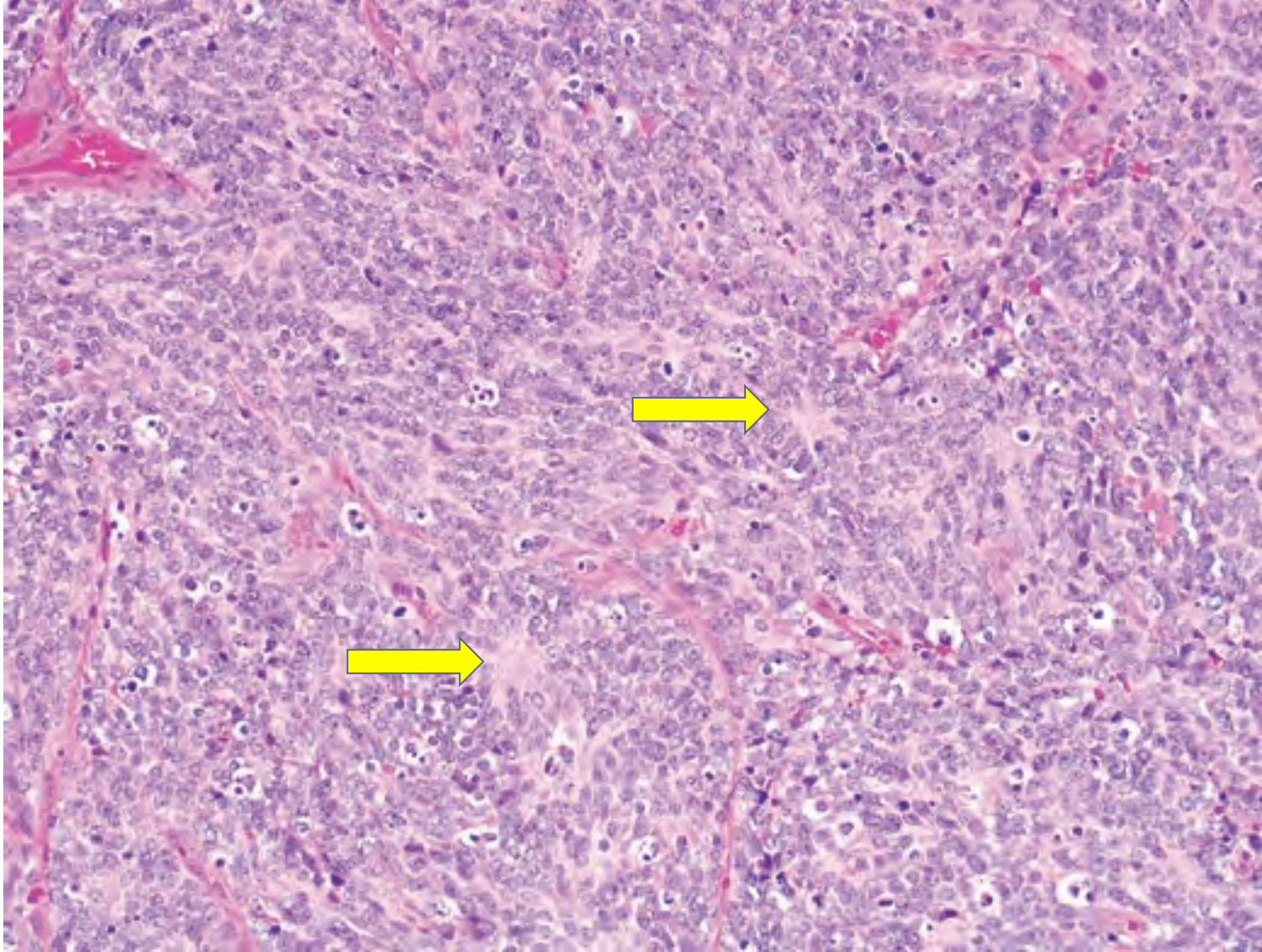
  - the expression of glial markers (GFAP) is less common.

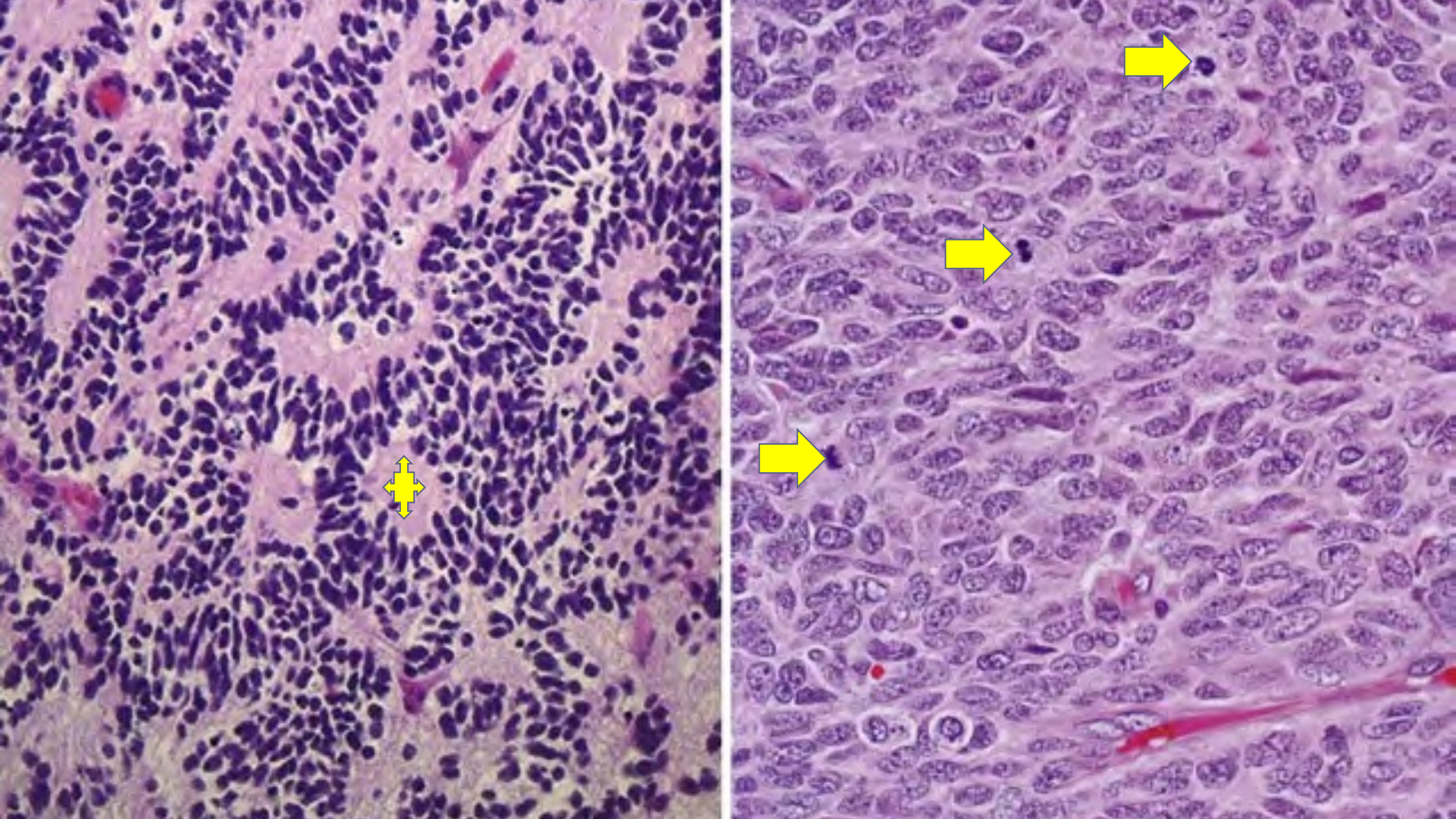
Morphology:

- **Homer Wright Rosettes:**
  - primitive tumor cells surrounding central neuropil (delicate pink material formed by neuronal processes).
  - Represents focal neuronal differentiation
  - Not specific; seen also in neuroblastoma and pineablastoma



Sheets of primitive small blue cells that form Homer Wright rosettes with central neuropil (arrows).





Oncogenic pathways in Medulloblastoma:

- **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.

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

- **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.**

- Medulloblastomas are classified according to **molecular characteristics** in addition to **histopathological features into:**

- Medulloblastoma, WNT activated
- Medulloblastoma, SHH activated and P53 wildtype
- Medulloblastoma, SHH activated and P53 mutant
- Medulloblastoma, non-WNT/non-SHH

Table 8.01 Medulloblastoma subtypes characterized by combined genetic and histological parameters

Genetic profile	Histology	Prognosis
Medulloblastoma, WNT-activated	Classic	Low-risk tumour; classic morphology found in almost all WNT-activated tumours
	Large cell / anaplastic (very rare)	Tumour of uncertain clinicopathological significance
Medulloblastoma, SHH-activated, TP53-mutant	Classic	Uncommon high-risk tumour
	Large cell / anaplastic	High-risk tumour; prevalent in children aged 7-17 years
	Desmoplastic/nodular (very rare)	Tumour of uncertain clinicopathological significance
Medulloblastoma, SHH-activated, TP53-wildtype	Classic	Standard-risk tumour
	Large cell / anaplastic	Tumour of uncertain clinicopathological significance
	Desmoplastic/nodular	Low-risk tumour in infants; prevalent in infants and adults
	Extensive nodularity	Low-risk tumour of infancy
Medulloblastoma, non-WNT/non-SHH, group 3	Classic	Standard-risk tumour
	Large cell / anaplastic	High-risk tumour
Medulloblastoma, non-WNT/non-SHH, group 4	Classic	Standard-risk tumour; classic morphology found in almost all group 4 tumours
	Large cell / anaplastic (rare)	Tumour of uncertain clinicopathological significance

Meningiomas

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

- **Age at presentation:** adults (women>men)

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

Meningiomas

- **Presentation:** Most common headache, seizures, weakness (depends on location)
- **Prognosis:** determined by the lesion size and location, surgical accessibility, and histologic grade.
- usually solitary, but multiple sites can be affected
- Meningiomas express **progesterone receptors** and may grow more rapidly during pregnancy, only to regress after delivery.

Pathogenesis

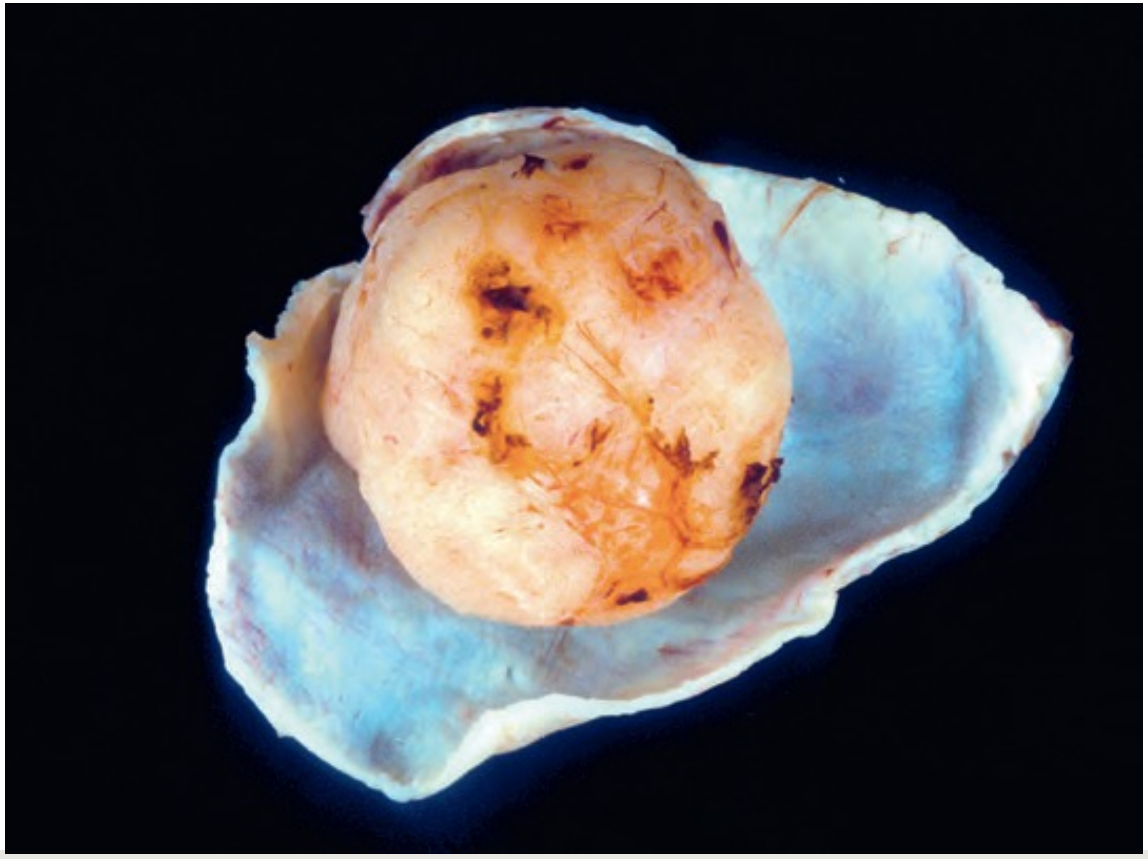
- The most common cytogenetic abnormality is loss of chromosome 22, especially the long arm (22q).

- The deletions include the region that harbors the NF2 gene

- meningiomas are a common lesion in the setting of NF2.

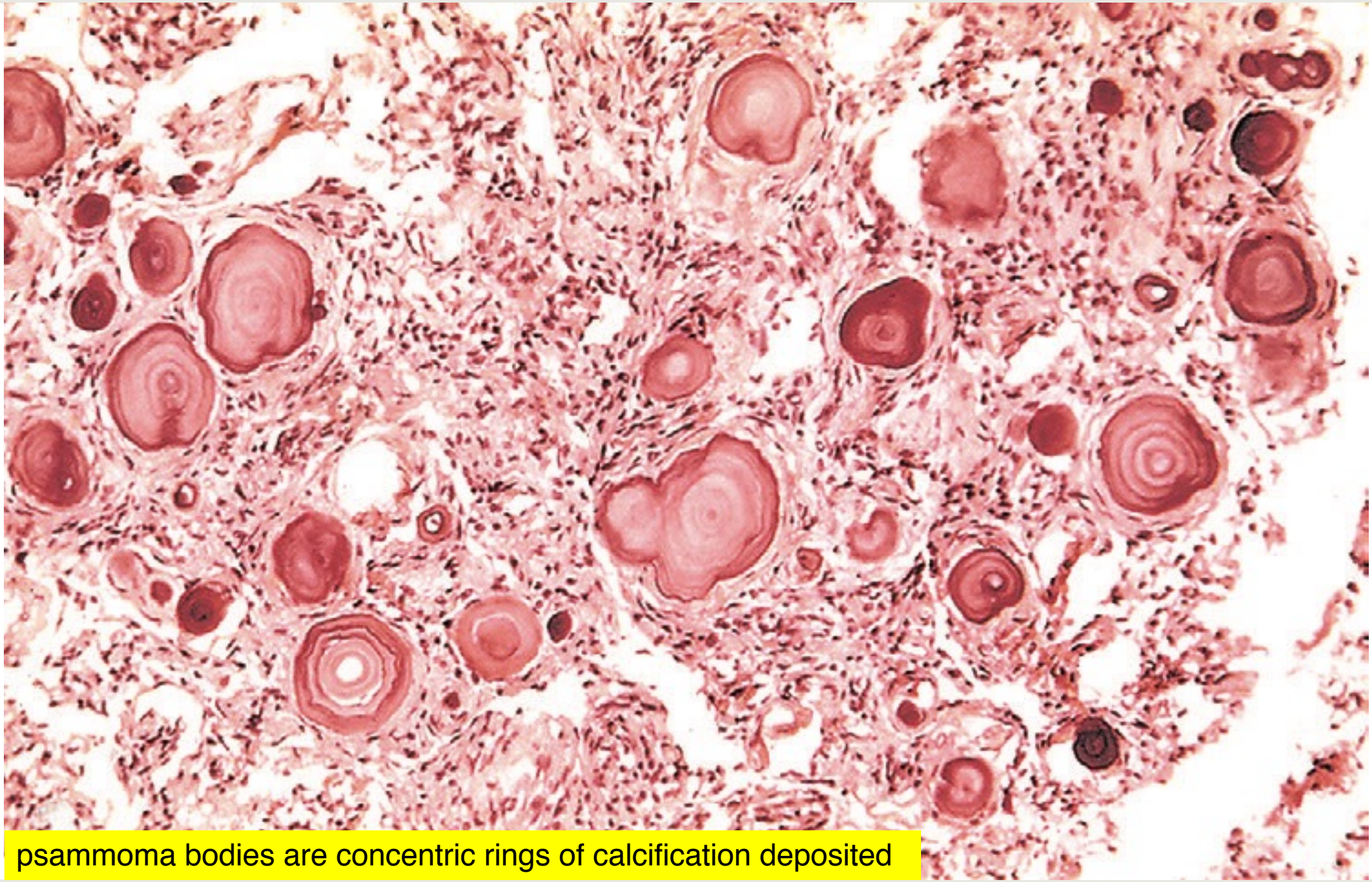
Macroscopic:

- rubbery, rounded, or bosselated dural masses that compress underlying brain
- Mostly separable from underlying brain, but some tumors are infiltrative



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
- Many histologic patterns, with no prognostic difference
  - meningothelial (most common)→clusters of epithelioid cells with fuzzy or indiscernible cell membranes
  - Other patterns include fibroblastic, transitional, and psammomatous



psammoma bodies are concentric rings of calcification deposited

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 a high N/C ratio, prominent nucleoli, patternless growth, or necrosis; **or**

3- **clear cell** or **chordoid subtypes of meningioma**

ANAPLASTIC MENINGIOMAS, WHO grade 3 (malignant):

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

1. **>20 mitoses/ 10HPF;** or

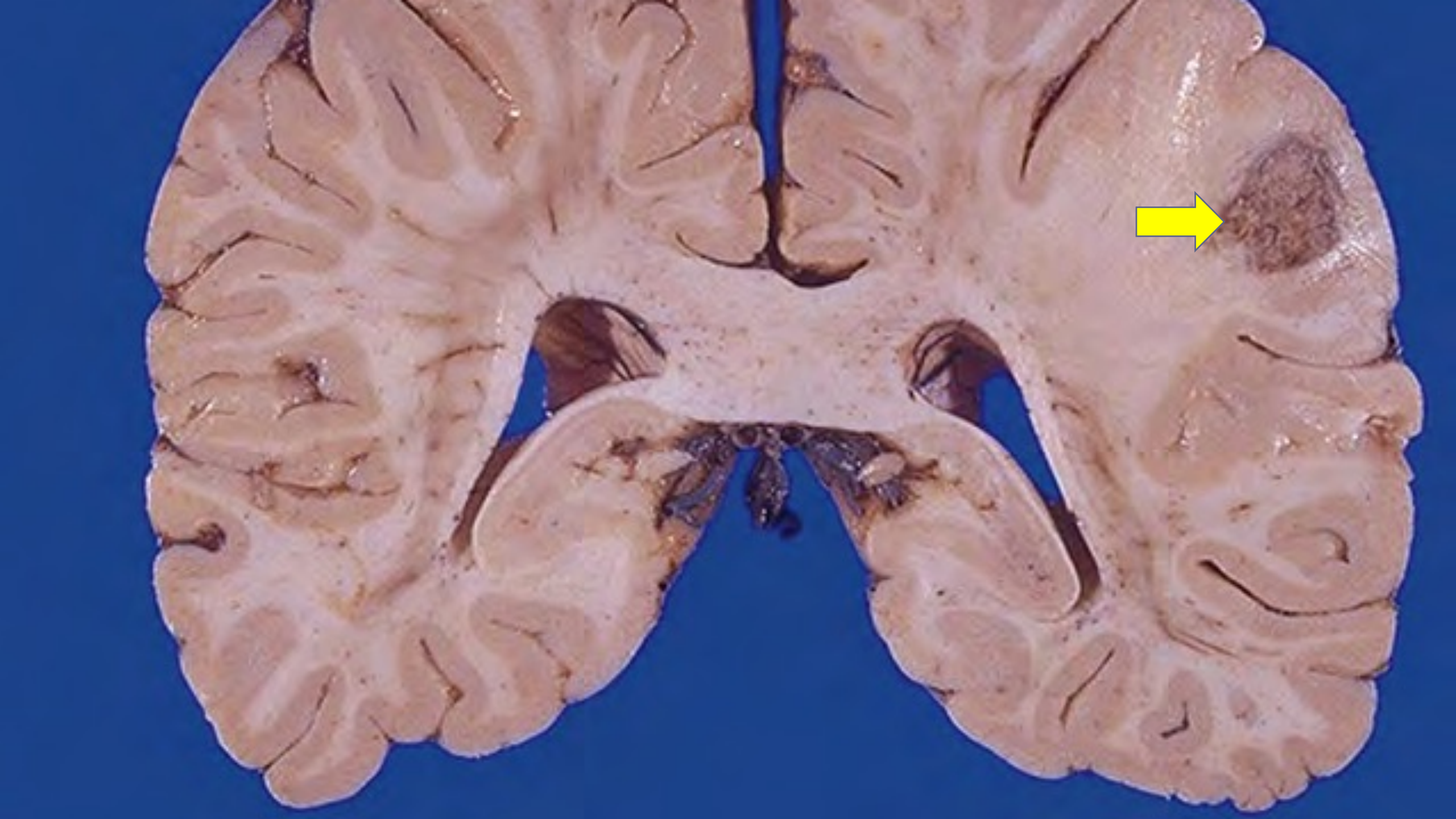
1. **Papillary;** or **rhabdoid meningioma.**

Metastatic Tumors:

- 25-50% of intracranial tumors.
- mostly **carcinomas**
- The most common primary sites are **lung, breast, skin (melanoma), kidney, and gastrointestinal tract (**80% of cases).

- **sharply demarcated masses**, often at the grey-white matter junction, and elicit local edema

- The boundary between tumor and brain parenchyma is sharp at the microscopic level with surrounding reactive gliosis.



OTHER PARENCHYMAL TUMORS

Primary Central Nervous System Lymphoma:

- **the most common CNS neoplasm in immunosuppressed individuals**

- In non-immunosuppressed populations, the frequency increases after 60 years of age.

- aggressive disease , poor response to chemotherapy (especially if compared with comparable histology that occur at non-CNS site)

- The most common type: **diffuse large B-cell lymphomas**

- **Primary brain lymphoma:**

  - multifocal
  - involvement outside of the CNS (in lymph nodes or BM) is a rare and late complication.
  - relatively **well defined** as compared with glial neoplasms but not as discrete as metastases.

Germ Cell Tumors

- Can be **primary or metastatic**

- **Primary brain germ cell tumors:**
  - **Locations:** along the **midline**, most commonly in the **pineal and the suprasellar** regions (post. Pituitary and infundibular stalk).

  - 90% during the **first 2 decades of life**.

Germ Cell Tumors

- The most common primary CNS germ cell tumor is **germinoma**, closely resembles testicular seminoma.

- Other germ cell tumors include: teratoma (mature and immuture), embryonal carcinoma, yolk sac tumor, chriocacinoma and mixed germ cell tumors


thank you