CNS tumors

CNS III

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Primary CNS Tumors

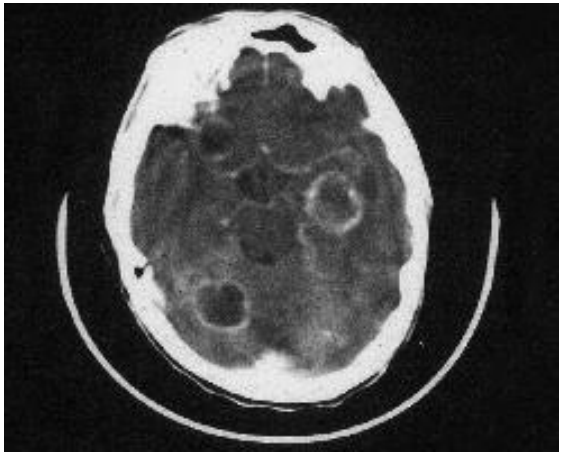
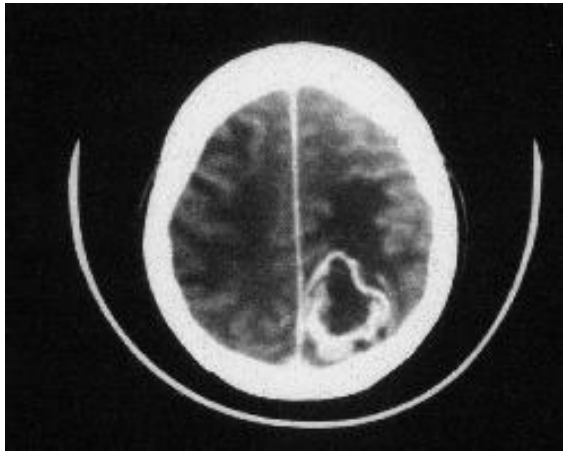
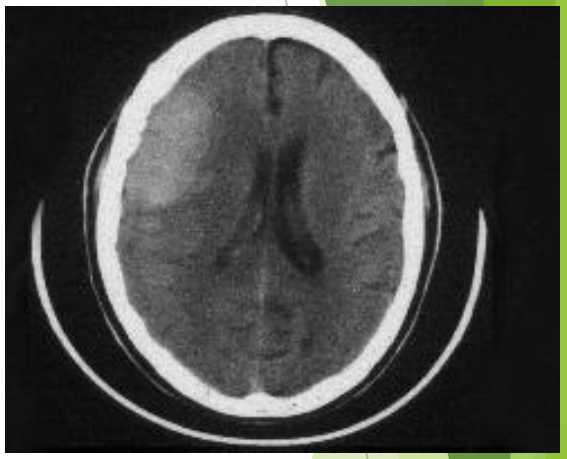
- 1- 2% of all CA, but 20% of CA in children.
- Incidence: Intracranial 10-17/100,000.
- Intraspinal 1-2/100,000.
- 50-75% are primary.
- In children, majority are infratentorial.
- In adults, majority are supratentorial.
- Do not have premalignant or in situ stage.
- Even low grade lesions can infiltrate widely.
- Anatomic site can influence outcome, regardless of type & grade due to local effect or non-resectability.

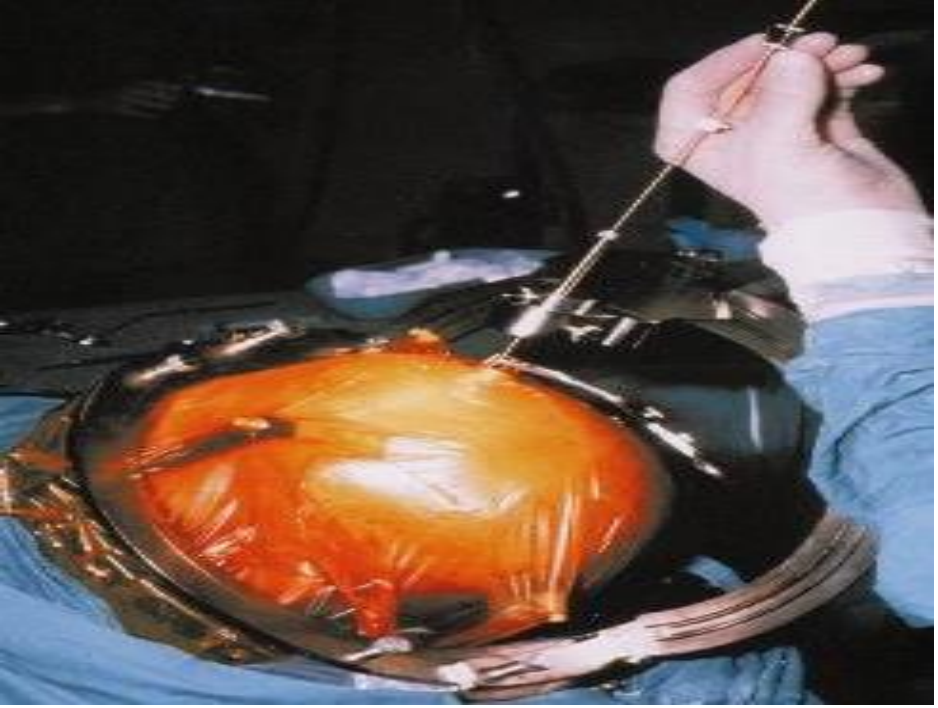
- Invasion ,”but no metastases”, occurs in most intra-axial tumors, regardless of tumor grade
- However, some spread through the CSF
- Some low grade gliomas dedifferentiate to higher grade.
- Complete surgical resection - doubtful even for tumors at the ‘benign’ end of spectrum

Presentation: Localizing signs ± ↑ ICP

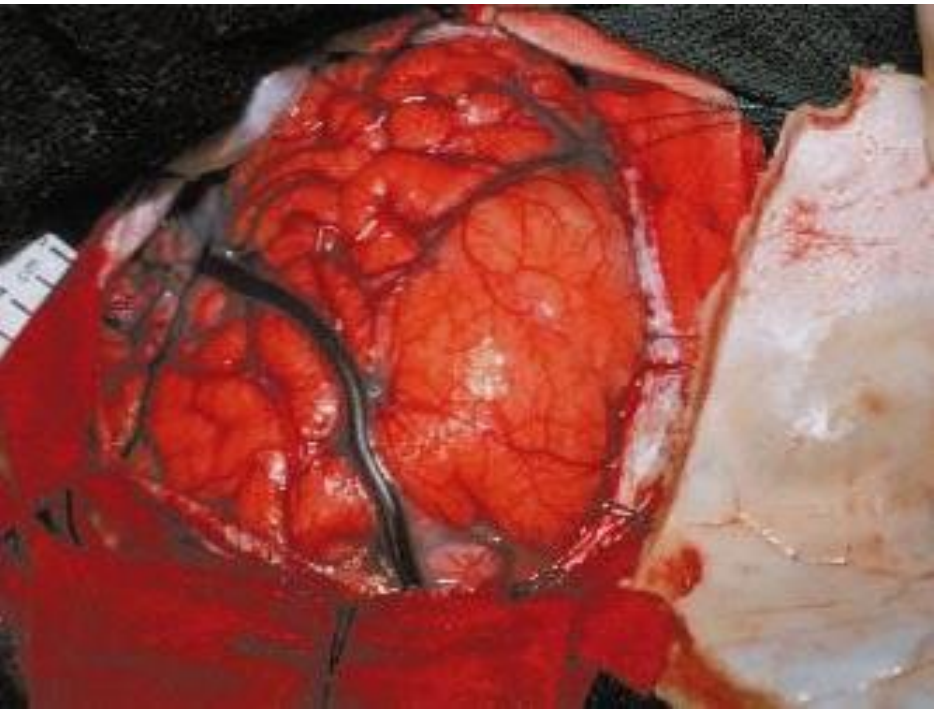
- Assessment:

- History
- Physical examination
- Neurologic exam
- LP (including cytology)
- CT
- MRI
- Brain angiography
- Biopsy



- Stereotactic Biopsy



- Craniotomy

Primary Tumors - Etiology

- **Radiation:** Often 5-25 years after treatment of pituitary adenoma or craniopharyngioma
- **Cell phones:** Mobile phones use electromagnetic radiation.
- In 2011, **International Agency for research on Cancer (IARC)** has classified mobile phone as possibly carcinogenic.
- That means that there "could be some risk" of carcinogenicity.

Primary Tumors - Etiology

- Inherited familial tumor syndromes : most AD linked to tumor suppressor gene inactivation
- Neurofibromatosis Type I & Type II – Variety of CNS & peripheral nerve tumors ± other systemic manifestations
- Tuberous sclerosis – CNS hamartomas, astrocytoma, subependymoma (TUBERS), extracerebral lesions including benign skin lesions, renal tumors....etc
- Von Hippel-Lindau – hemangioblastoma, renal carcinoma, renal cysts .. etc
- Li-Fraumeni – inherited p53 mutation ▫ glioma, many types of tumors
- Immunosuppression

Classifications:

- Classified according to cell of origin & degree of differentiation. However, slowly growing entities may undergo transformation into more aggressive tumors.

- WHO grading system: Important for treatment

Classification of NS Tumors:

1- Gliomas:

- Astrocytoma & variants
- Oligodendroglioma
- Ependymoma

2- Neuronal Tumors

- Central neurocytoma
- Ganglioglioma
- Dysembryoplastic neuroepithelial tumor

3- Embryonal (Primitive) Neoplasms

- Medulloblastoma

4- Other Parenchymal Tumors:

- Primary CNS Lymphoma
- Germ Cell Tumors

5- Meningiomas

6- Nerve Sheath Tumors:

- Schwannoma
- Neurofibroma

7- Metastatic Tumors

Most common intracranial tumors in adults:

1- Metastatic

2- Glioblastoma multiforme (GBM)

3- Anaplastic astrocytoma

4- Meningioma

Most common intracranial tumors in children:

1- Astrocytoma

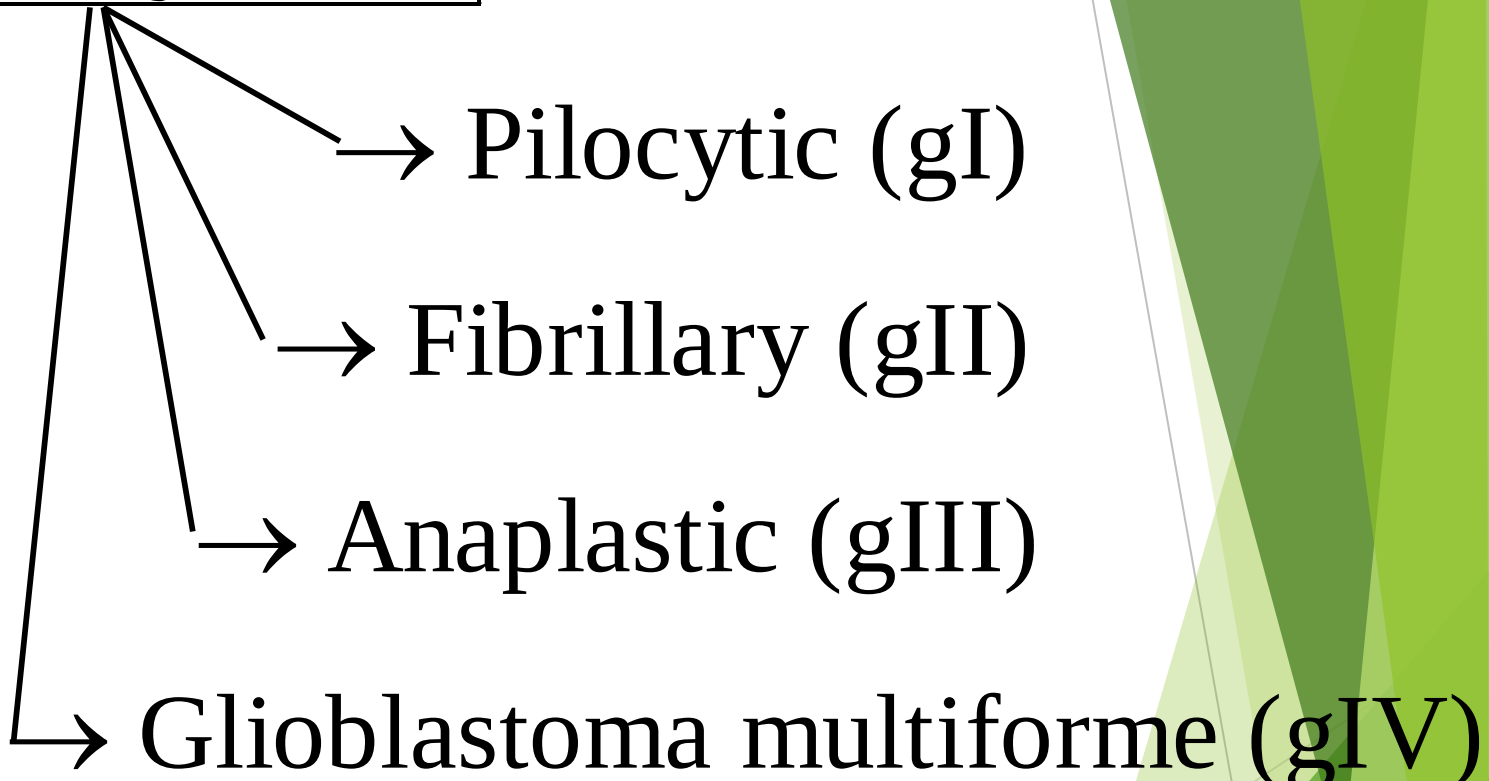
2- Medulloblastoma

3- Ependymoma

ASTROCYTOMA

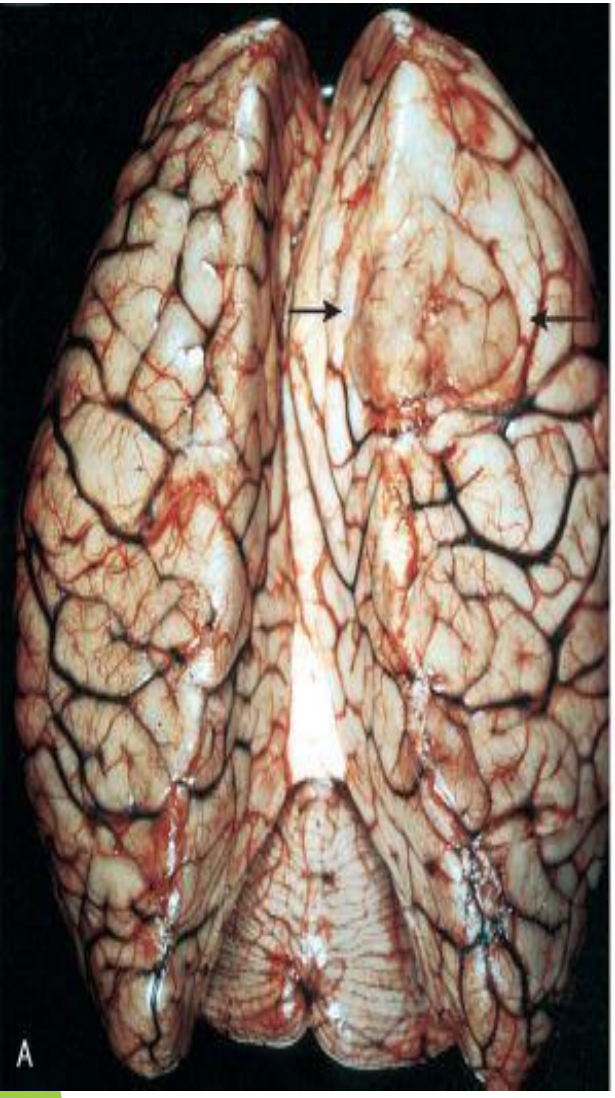
- Commonest glioma (glial tumor)
- Different types
- Different age groups
- Many mutations especially in p53, RB, PI3K, IDH-1 & IDH-2
- Positive immunostaining for IDH1 is important in identifying low grade
- Ki-67 usually done for all cases

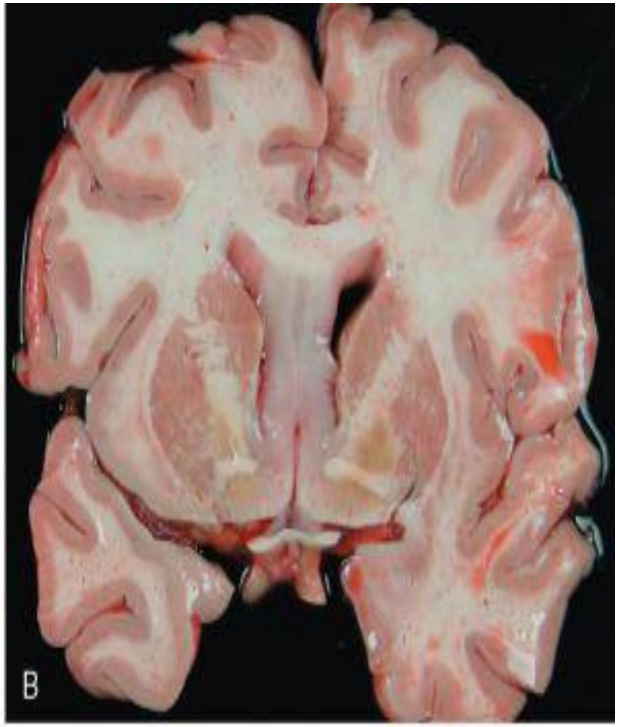
(I) Astrocytomas:



- **Gross Appearance:**
  - Solid or cystic
  - ± calcification
  - ± necrosis

- No clearly defined margin in low grade tumors

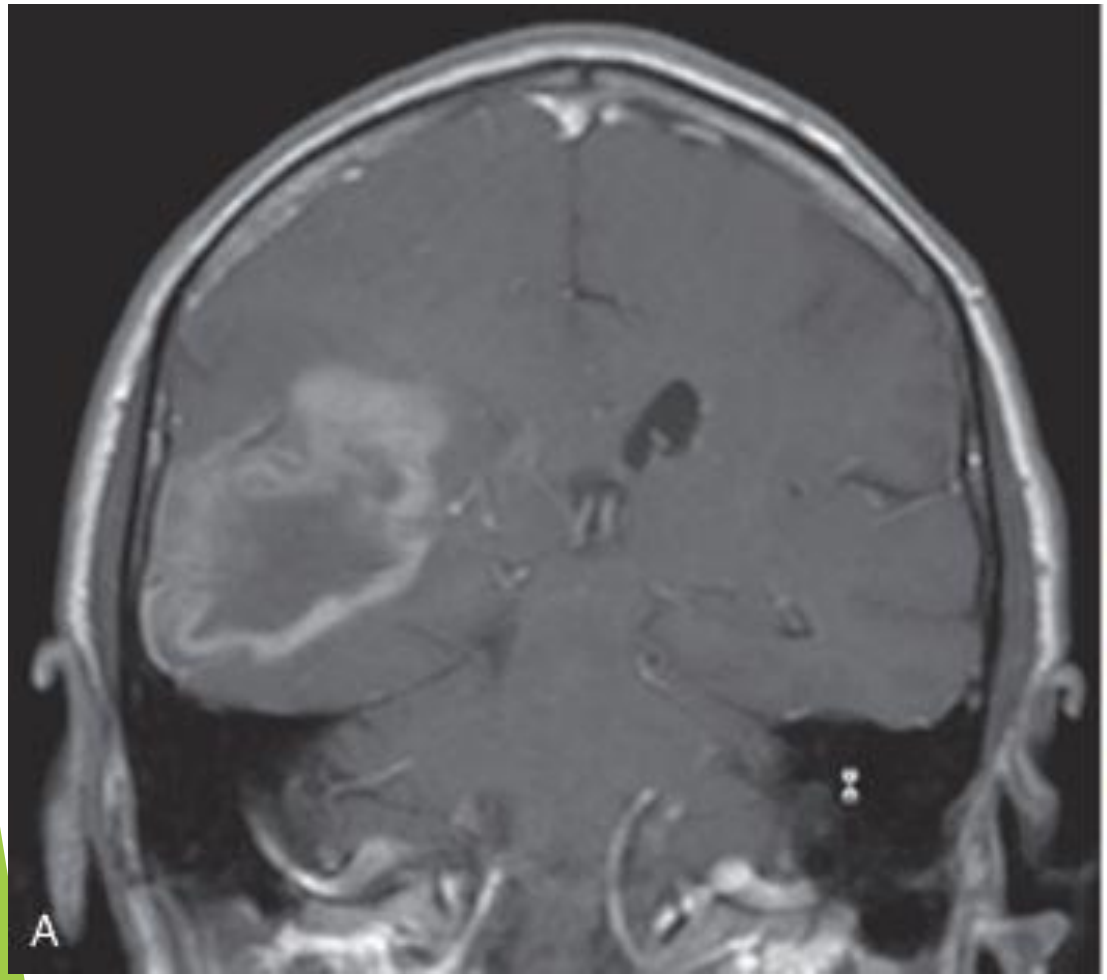


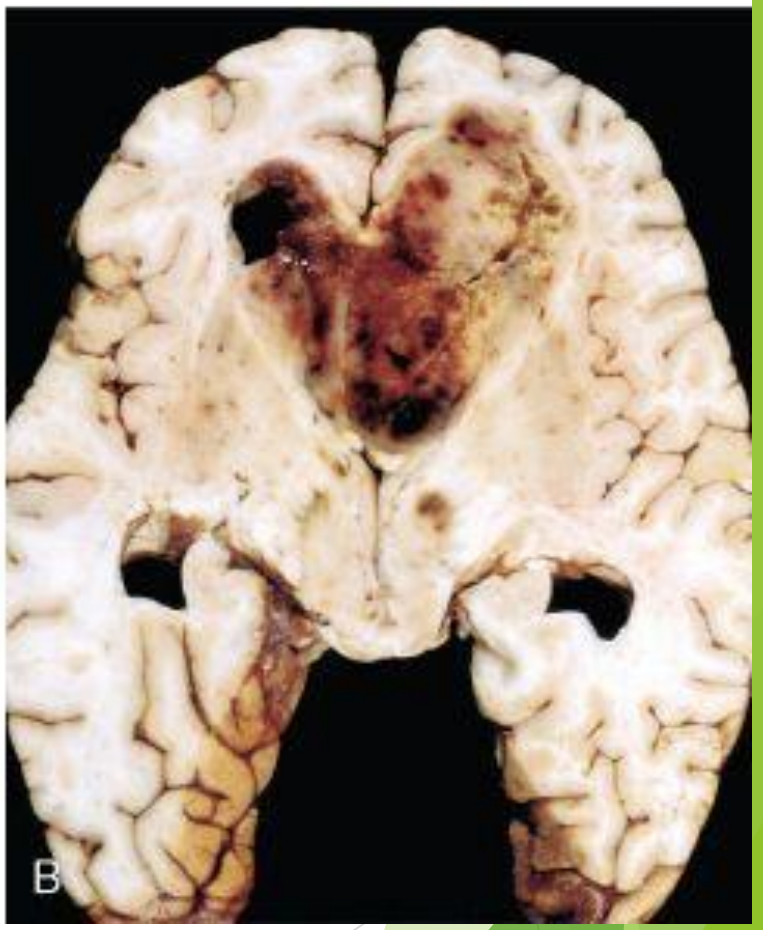


- Diffuse astrocytoma.

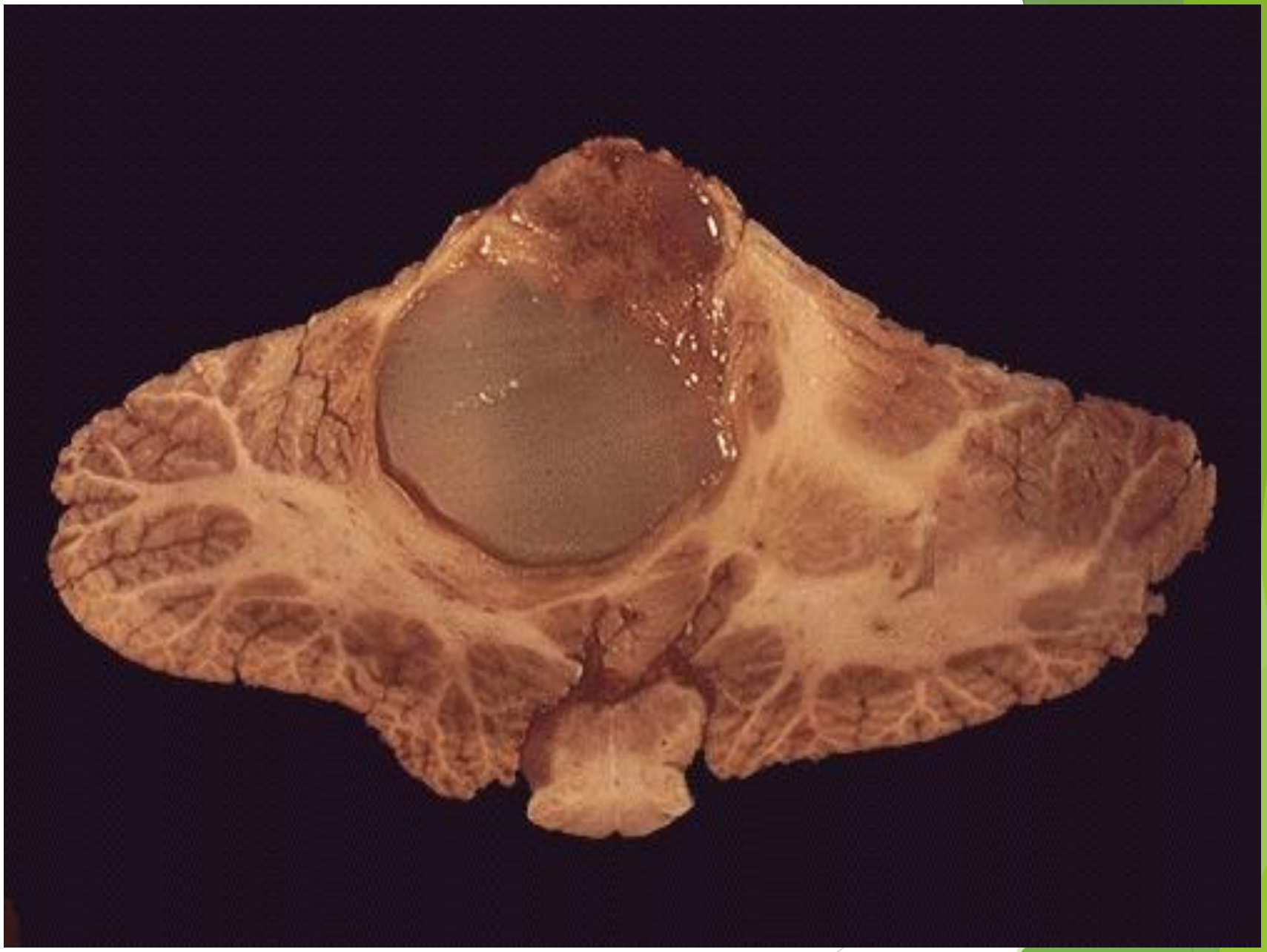
A, The right frontal tumor has expanded gyri, which led to flattening (arrows).

B, There is bilateral expansion of the septum pellucidum by gray, glassy tumor.





A, Post-contrast T1-weighted coronal MRI shows a large mass in the right parietal lobe with "ring" enhancement. B, Glioblastoma appearing as a necrotic, hemorrhagic, infiltrating mass.



Pilocytic astrocytoma - A relatively well-defined cystic tumor

ASTROCYTOMA/ GRADE

- WHO Grading:
  - Mitotic activity
  - Vascular proliferation
  - NECROSIS
- Some high grade tumors (Glioblastoma) occur de novo & not from transformation of low grade

Astrocytoma / Types:

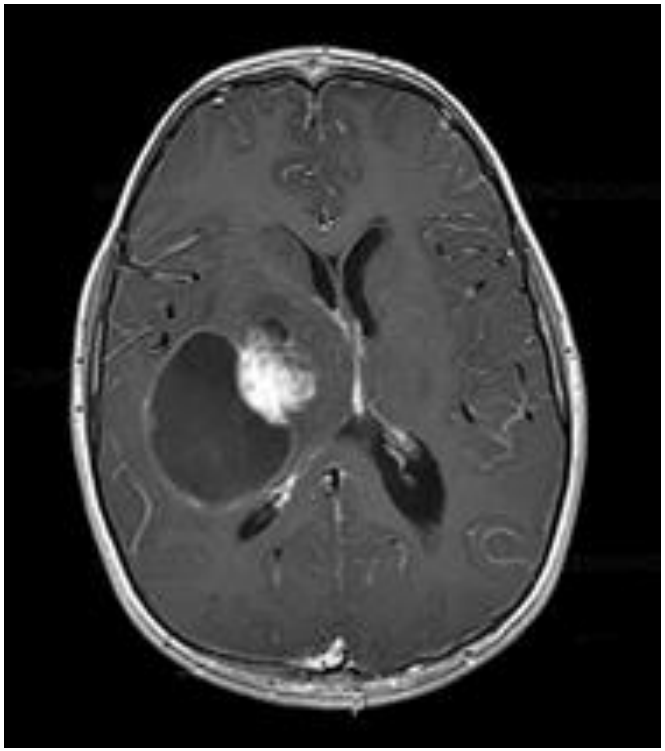
- WHO Grade I; Pilocytic Astrocytoma:

- Most in children, Cerebellum, optic pathways, 3rd ventricle... etc
- Radiology: Often cystic with mural enhancing nodule
- Low grade (relatively benign), no mitoses

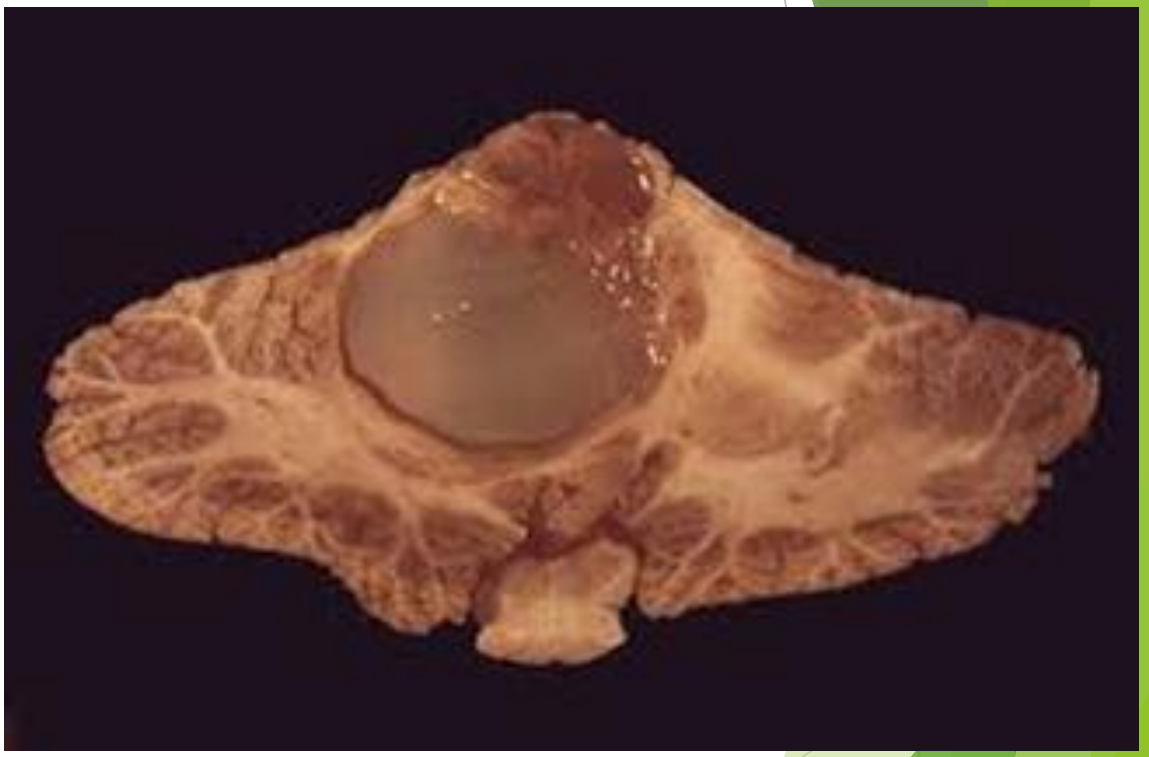
- Morpholpgy: Bipolar astrocytes, Microcysts & Rosenthal Fibers, eosinophilic granular bodies

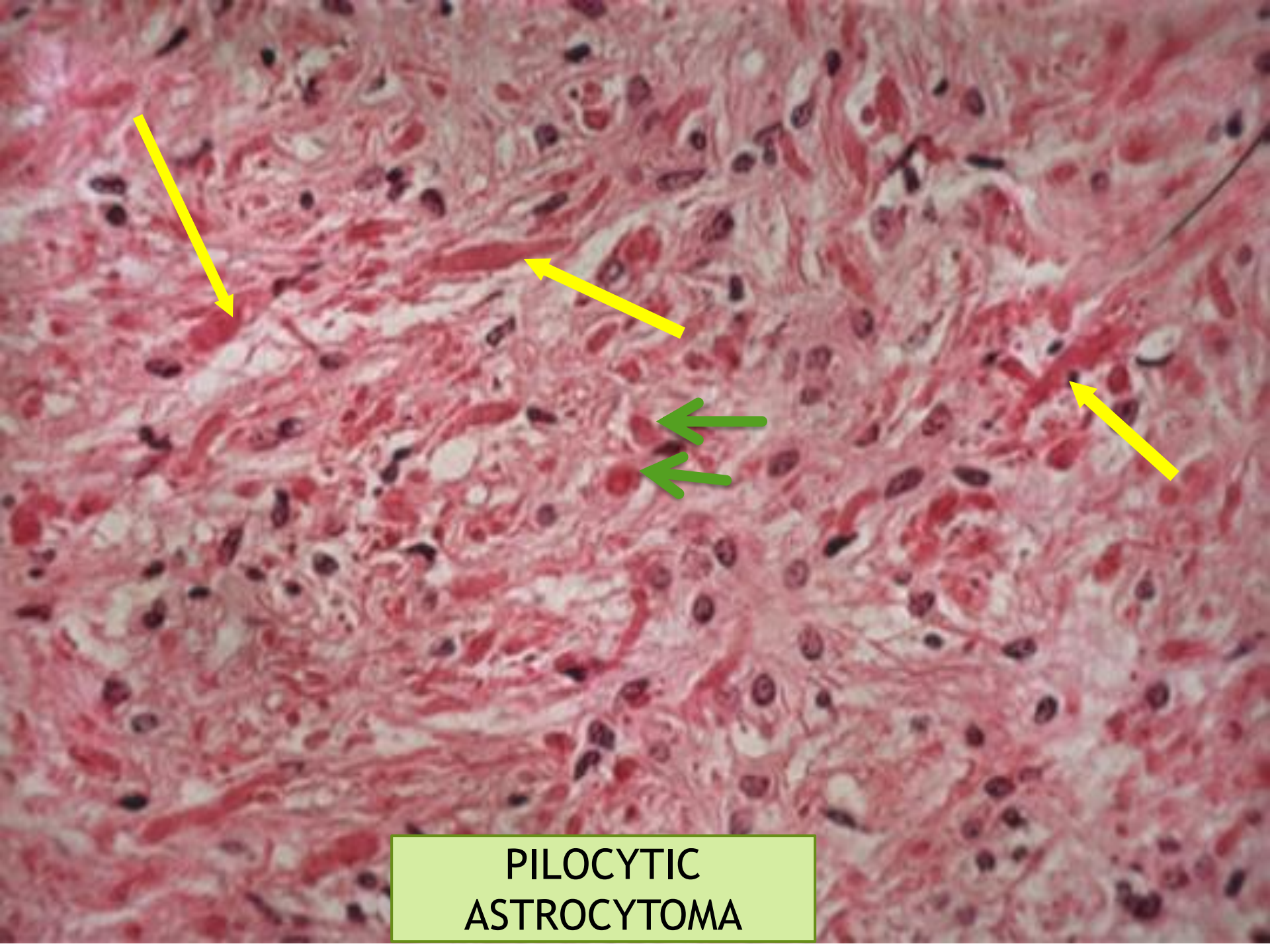
- Molecular: KIAA1549-BRAF fusion is the most common genetic event in pilocytic astrocytoma. It is Negative for IDH mutations; May be positive for BRAF mutation

MRI picture

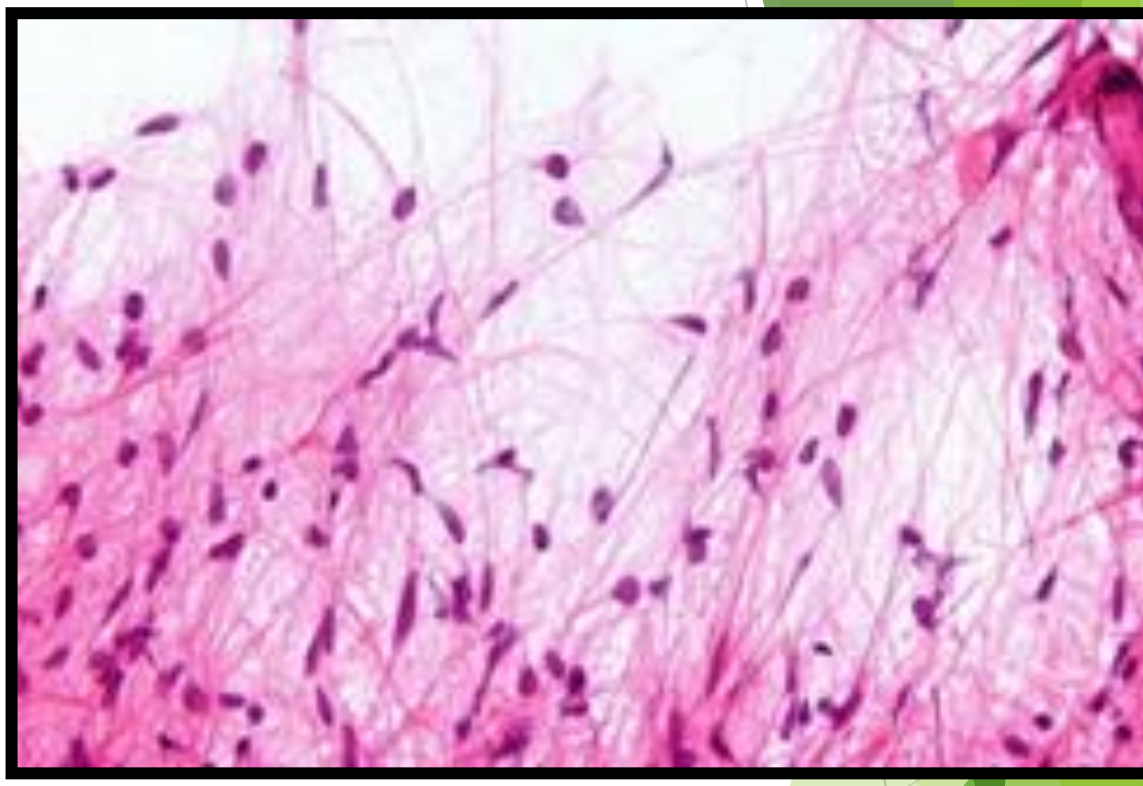


gross picture



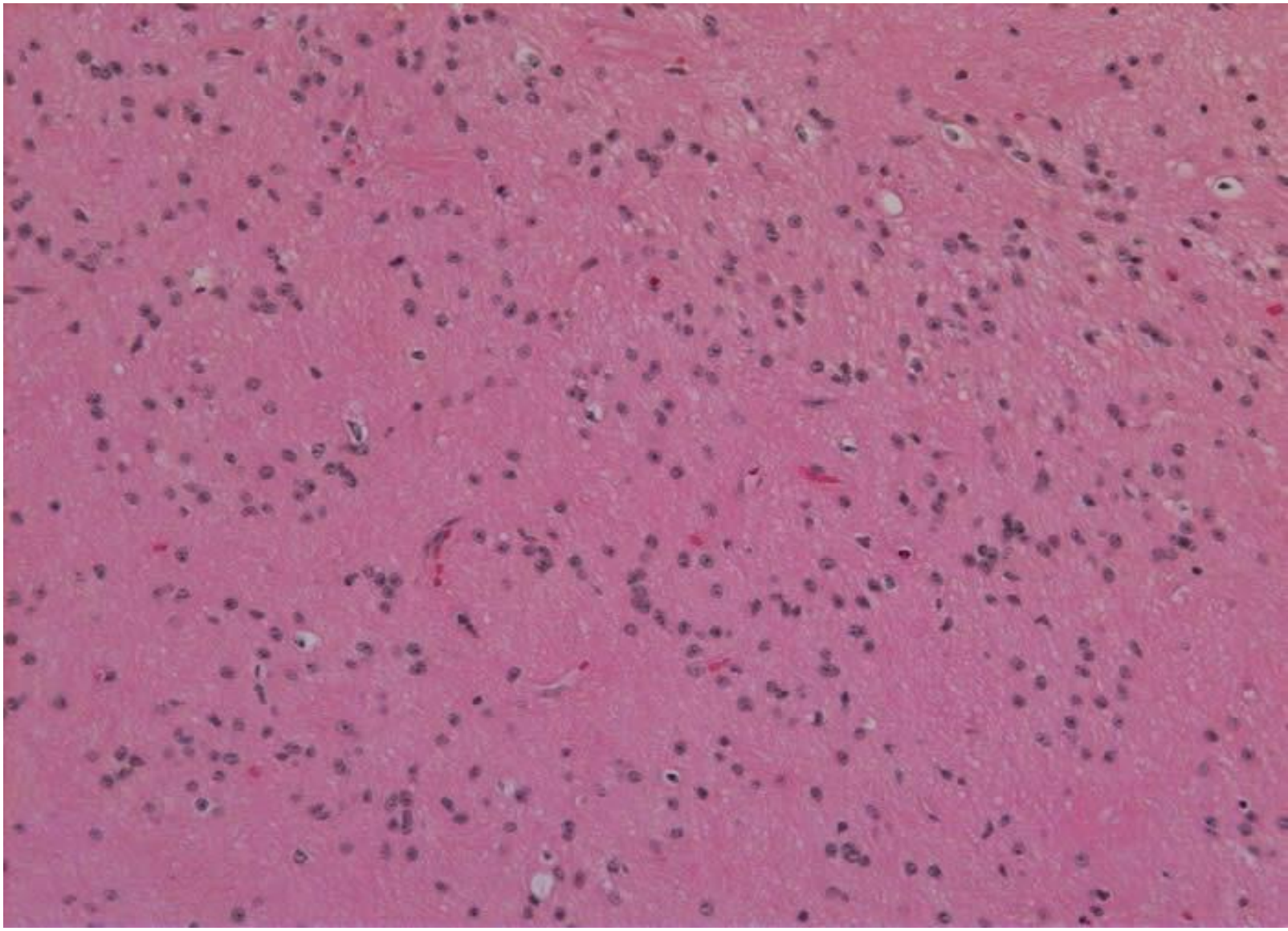

PILOCYTIC
ASTROCYTOMA

- Bipolar cells with:
- Long, thin processes.



WHO Grade II; Diffuse Astrocytoma

- Commonest (up to 80% adult gliomas)
- Any age, more in adults, more in cerebrum
- Well differentiated/low grade
- Fine fibrillary network with minimal pleomorphism
- - Proliferation of astyrocytes.
- - Pleomorphic, hyperchromatic no mitotic figures.
- - Admixed in a fibrillary stroma
- up to 80% of WHO grade II and III gliomas have IDH mutations



Diffuse Astrocytoma:
? Gliosis versus Glioma

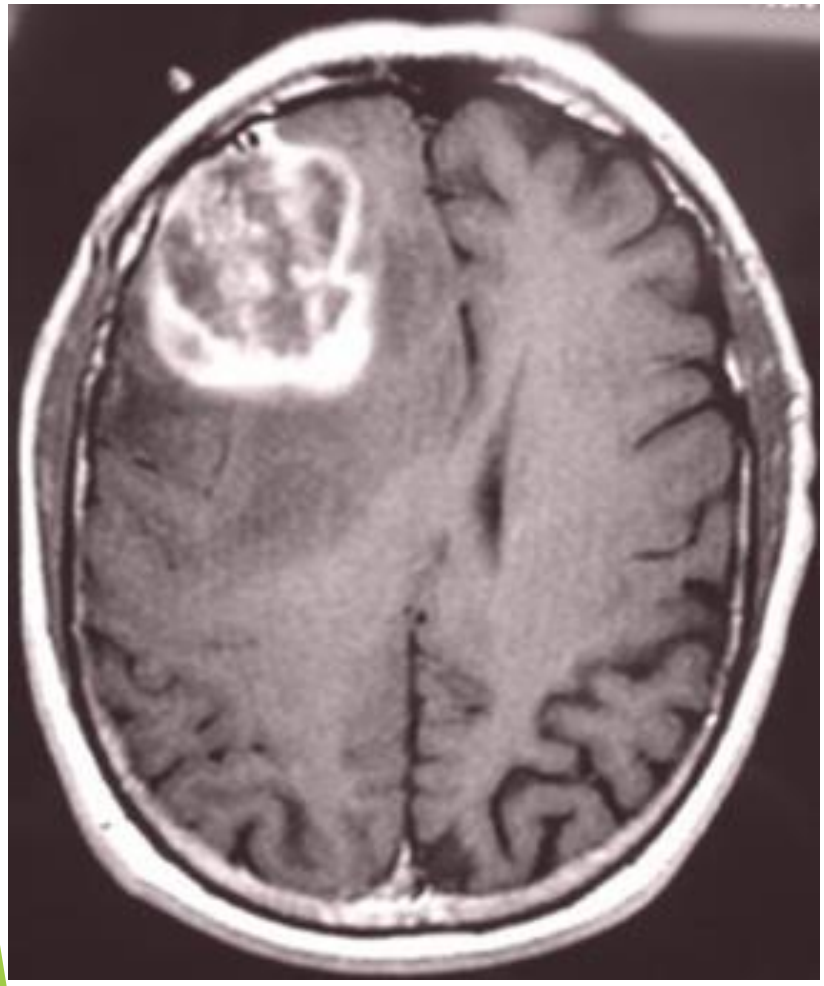
WHO Grade III - Anaplastic Astrocytoma

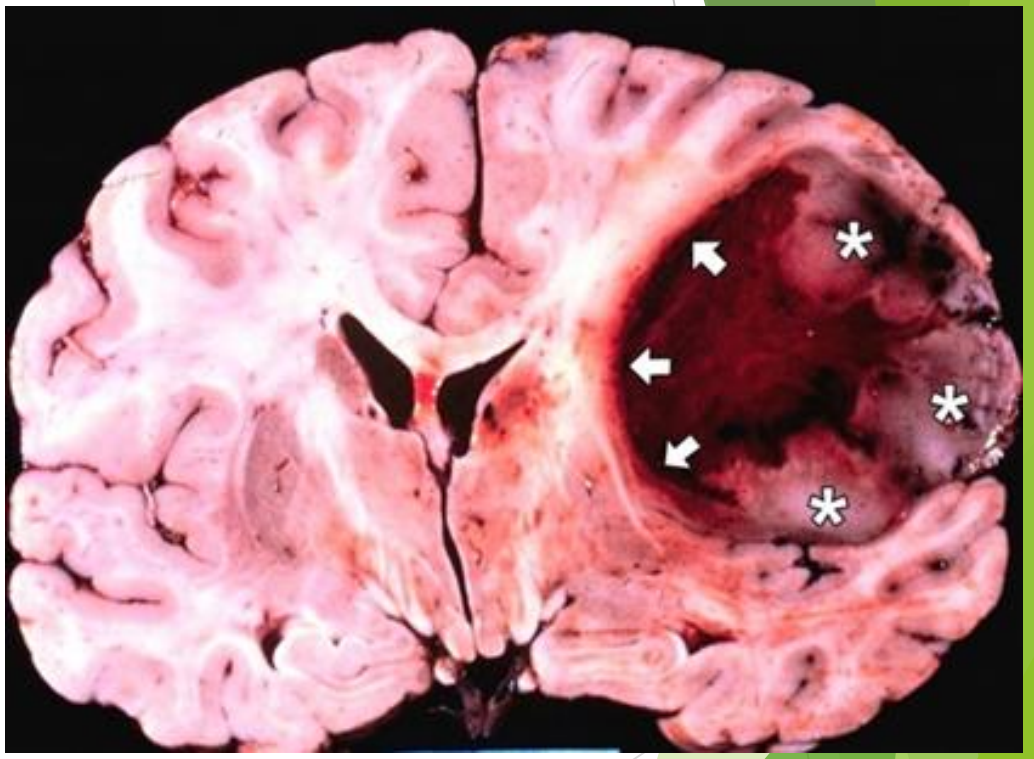
- Aggressive Adult tumor, supratentorial but can occur anywhere in the brain.
- More cellular and pleomorphic
- May show numerous Gemistocytes
- No microvascular proliferation or palisading necrosis

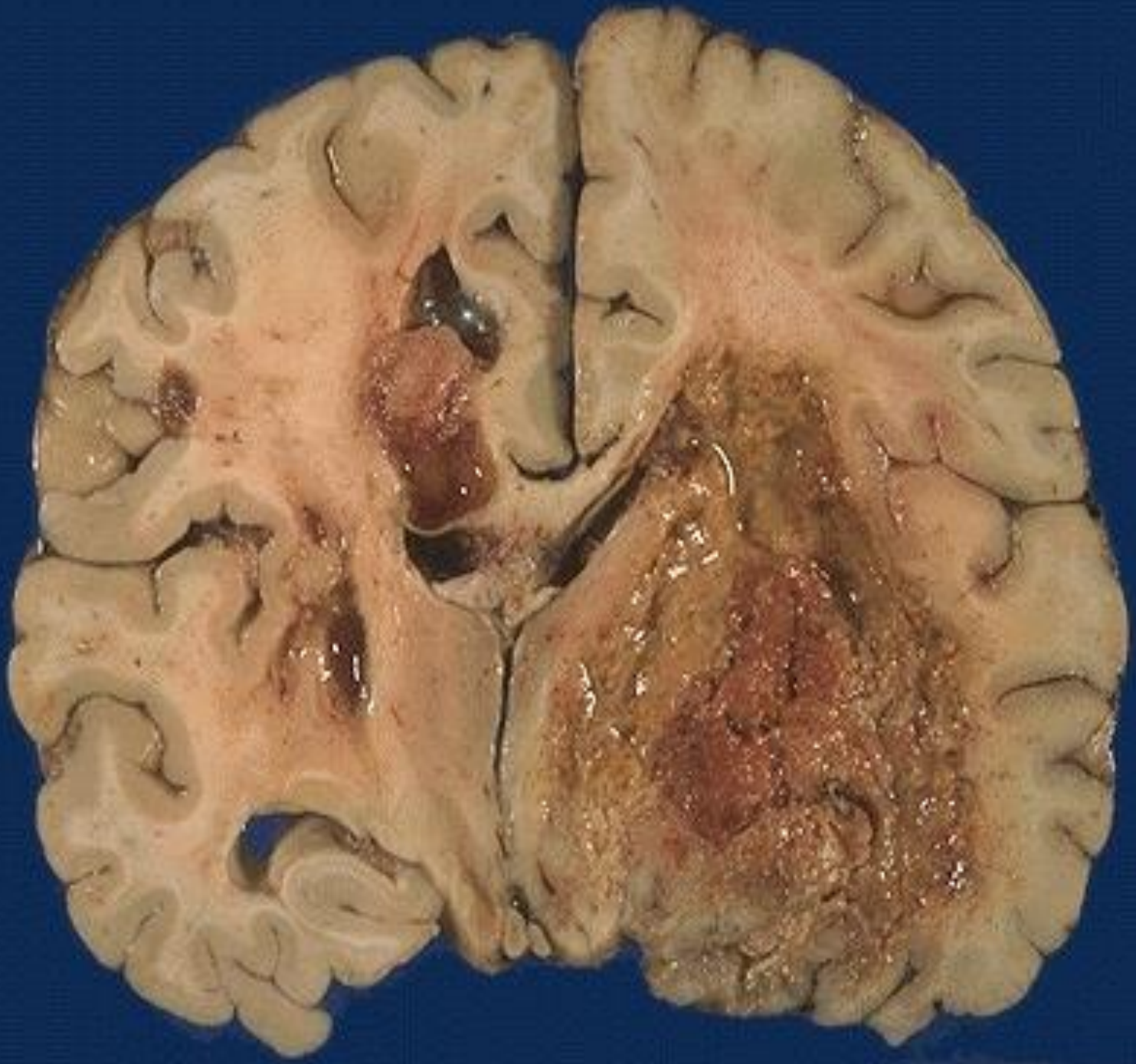
WHO Grade IV; Glioblastoma

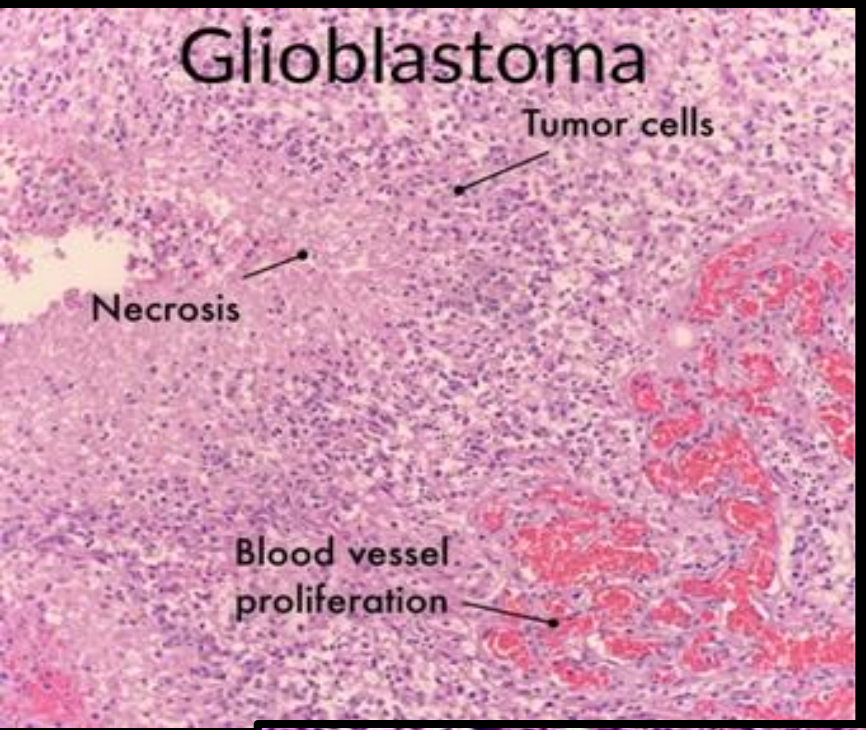
- More in adults
- Supratentorial enhancing tumor with edema
- Cellular pleomorphic tumor with prominent mitoses
- Microvascular proliferation present
- PALISADING NECROSIS present

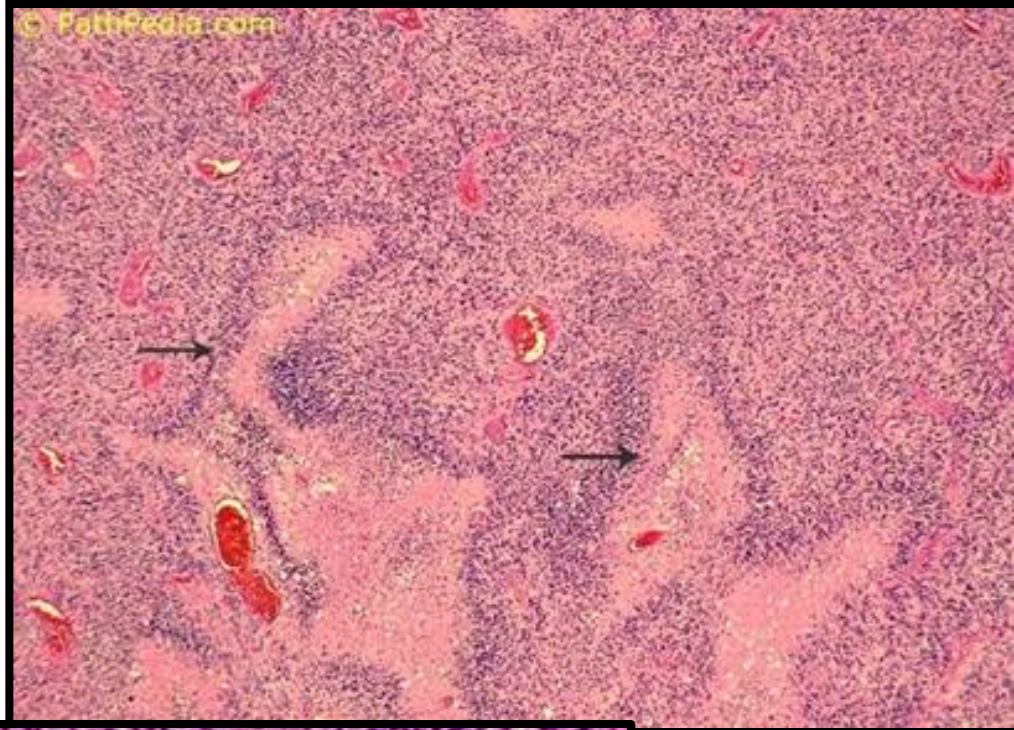
- The WHO grading system is important in prognosis & in outlining type of therapy
- All astrocytomas are GFAP+, variable Ki-67.

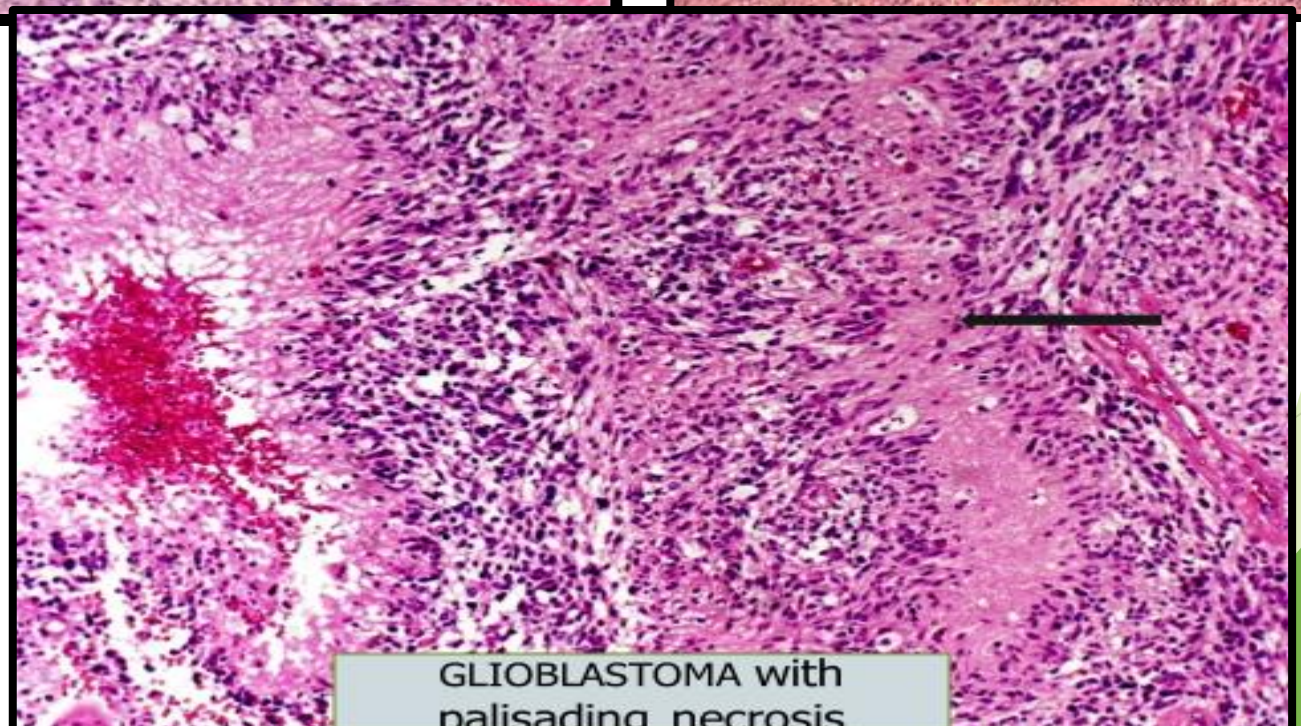











GLIOBLASTOMA with
palisading necrosis

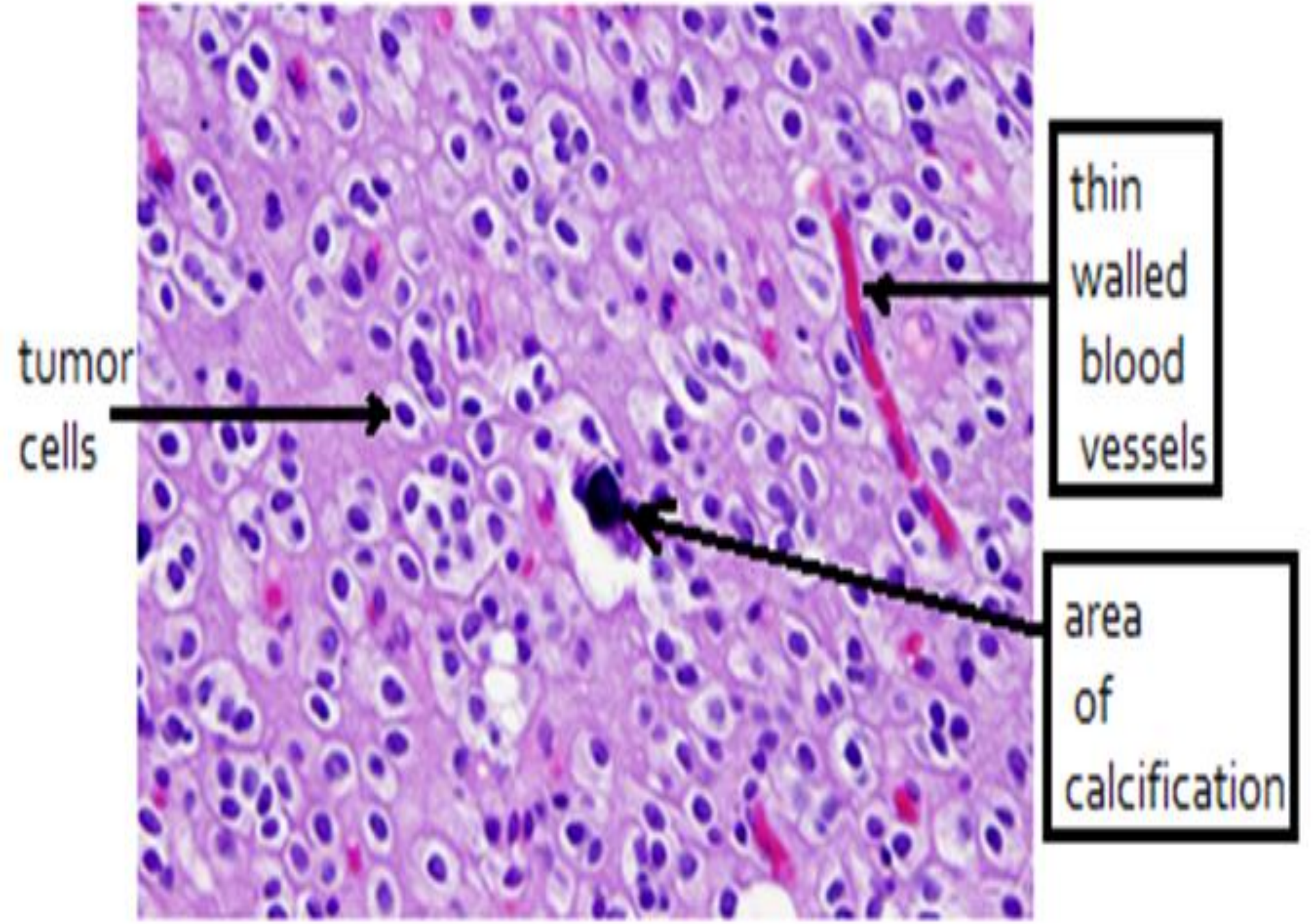
Glioma

- Prognosis depend on grade, site & Age (child versus > 65)
- Low grade:
- Surgery
- Radiotherapy in selected cases

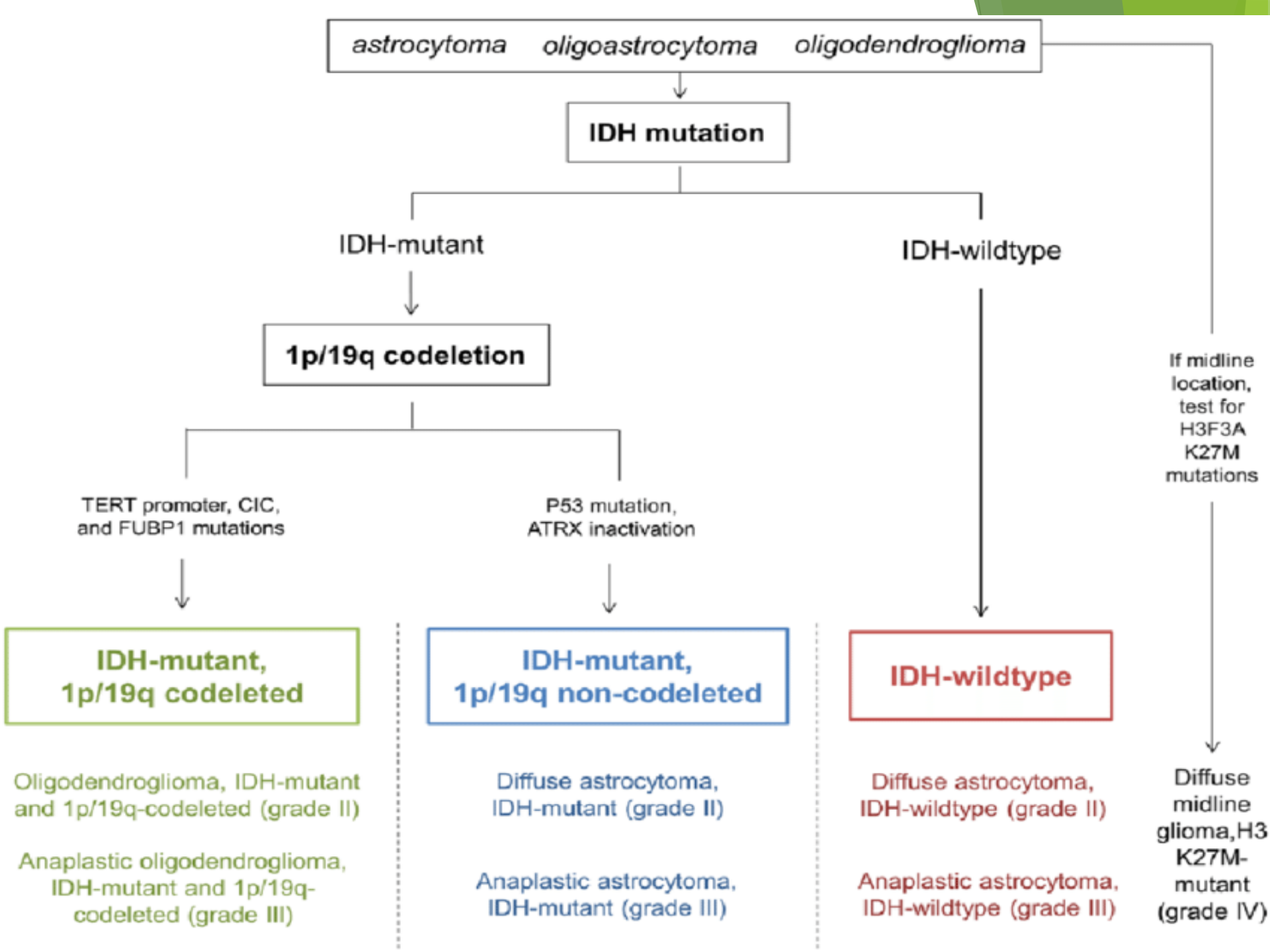
- High grade:
- Dexamethasone
- Surgery: Extent of tumour resection correlates with survival
- Radiotherapy
- Chemotherapy

OLIGODENDROGLIOMA

- More in adults & in cerebrum
- Calcification is common
- **Histology:**
  - Small uniform cells with clear cytoplasm
  - Debate on !!Some mixed with astrocytoma!!
  - Absent or minimal mitoses
  - Typical FRIED EGG APPEARANCE
- **WHO Grade:**
  - Grade II
  - Anaplastic oligodendroglioma - Grade III
- Better prognosis than astrocytoma similar grade
- 1p/19q co-deletion as well as IDH mutation is mandatory for diagnosis


tumor cells
thin walled blood vessels
area of calcification

TYPE \ GRADE	WHO grade I	WHO grade II	WHO grade II	WHO grade IV
	CIRCUMSCRIPT	DIFFUSE		
		Low grade	High grade	
Astrocytoma	Pilocytic-Astrocytoma Subependymal giant cells astrocytoma	Low-grade Astrocytoma	Anaplastic Astrocytoma	Glioblastoma
Oligodendroglioma		Low-grade Oligodendroglioma	Anaplastic oligodendroglioma	


astrocytoma oligoastrocytoma oligodendroglioma
IDH mutation
IDH-mutant
IDH-wildtype
1p/19q codeletion
If midline location, test for H3F3A K27M mutations
TERT promoter, CIC, and FUBP1 mutations
P53 mutation, ATRX inactivation
IDH-mutant, 1p/19q codeleted
IDH-mutant, 1p/19q non-codeleted
IDH-wildtype
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted (grade II)
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted (grade III)
Diffuse astrocytoma, IDH-mutant (grade II)
Anaplastic astrocytoma, IDH-mutant (grade III)
Diffuse astrocytoma, IDH-wildtype (grade II)
Anaplastic astrocytoma, IDH-wildtype (grade III)
Diffuse midline glioma,H3 K27M-mutant (grade IV)

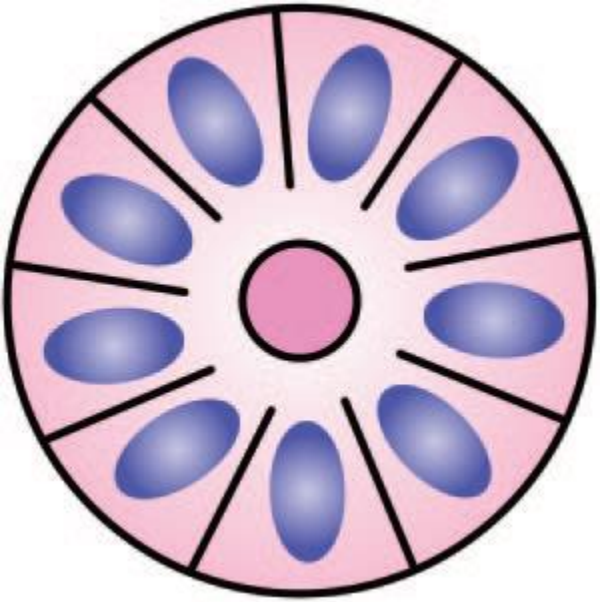
EPENDYMOMA

- **- Slow growing tumor.**
- **- Age: Children, young adults.**
- **Cell of origin: ependymal cells lining the ventricles.**
- **Gross: gray, fleshy mass**
- **Radiology:** Uniformly enhancing mass, well demarcated usually in ventricle or spinal cord
- WHO Grade:
- **Grade II or Anaplastic Grade III**
- Can metastasize via CSF
- May cause obstructive hydrocephalus
- Rx: Surgery, Radiotherapy

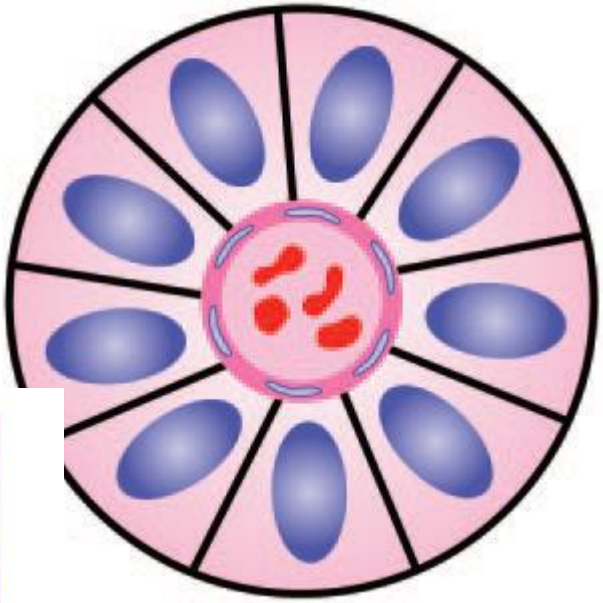
EPENDYMOMA

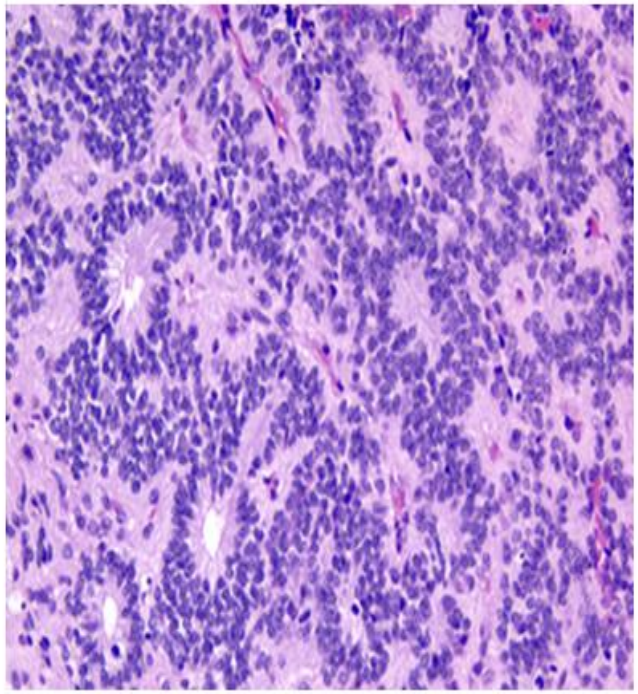
- Age: Children & Young adults
- Location: mostly 4th. Ventricle in 0-20years of age, in ≥ 20 years Lumbosacral region OR lat. or 3rd.ventricle
- Histology: Classical or Myxopapillary (usually located in lumbosacral region).
    - Ependymal true rosettes qand canals
    - Perivascular pseudorosettes
    - Myxopapillary is more loose & mucoid

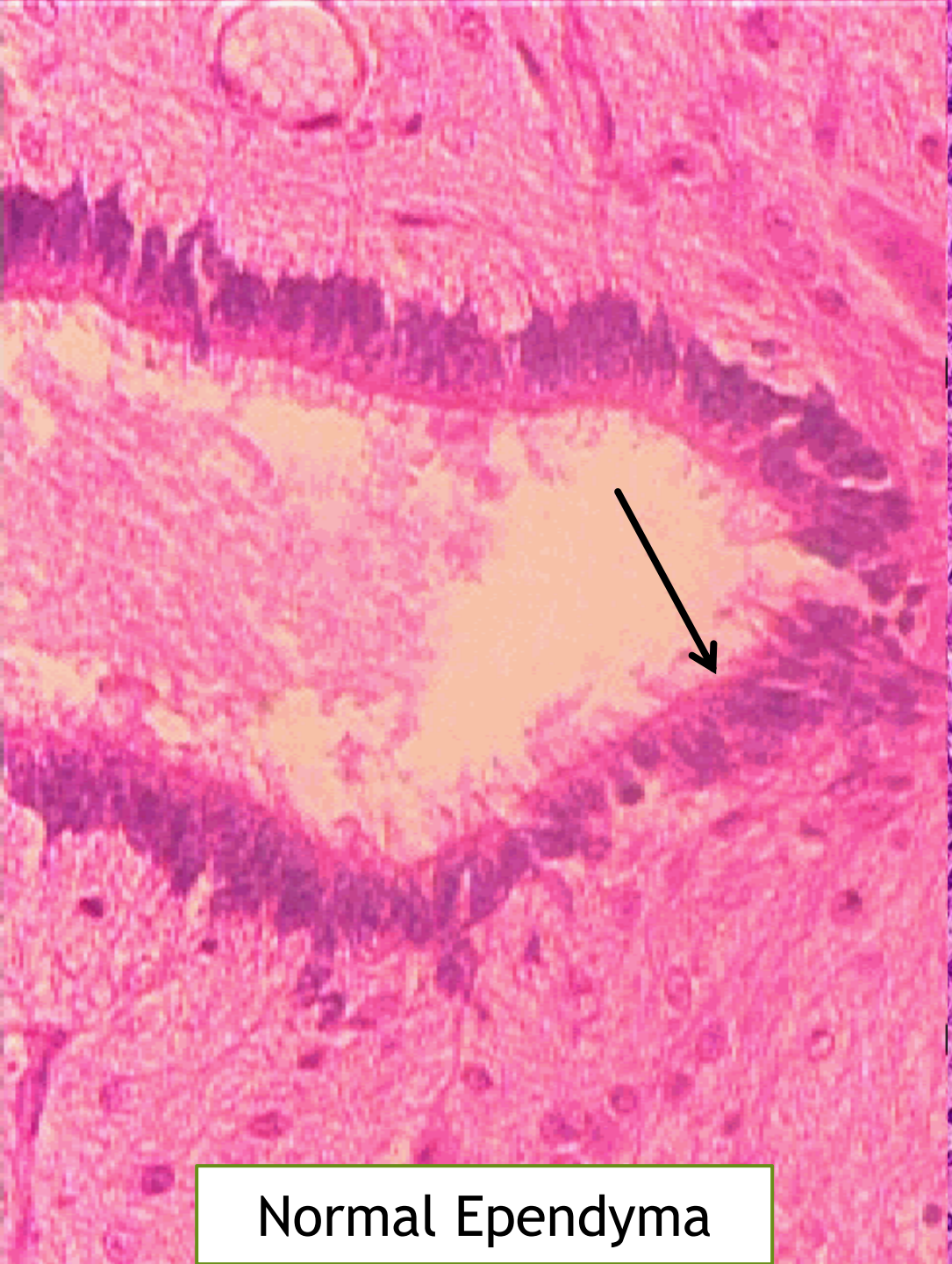
True Rosette



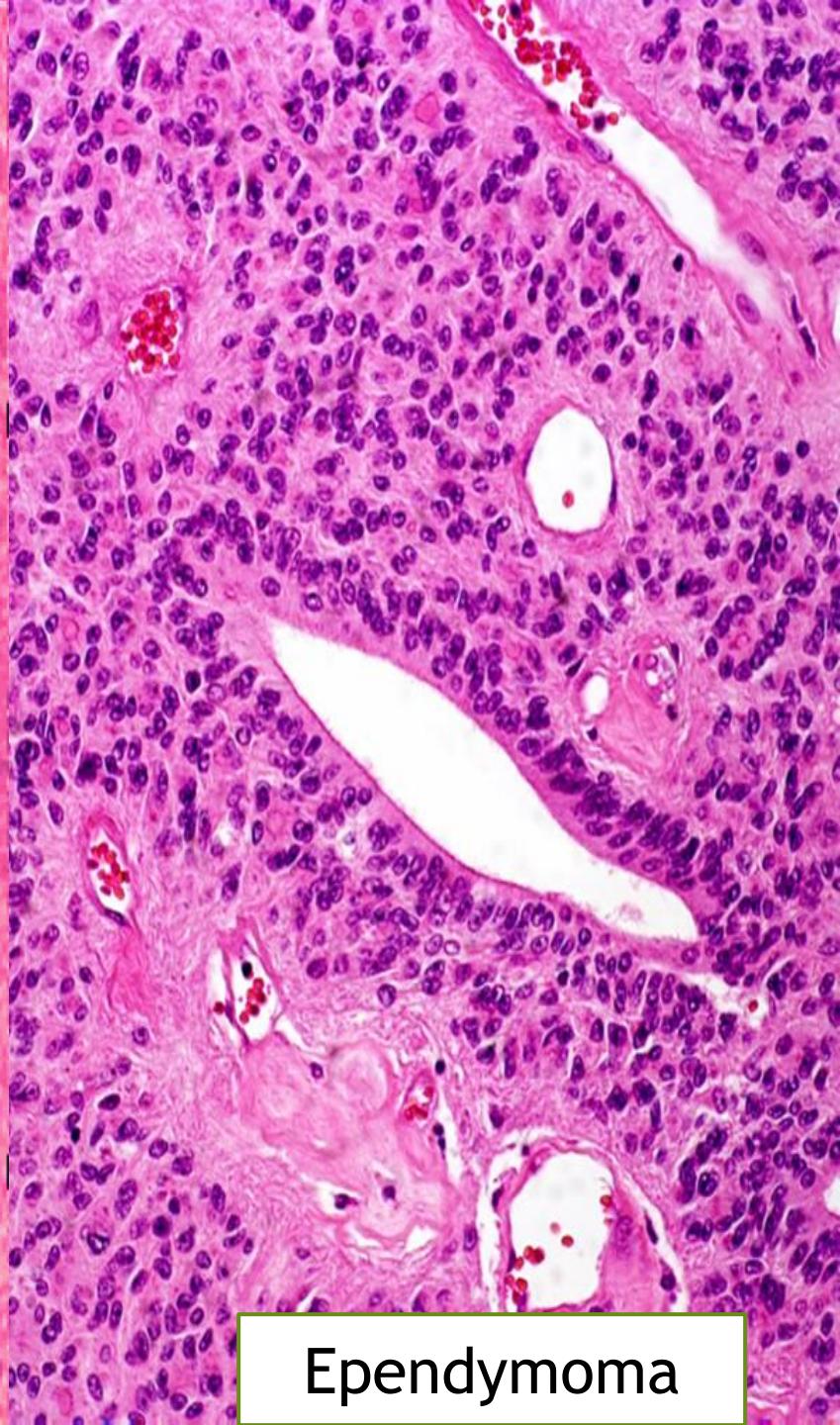
Perivascular Pseudorosette







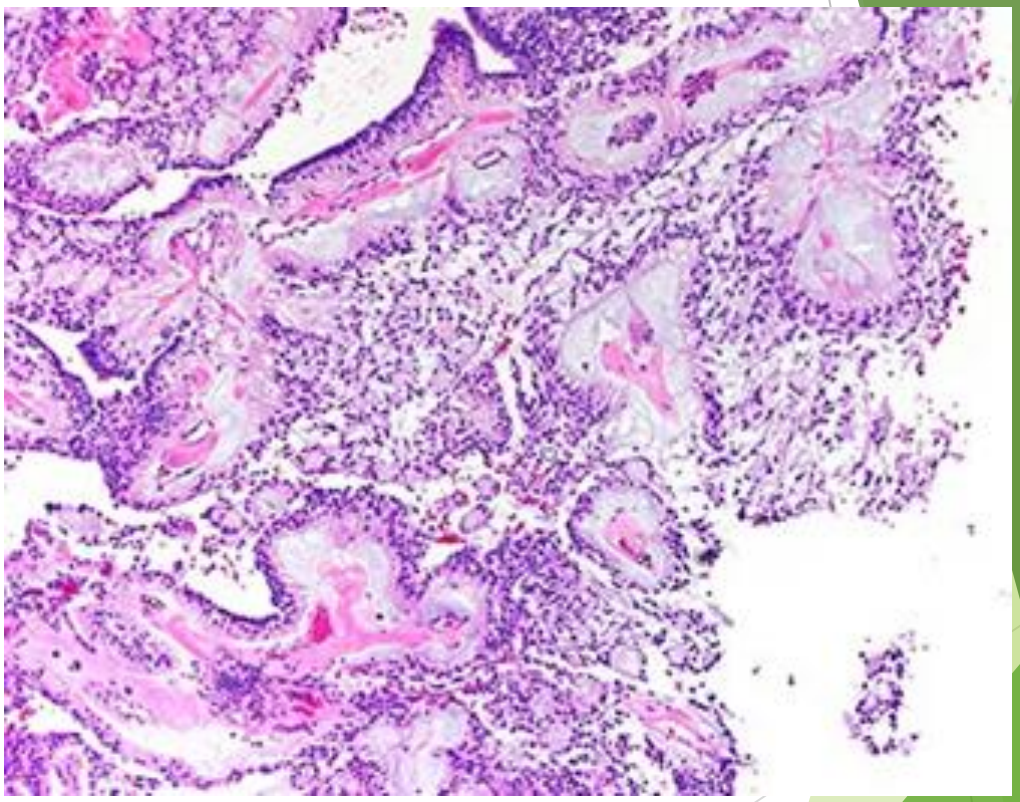
Normal Ependyma



Ependymoma

-M/E:

papillae with myxomatous changes.



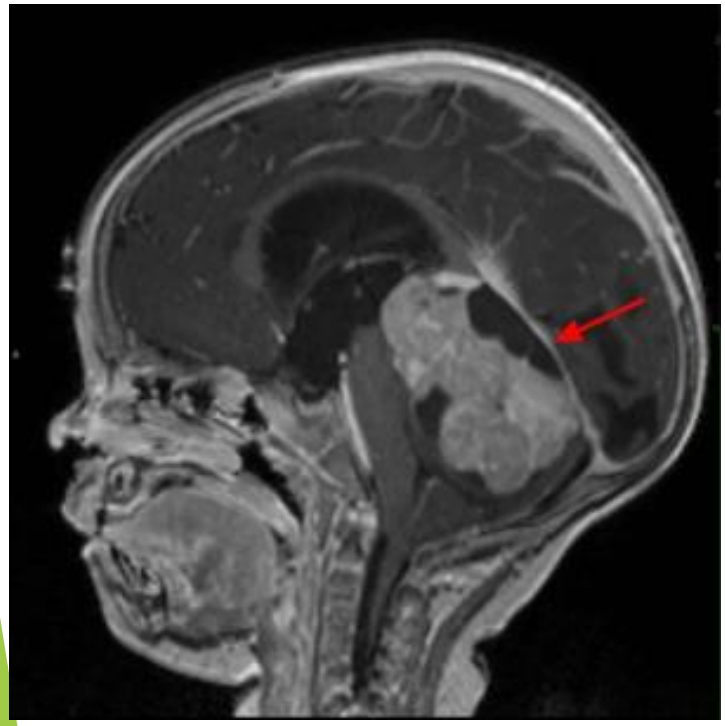
Medulloblastoma

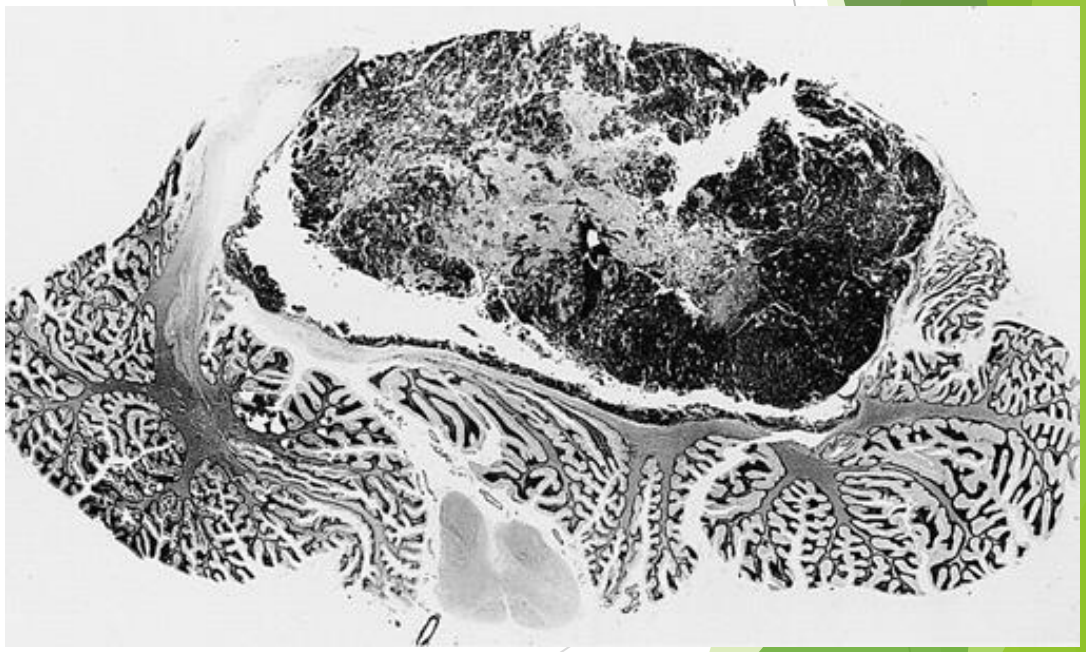
- 20% of pediatric brain tumors
- Primitive small cell (blue cell) tumor
- Any midline cerebellar or roof of 4^{th}. ventricle tumor in a child is a medulloblastoma till proven otherwise!
- Can be lateral cerebellar, more in young adults
- Hydrocephalus & ↑ICP occur early

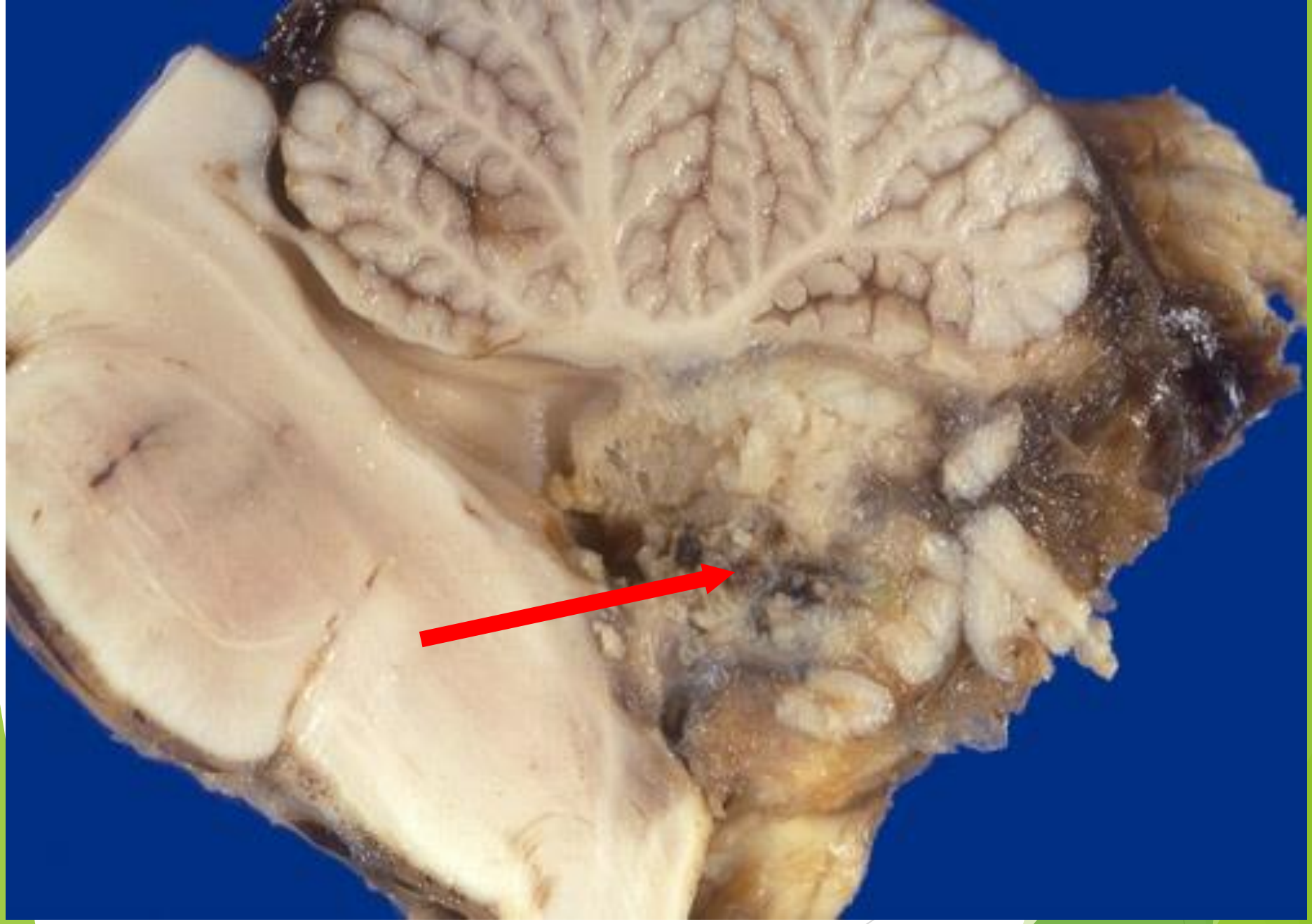
-Rapidly growing tumor.

-**Age:** children.

-**Site:** Roof of the 4th ventricle, obstructing pathway of C.S.F



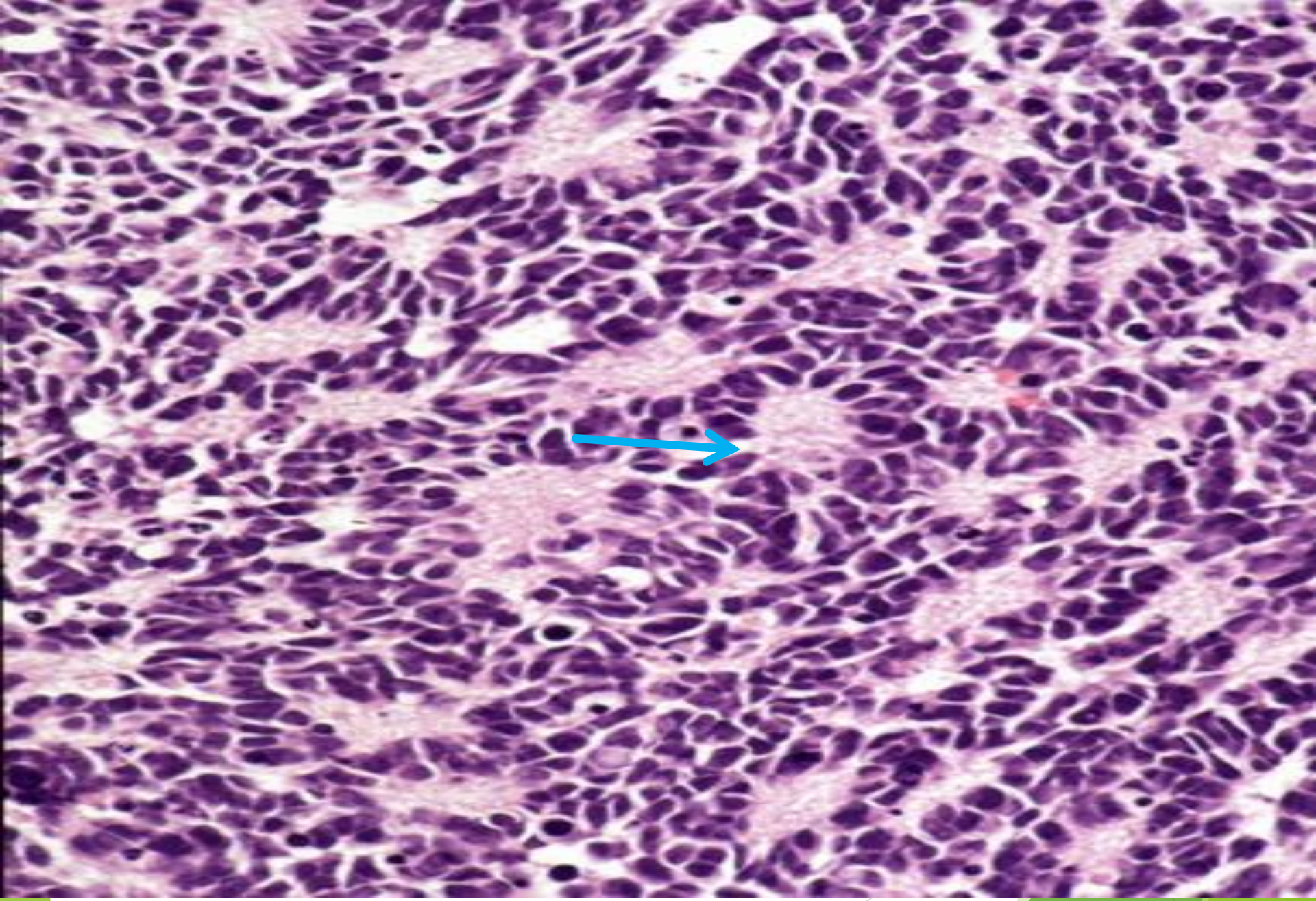




Medulloblastoma

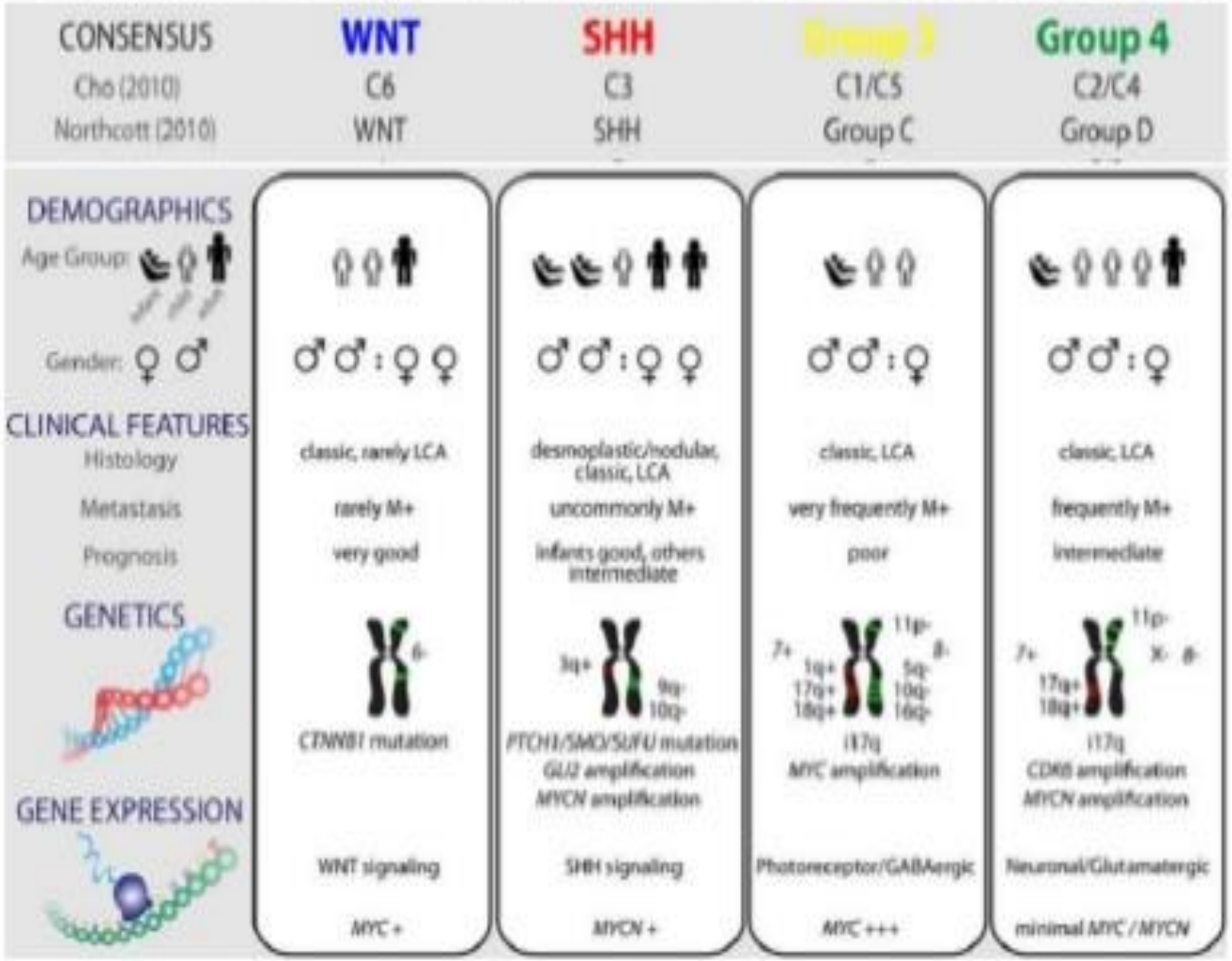
Microscopic features:

- Sheets of small undifferentiated blue hyperchromatic cells with numerous mitoses
- Homer-Wright Rosettes
- Neurofibrillary background
- WHO Grade IV
- MYC amplification– poor. WNT - favorable
- Rx.: Resection + Radiation entire neuraxis since spreads along CSF



Medulloblastoma/ Rosettes

Molecular subgroups of Medulloblastoma



5 yr OS	~95%	~75%	~ 50%	~ 75%

Taylor et al Acta Neuropathol (2012) 123:465–472

MENINGIOMA

- Arises from meninges on surface of brain or spinal cord.
- Most in adult females
- Tumor cells contain PR receptors
- NF2 gene inactivating mutation, even in 50% of non-NF2 meningiomas
- Sites: Parasagittal, Falx, sphenoid, ventricles.. etc

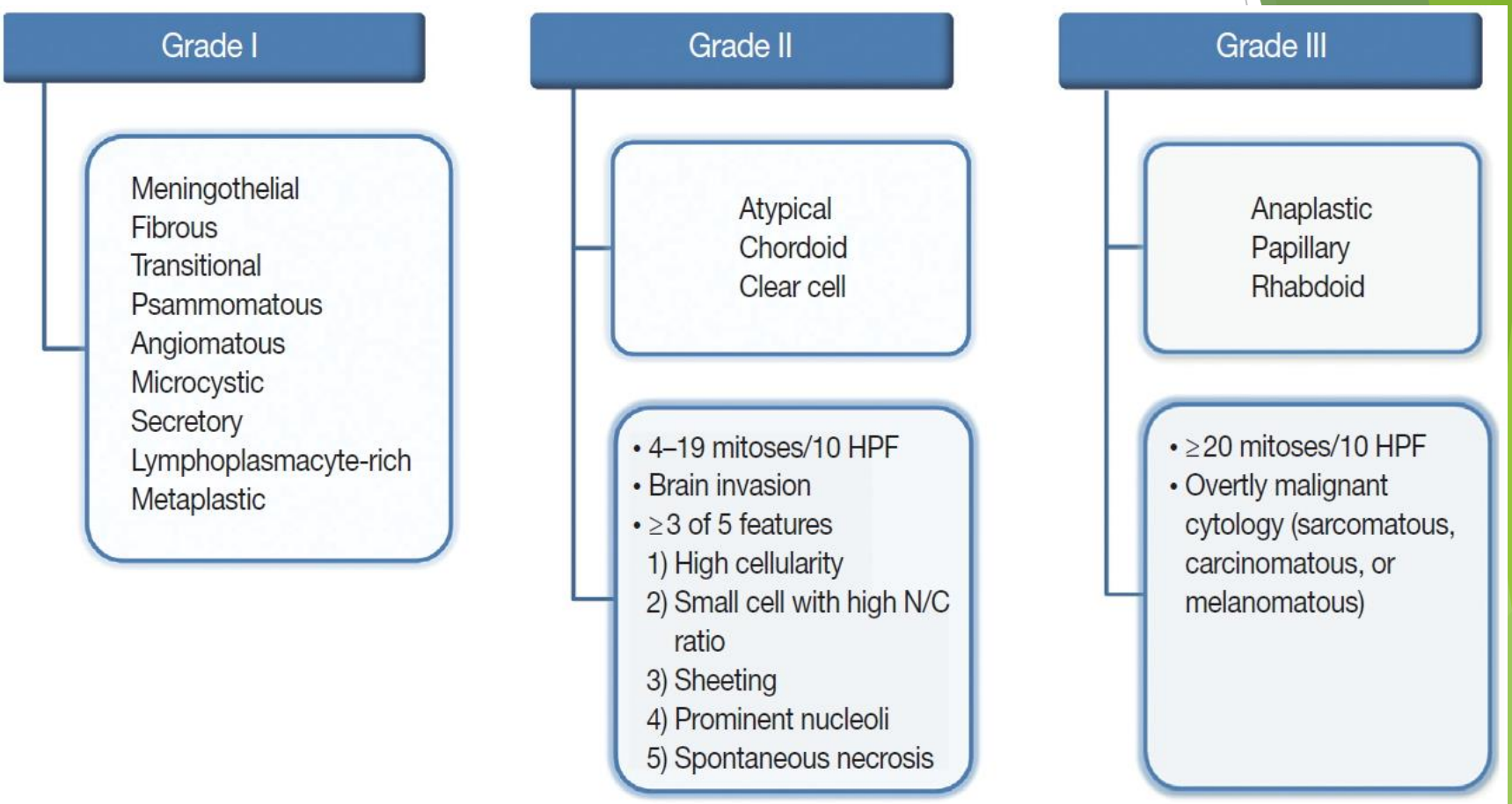
Gross features:

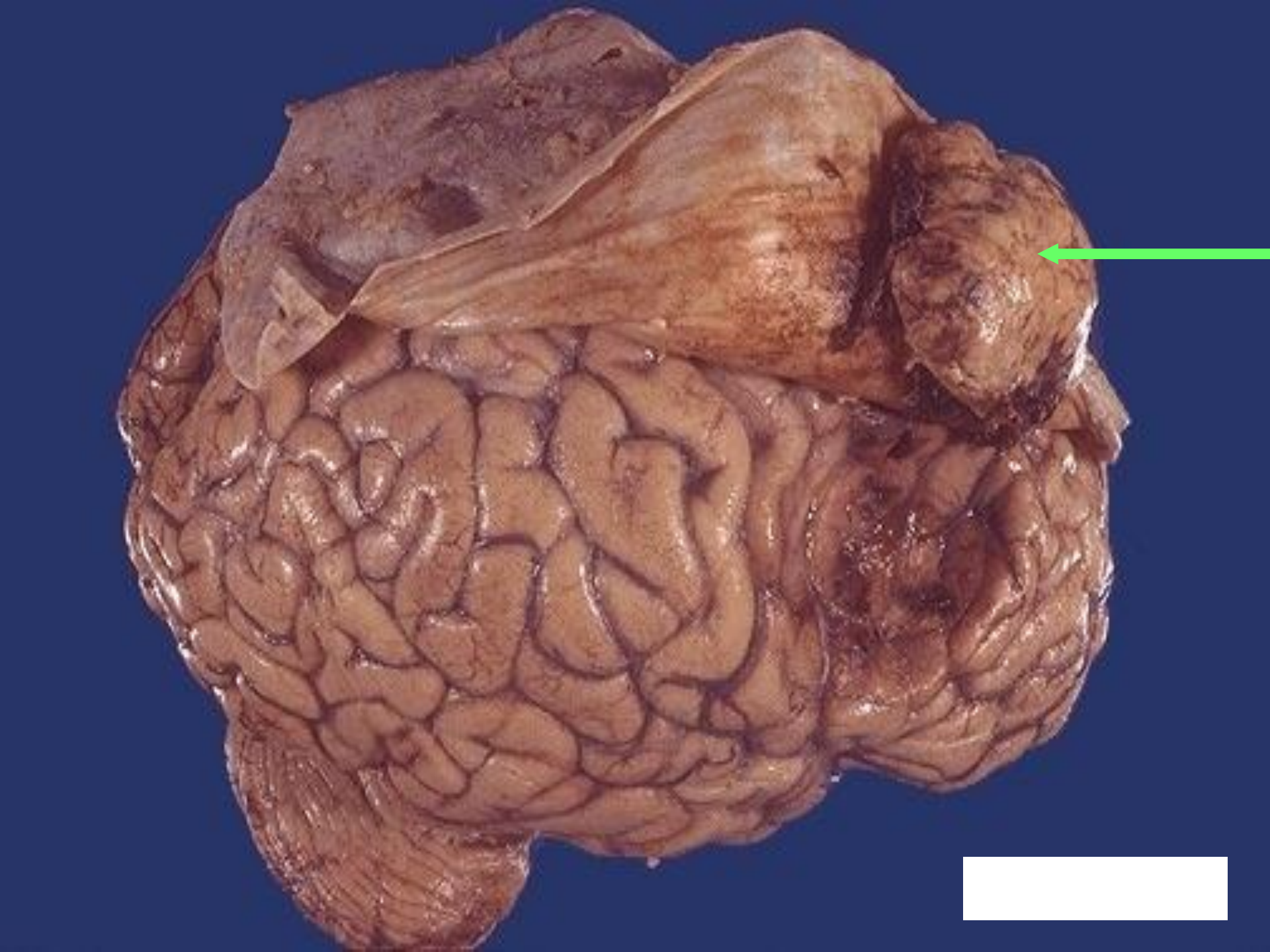
- Well-defined solid dural-based mass
- Compressing brain but easily removed
- Can invade the Skull & Venous sinuses, but this does not affect grade
- Can invade the underlying brain: IMPORTANT in prognosis: increased recurrence rate

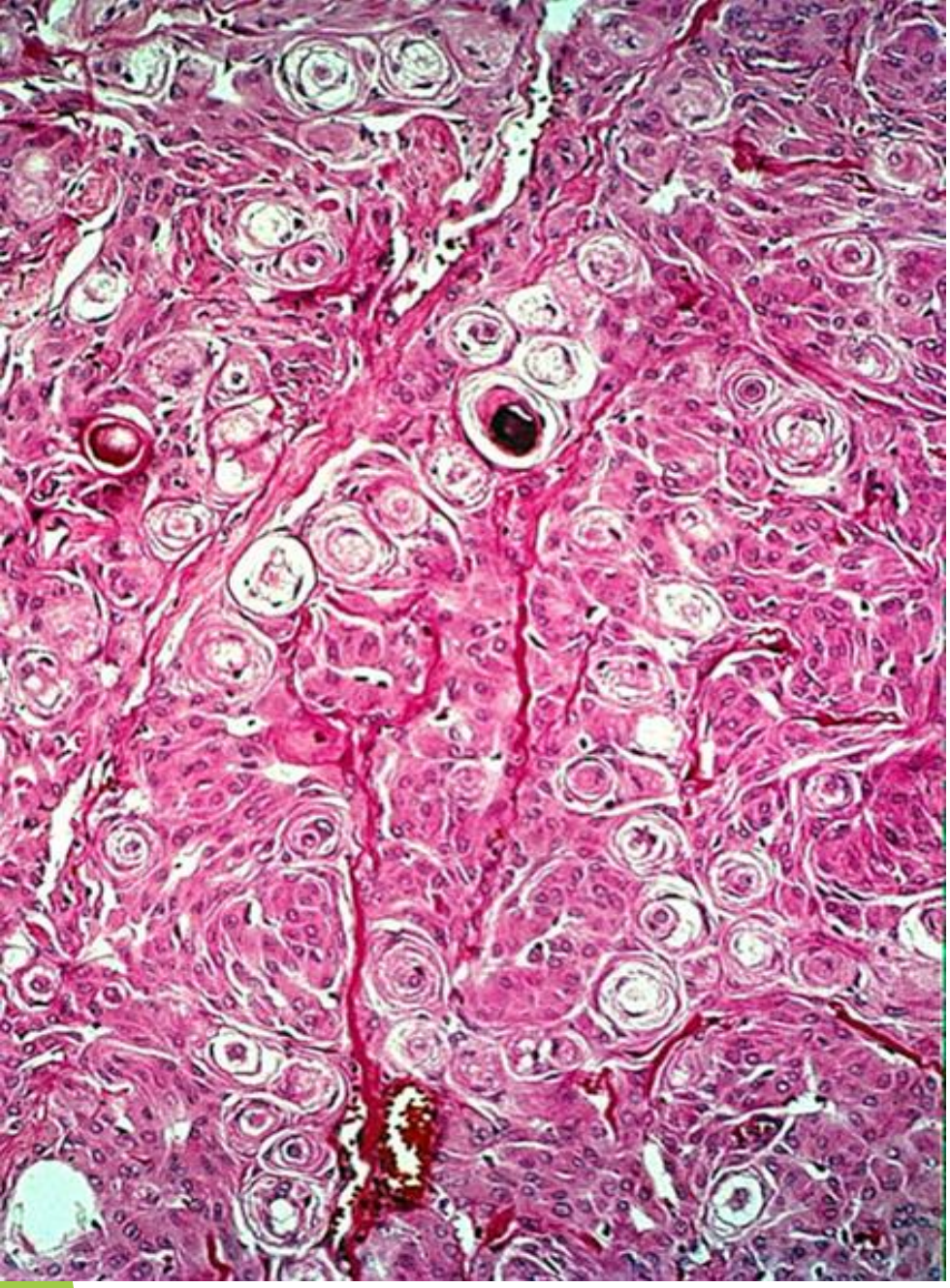
Many subtypes:

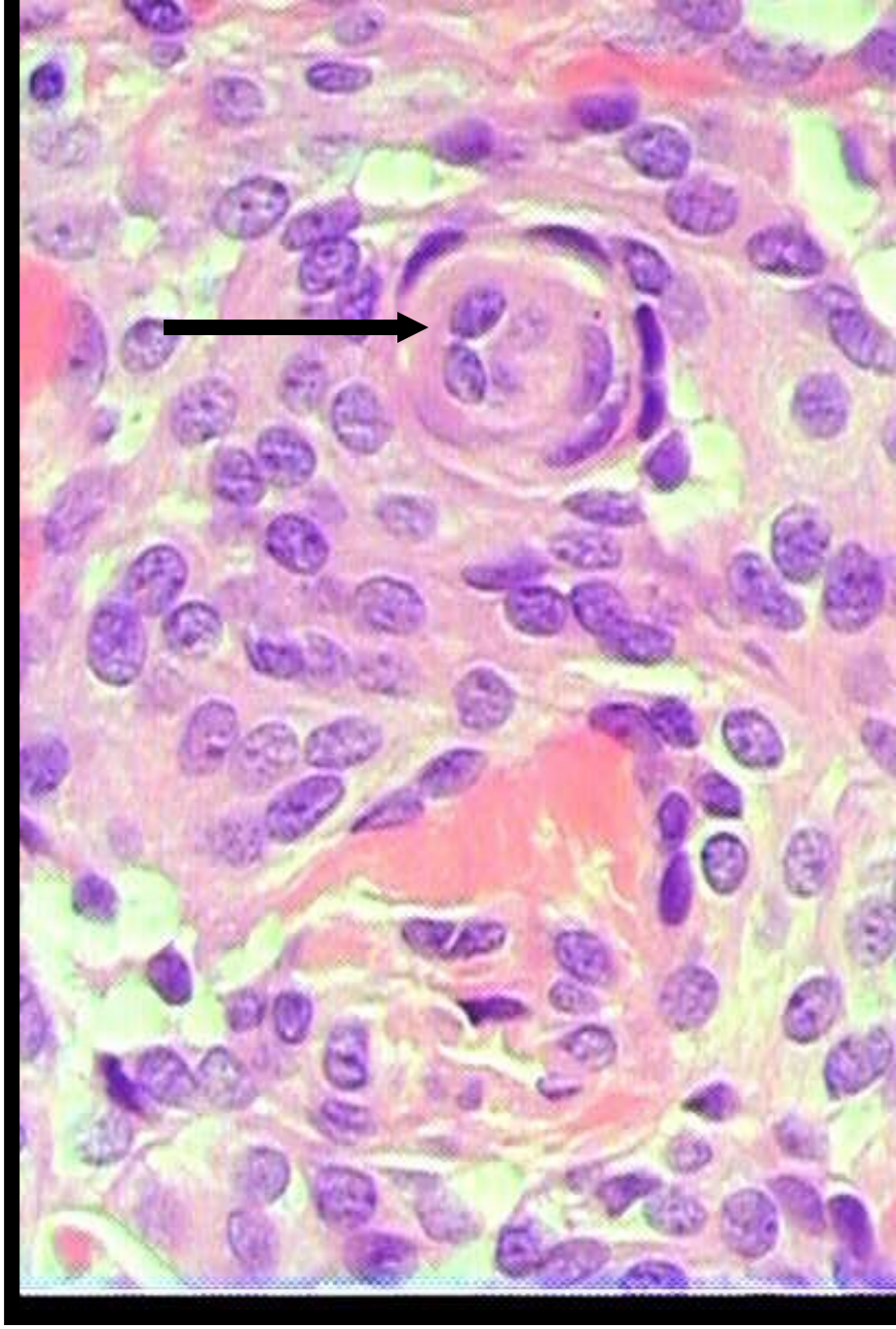
- Syncytial
- Fibroblastic
- Transitional
- Psammomatous (PSAMMOMA BODIES)
- Secretory
- Many Others

- Majority are benign but may recur
- Some types more likely to be aggressive
- Prognosis depends on SIZE, LOCATION, GRADE & Surgical ACCESSIBILITY


Grade I
Meningothelial
Fibrous
Transitional
Psammomatous
Angiomatous
Microcystic
Secretory
Lymphoplasmacyte-rich
Metaplastic
Grade II
Atypical
Chordoid
Clear cell
• 4–19 mitoses/10 HPF
• Brain invasion
• ≥3 of 5 features
1) High cellularity
2) Small cell with high N/C ratio
3) Sheeting
4) Prominent nucleoli
5) Spontaneous necrosis
Grade III
Anaplastic
Papillary
Rhabdoid
• ≥20 mitoses/10 HPF
• Overtly malignant cytology (sarcomatous, carcinomatous, or melanomatous)







Psammoma bodies are diagnostic of meningiomas in brain tumors

Neuronal tumors

- **Central neurocytoma:**
  - Low grade intraventricular (3rd or Lat)
  - Neuropil
- **Ganglioglioma:**
  - Age ≤ 30yrs, presents with seizures
  - Mixture of low grade Astro. + mature neurons
  - Anywhere but most temporal
- **Dysembryoplastic neuroepithelial tumor**
  - Low grade childhood tumor
  - Nodular tumor in superficial temporal lobe
  - Seizure

LYMPHOMA

- Primary usually multiple peri-ventricular nodular tumor (1% of IC-tumors)
- High grade B cell Lymphoma
- Most common CNS tumor in immunosuppressed
- Most frequent in AIDS patients with EBV infection.
- Poor response to chemoRx
- May be secondary lymphoma due to spread from peripheral lymphoma to CNS is usually to meninges rather than into brain

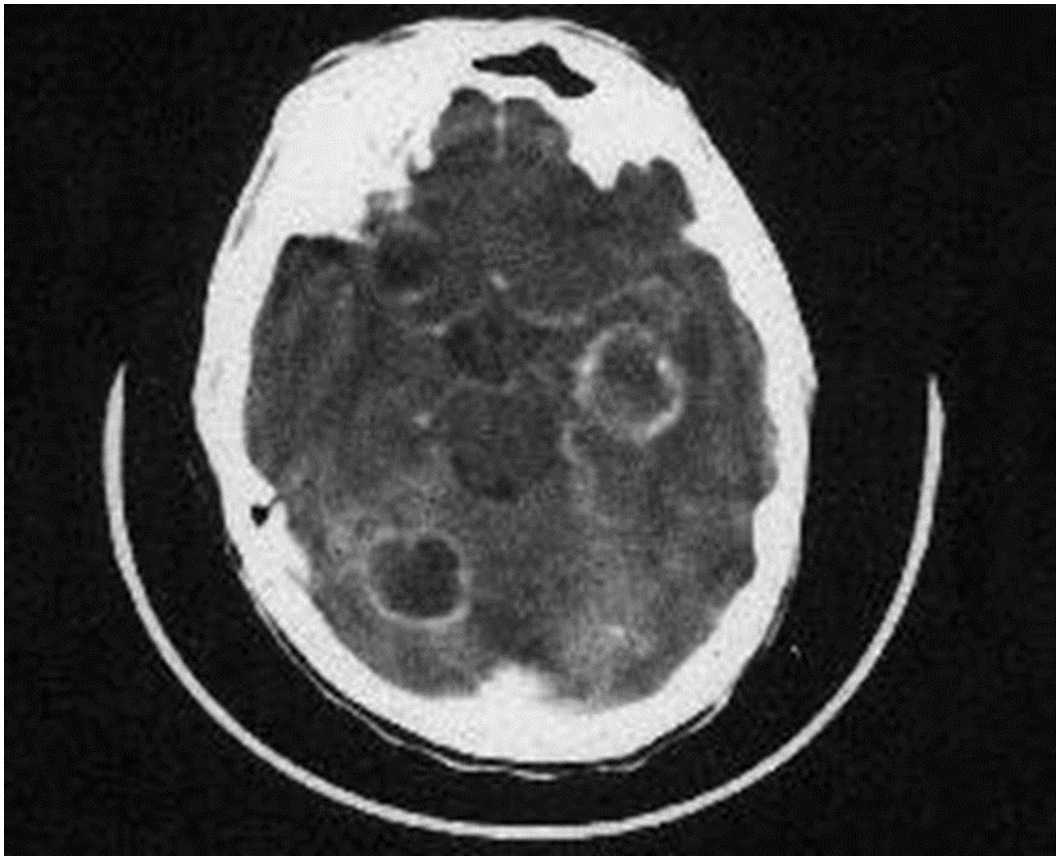
GERM CELL TUMORS

- Primary – midline (pineal & suprasellar)
-
- 90% - First 2 decades of life
- Most common type: Germinoma

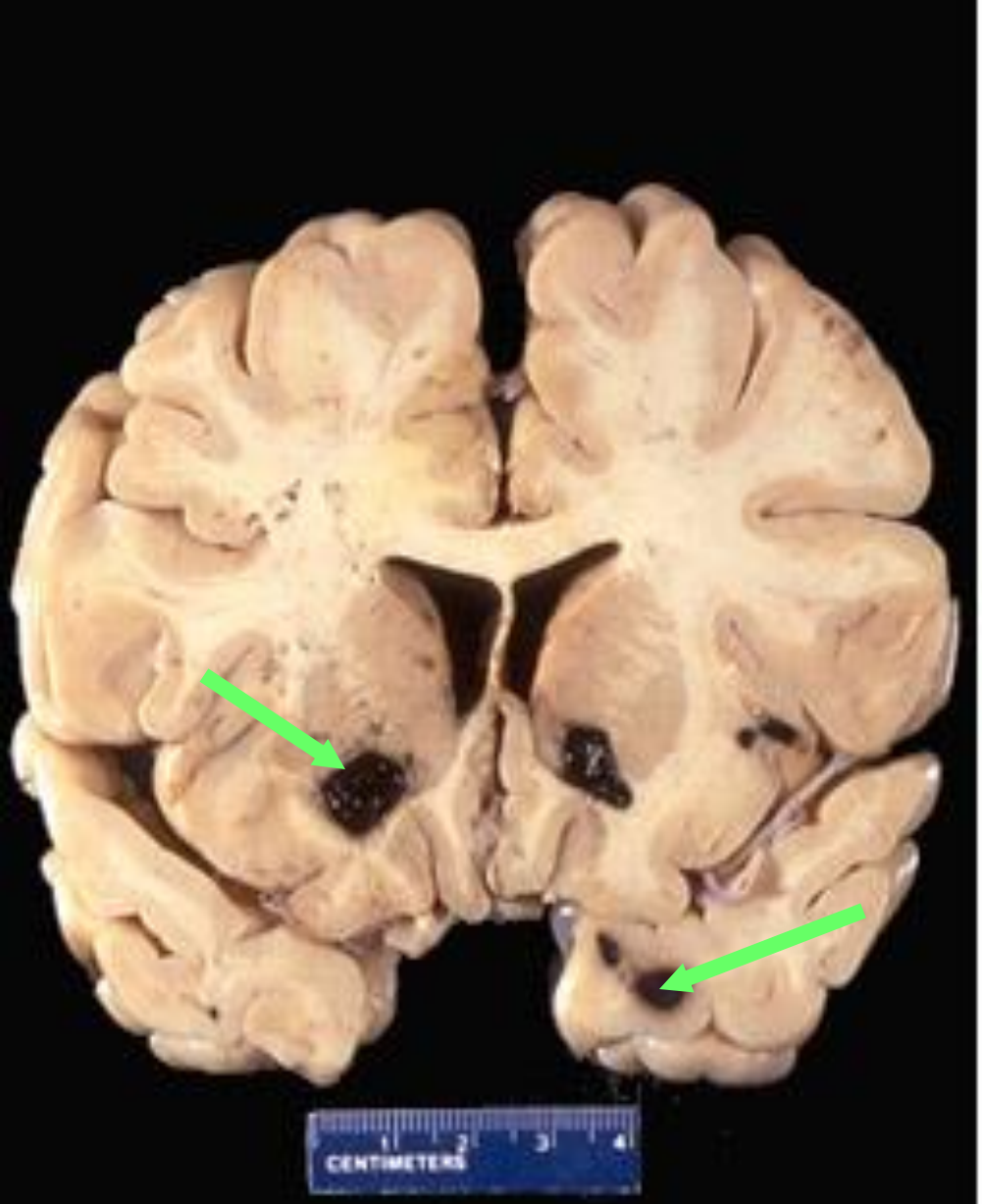
METASTATIC TUMORS

A- Brain metastases

- More common than primary ?
- Often multiple
- Majority of tumors disseminate by blood & parallel anatomic distribution of regional blood flow:
  - Grey-white matter junction
  - Border zone between MCA and PCA distributions
  - Often MULTIPLE
- Marked edema is seen around metastasis



- Origin of solid primary tumors:
  - Lung (most common)
  - Breast
  - Gastrointestinal
  - Kidney
  - Melanoma
- Less common but with special propensity to metastasize to brain
  - Germ cell tumors
  - Thyroid


CENTIMETERS
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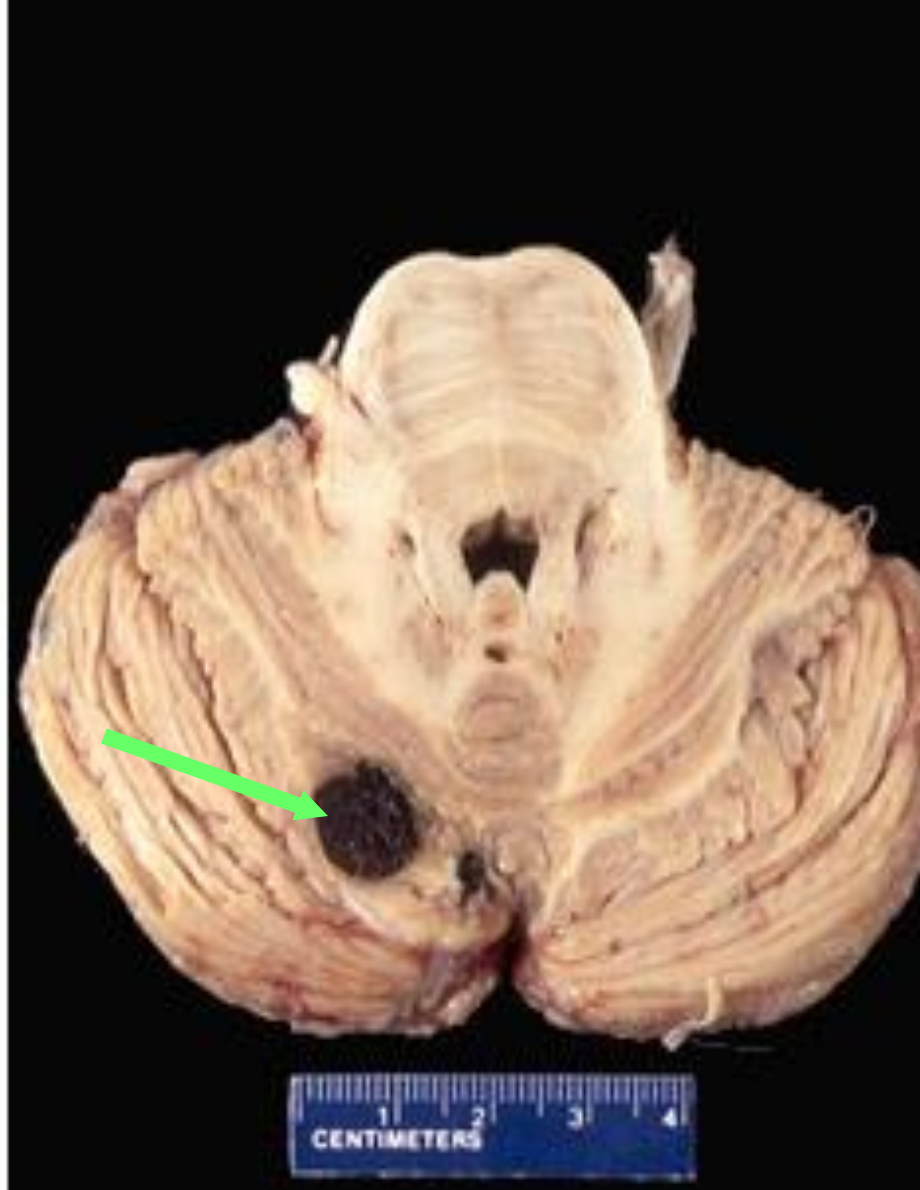
3
4


CENTIMETERS
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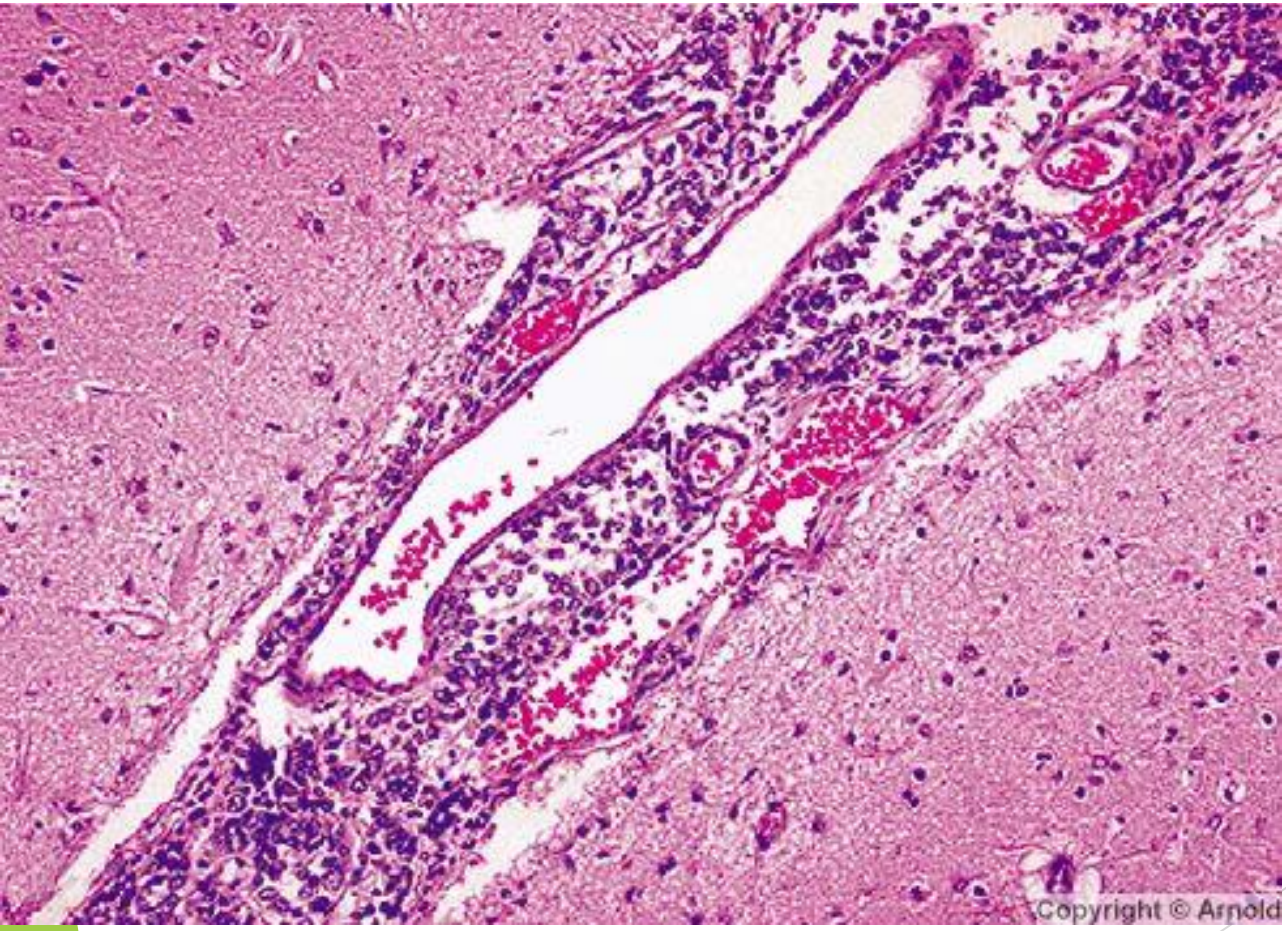
B- Leptomeningeal Metastases

- Clinically evident in 8% of patients with metastases
  - Breast, lung, gastrointestinal adenocarcinoma
  - Melanoma
  - Lymphoma & Leukemia

- Mode of spread
  - Haematogenous
  - Shedding of cells into subarachnoid space from superficial brain metastasis
  - Growth along peripheral nerves (squamous cell carcinoma, non-Hodgkin lymphoma)

- Meningeal carcinomatosis

METASTATIC TUMORS
leptomeningeal carcinomatosis



Spinal Cord tumors

- Extraspinal: Metastatic, Lymphoma
- Extradural intraspinal: Metastatic, Lymphoma
- Intradural:

  Extramedullary: Schwannoma

  Meningioma

  Intramedullary: Ependymoma

  Astrocytoma

The End

Good luck