

CENTRAL NERVOUS SYTEM TUMORS(3)



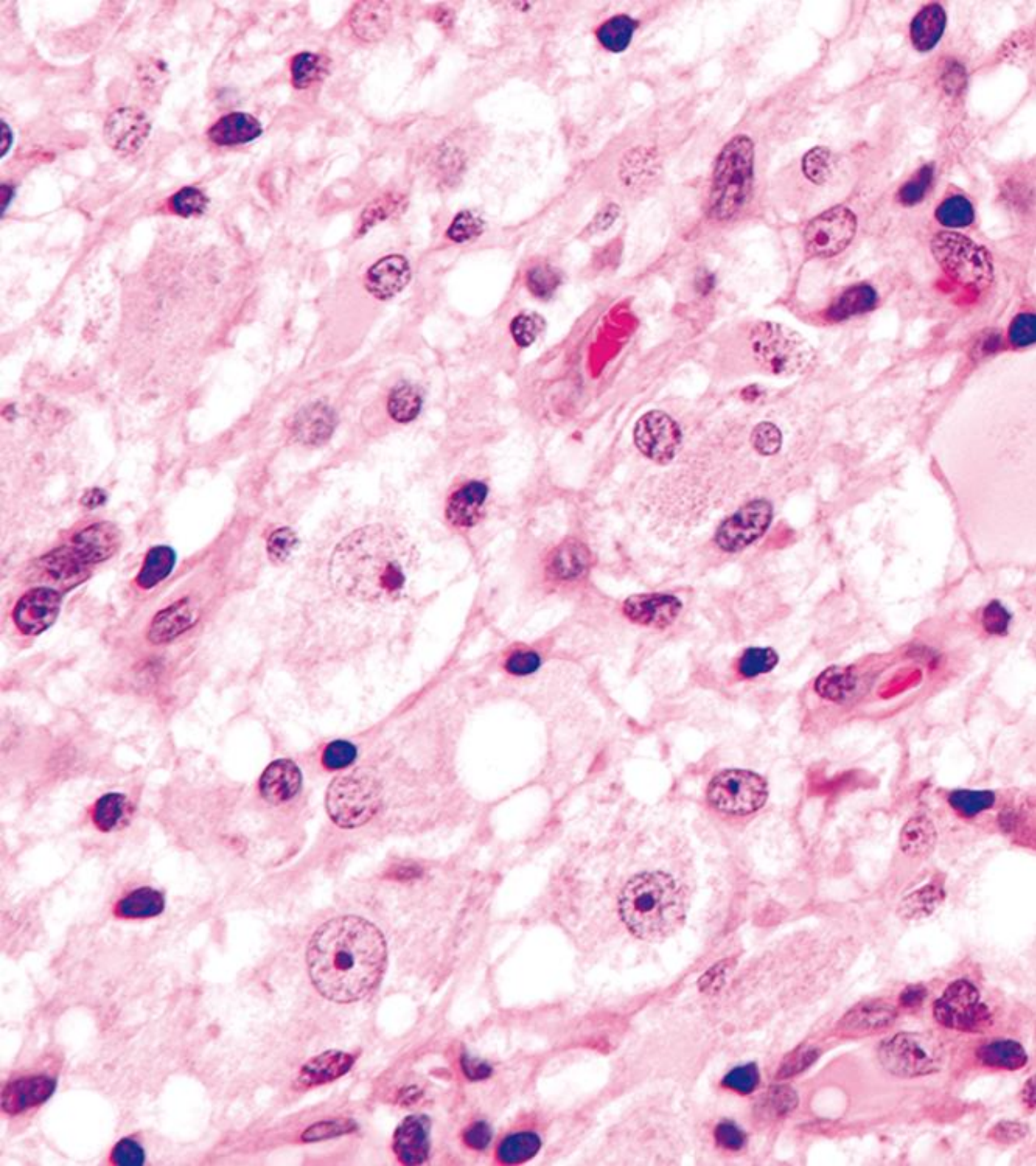
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Neuronal Tumors

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





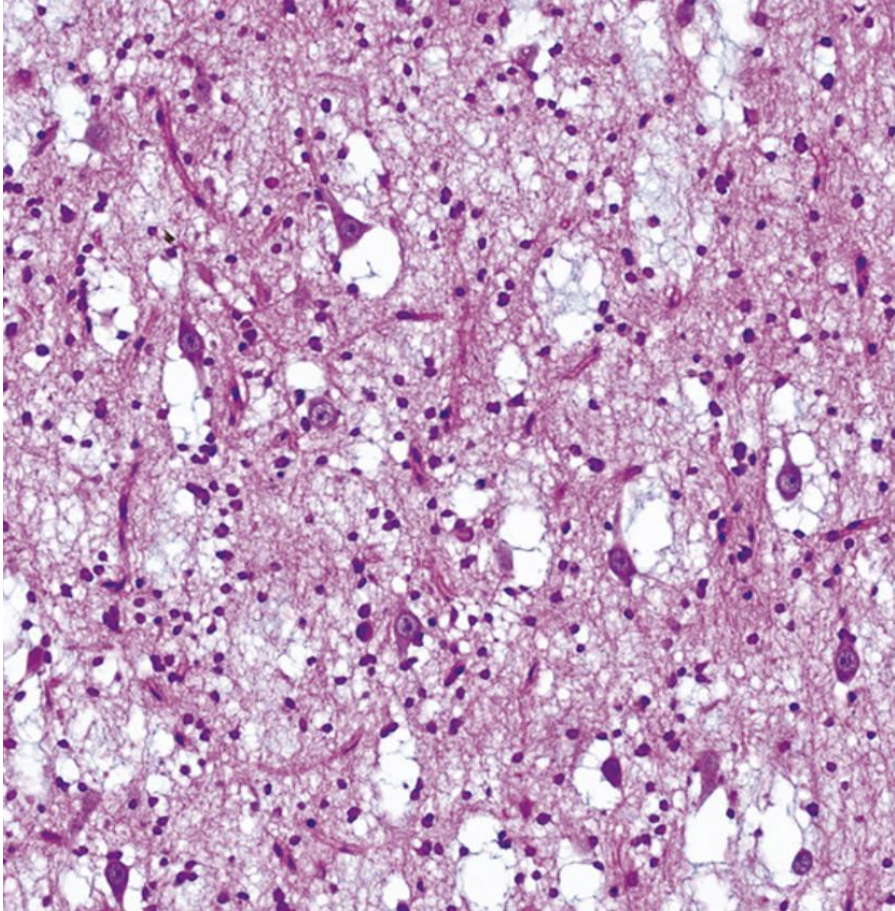
Gangliogliomas, WHO grade 1:

- children and young adults.
- Slow growing tumor
- composed of a mixture of neoplastic ganglion and glial cells
- most commonly in the temporal lobe.
- 20-50% have mutations in BRAF gene



Dysembryoplastic neuroepithelial tumor (DNT),

WHO grade 1:



- Rare
- children and young adults
- Slow growing tumor
- Present with seizure
- 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



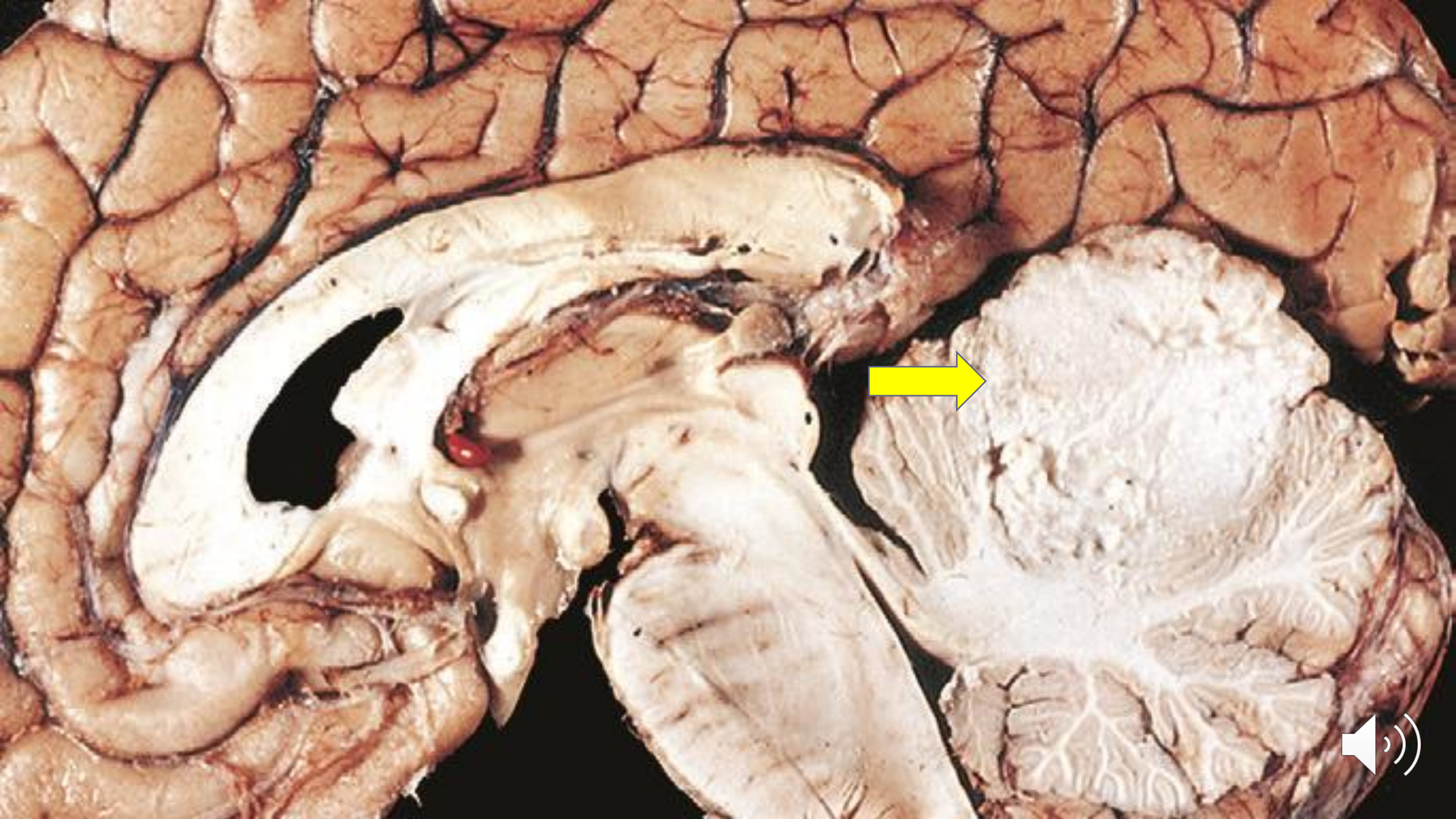
- predominantly in **children**
- mainly in **cerebellum**
- **All are highly malignant, WHO grade 4**
- **radiosensitive.**
- the prognosis for untreated patients is **dismal**
- **5-year survival rate may be as high as 75%** with total excision, chemotherapy, and irradiation



Macroscopic:

- In children (midline) while in adults (lateral)
- well circumscribed (often)
- may extend to the cerebellar surface and involve the Leptomeninges
- **complication:**
 - Medulloblastomas have tendency to spread to the subarachnoid space
→ Dissemination through the CSF





Morphology:

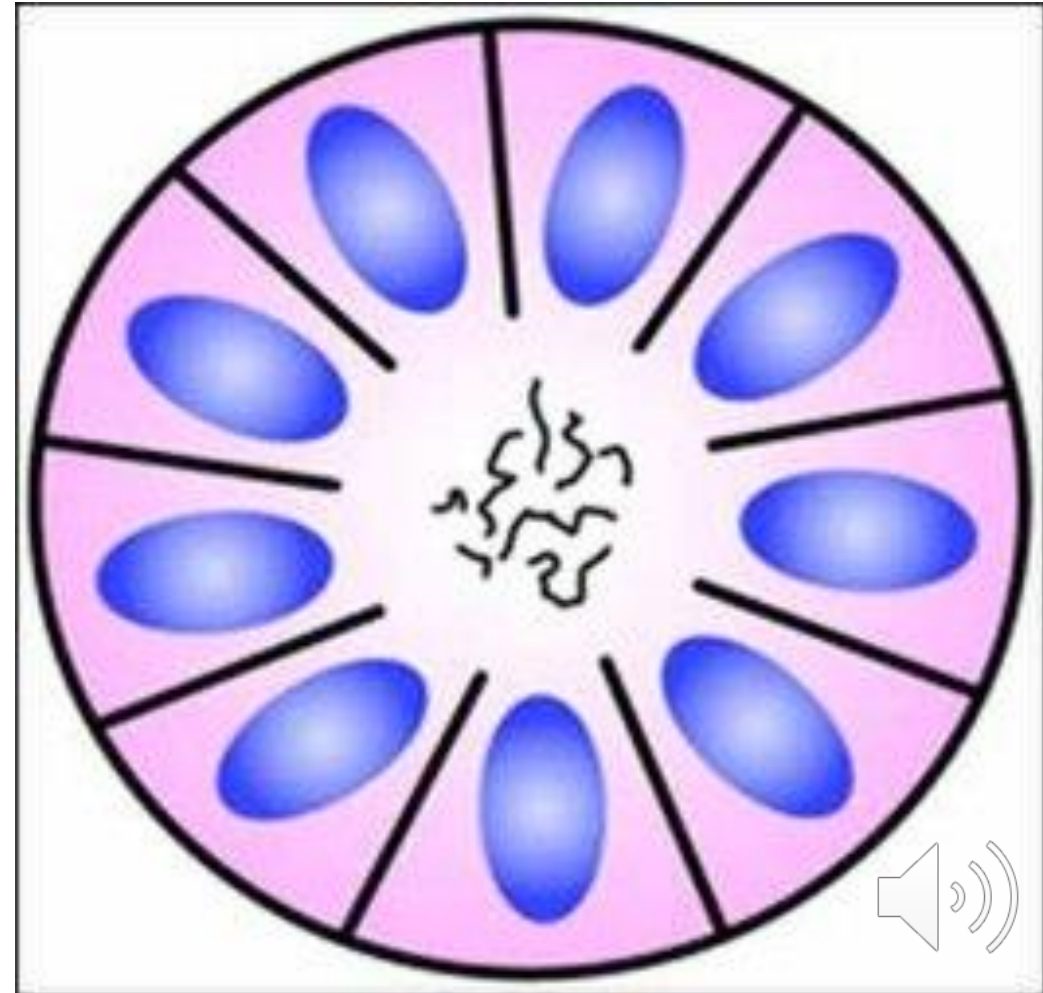
- Very Cellular
- sheets of small primitive cells (“small blue”), Each cell with little cytoplasm and hyperchromatic elongated or crescent-shaped nuclei
- mitoses are abundant.
- often express neuronal markers such as synaptophysin, expression of glial markers (GFAP) is less common.



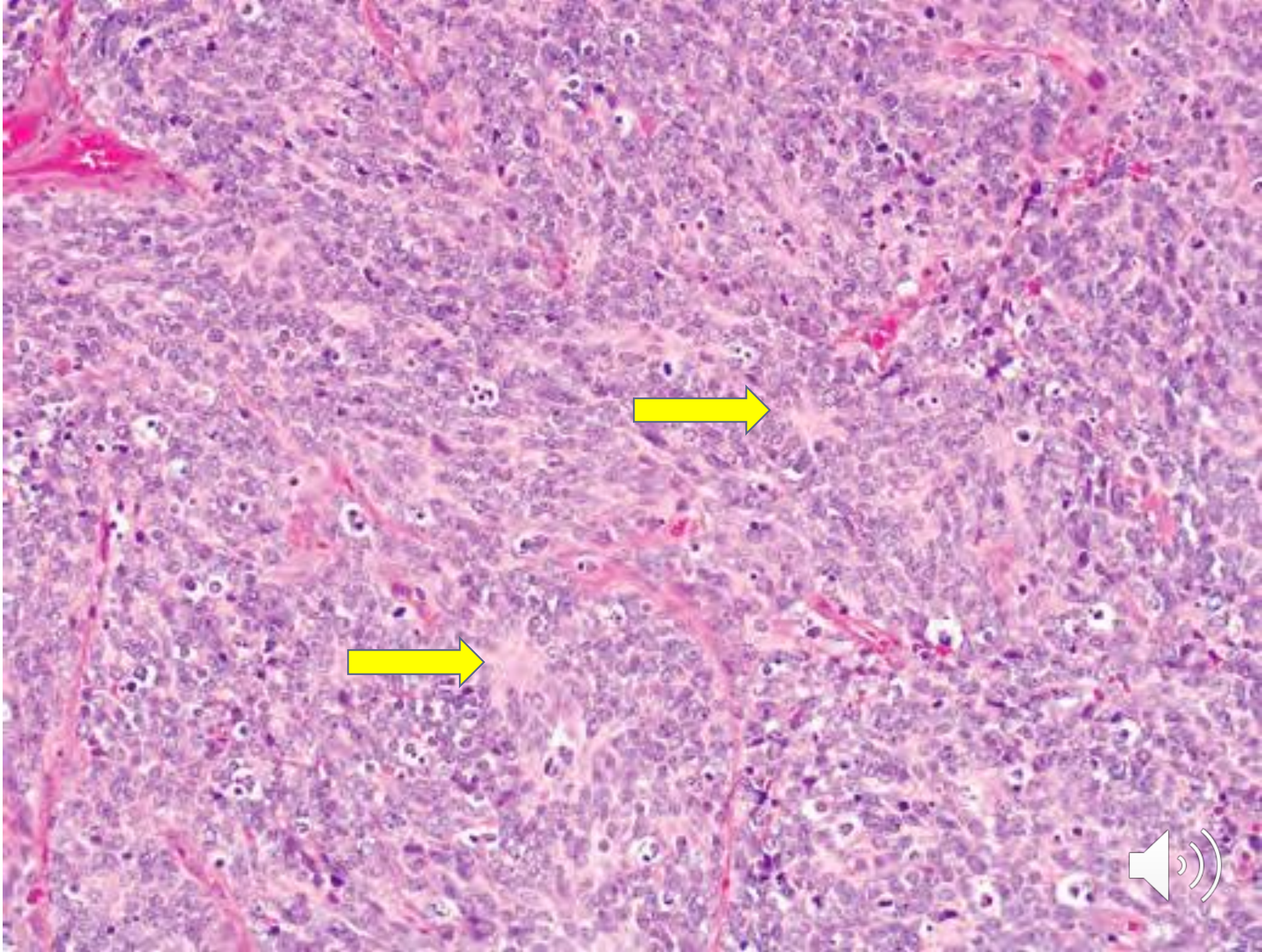
Morphology:

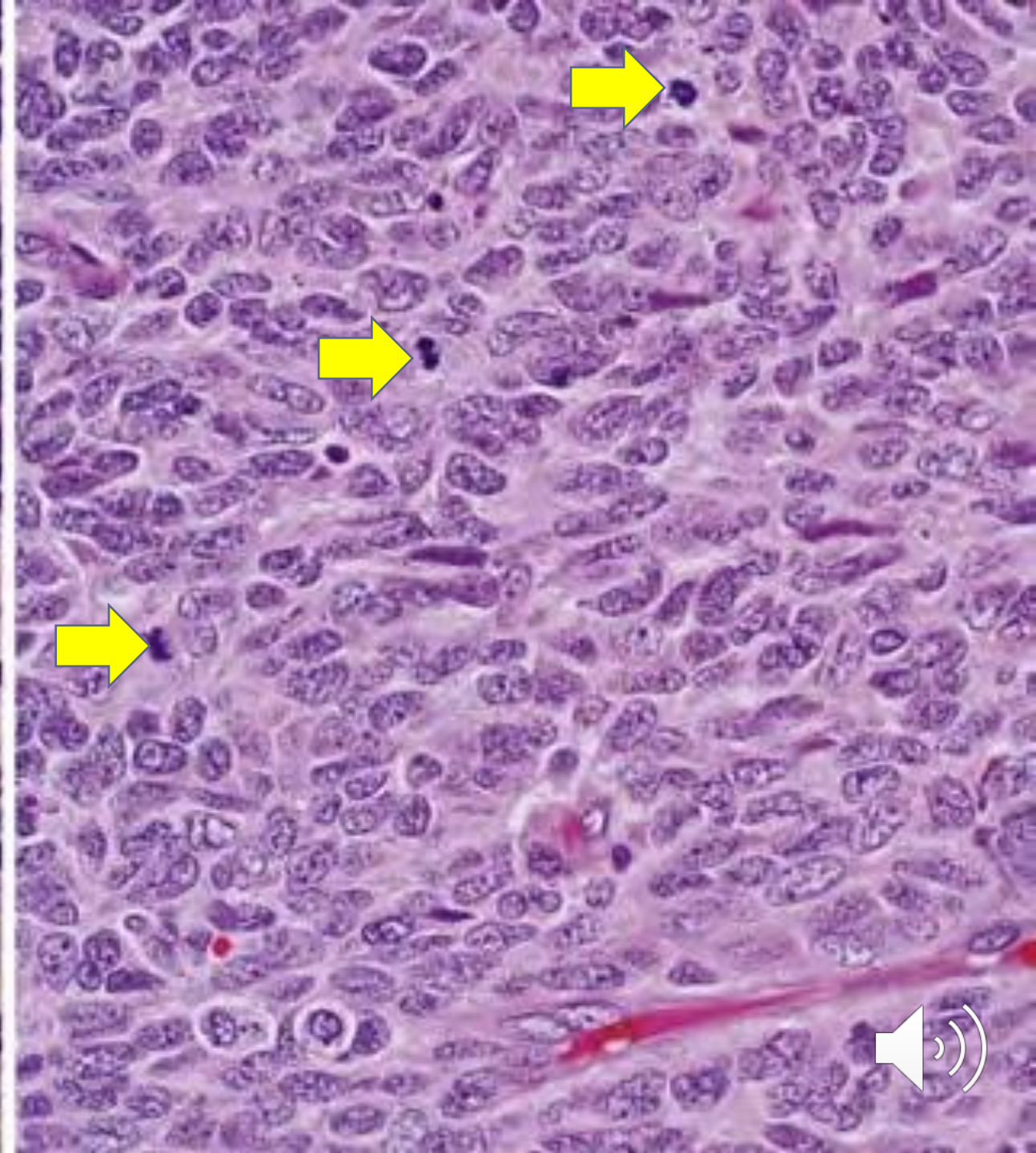
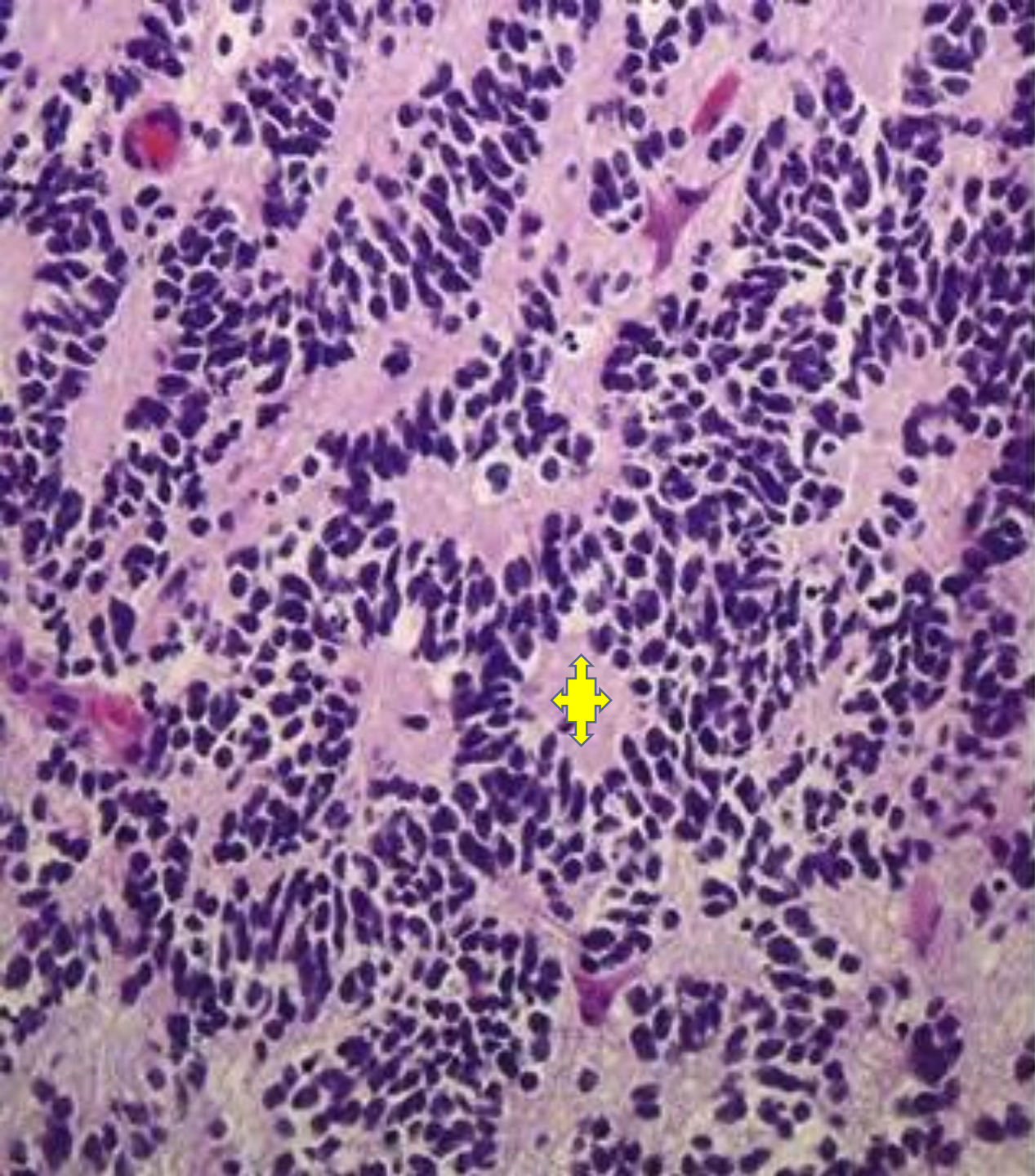
- **Homer Wright Rosettes:**

- 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).





Meningiomas, WHO grades 1-3

- tumors that arise from meningotheelial cells of the arachnoid matter and usually attached to the dura
- **Age at presentation:** adults (women>men)
- **Location:** any of the external surfaces of the brain, spinal cord, within the ventricular system, from the stromal arachnoid cells in the choroid plexus.



- **Presentation:** Most common headache, seizures, weakness (depends on location)
- **Prognosis:** determined by the lesion size and location, surgical accessibility, and histologic grade.
- Most meningiomas are easily separable from the underlying brain but some tumors are infiltrative (associated with increased risk of recurrence)
- Meningiomas express **progesterone receptors** and may grow more rapidly during pregnancy, only to regress after delivery.



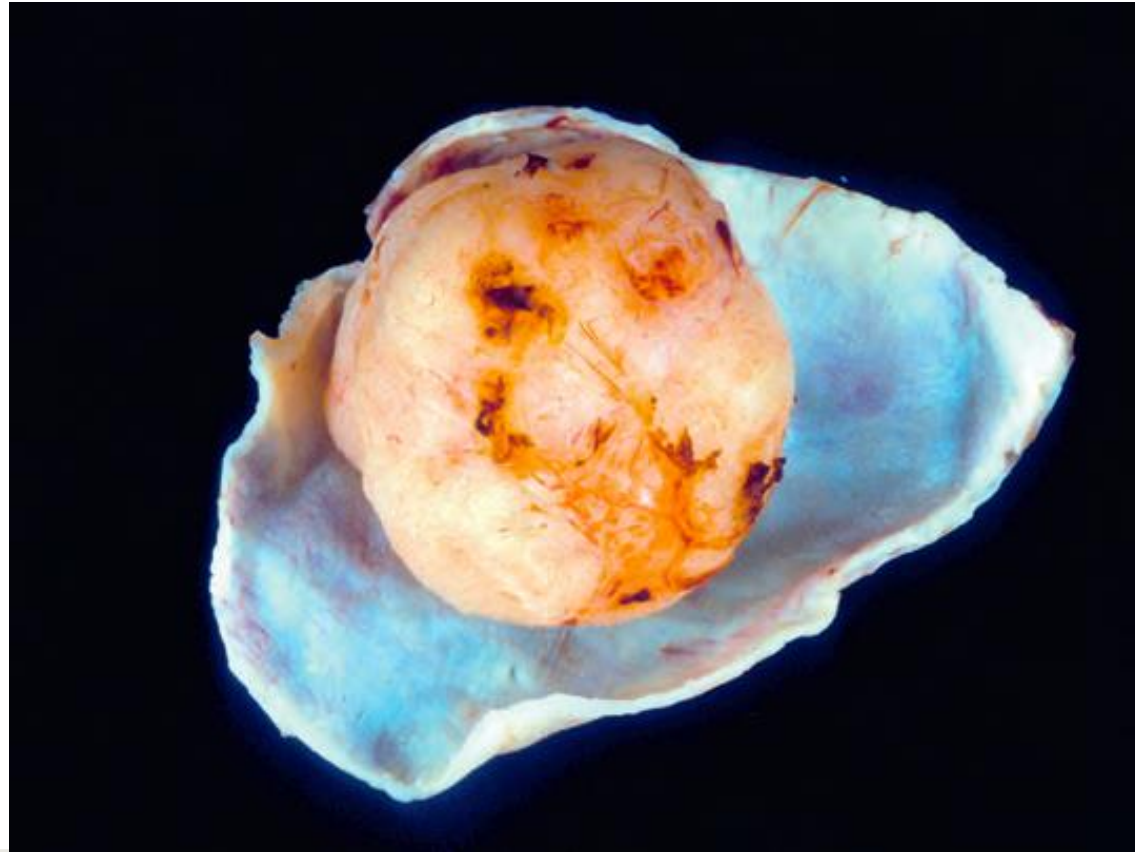
Pathogenesis

- 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.
- Of sporadic meningiomas, 50% to 60% harbor mutations in the NF2 gene
- Multiple meningiomas + 8th nerve schwannoma or glial tumor → common in the setting of NF2.



Macroscopic:

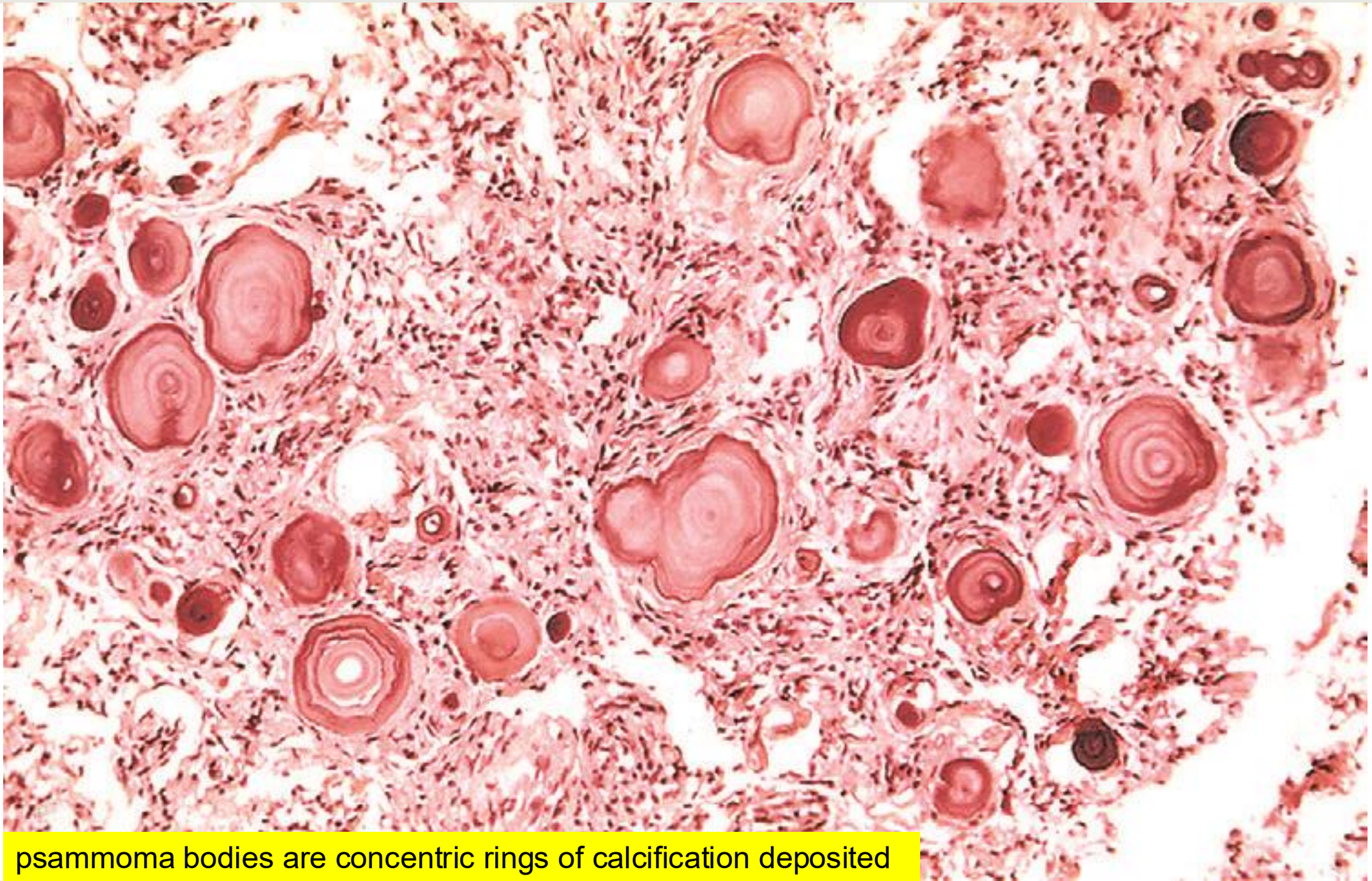
- rubbery, rounded, or bosselated dural masses that compress underlying brain
- Mostly separable from underlying brain, but some tumors are infiltrative



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 subtype, with no prognostic difference, including:
 - meningothelial (most common) → clusters of epithelioid cells with fuzzy or indiscernible cell membranes
 - Other patterns include fibrous, transitional, angiomatous, microcystic, lymphoplasmacyte rich, metaplastic, secretory and psammomatous





psammoma bodies are concentric rings of calcification deposited



MENINGIOMAS, WHO grade 2

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

1- 4 to 19 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; or

4- unequivocal brain invasion



MENINGIOMAS, WHO grade 3:

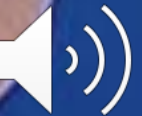
- Rare, highly aggressive, resemble a high-grade sarcoma or carcinoma or melanoma morphologically.
1. **≥ 20 mitoses/ 10HPF; or**
 2. Frank anaplasia (sarcoma, carcinoma or melanoma like); or
 3. TERT promotor mutation; or
 4. Homozygous deletion of CDKN2A/B
 5. **Papillary; or rhabdoid meningioma.**



Metastatic Tumors:

- >50% of intracranial tumors.
- mostly **carcinomas**
- The most common primary sites are **lung, breast, skin (melanoma), kidney, and colon** (80% of cases).
- **sharply demarcated masses**, often at the grey-white matter junction, and elicit local edema and 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.



Familial Tumor Syndromes

- inherited syndromes caused by mutations in tumor suppressor genes and associated with increased risk of neoplasms
- tumors of the nervous system make a prominent aspect of some of these syndromes, including:
 - ✓ **Tuberous Sclerosis**
 - ✓ **Von Hippel-Lindau Disease**



Tuberous Sclerosis

- autosomal dominant syndrome
- 1 in 6000 births
- characterized by:
 - **development of hamartomas and benign neoplasms involving the brain and other tissues**
 - **Extracerebral lesions:**
 - renal angiomyolipomas, retinal glial hamartomas, pulmonary lymphangiomyomatosis, and cardiac rhabdomyomas develop during childhood and adolescence.



Cysts at various sites, including the liver, kidneys, and pancreas.

- **Cutaneous lesions:**

- Angiofibromas
- localized leathery thickenings (shagreen patches)
- hypopigmented areas (ash-leaf patches)
- subungual fibromas.



CNS hamartomas

- Hamartomas within the CNS take the form of **cortical tubers and subependymal nodules**
- **Cortical tubers** are epileptogenic, and surgical resection can be beneficial.
- Hamartomas consist of glioneuronal hamartomas and subependymal hamartomas including **subependymal giant cell astrocytomas (SEGA)**



Von Hippel-Lindau Disease:

- autosomal dominant disease
- 1 in 30,000 to 40,000.
- **Associated with:**
 - hemangioblastomas of the CNS
 - in the cerebellum and retina, brainstem, spinal cord and nerve roots.
 - cysts in pancreas, liver, and kidneys
 - Increased risk of renal cell carcinomas
 - pheochromocytomas



Hemangioblastomas

- highly vascular neoplasms consists of numerous capillary-size or larger thin-walled vessels with intervening neoplastic cells that have vacuolated, lipid-rich cytoplasm.
- The neoplastic stromal cells express inhibin (useful diagnostic marker).



