



Lecture II

TUMORS



Overview

- 10-17/100,000; intracranial
- 1-2/100,000; intraspinal
- The majority are primary
- 20% of all cancers of childhood ✓✓
- 70% of childhood CNS tumors arise in the posterior fossa *→ Infratentorial*
- A comparable number of supratentorial tumors in adult

Tumors are usually classified into { Benign
Malignant }

→ Some categories (e.g. ovarian tumors, BLs tumors) are classified into { Benign
Intermediate (Borderline)
Malignant }

→ Brain Tumors are different

Overview

- Different concept of benign and malignant
- Even benign may prove fatal → lipoma هي نوع من أنواع tumor يمكن تكون fatal
- Mostly not amenable for complete resection
- Vital centers → CVS, Respiratory centers will be affected
- Rare metastasis outside → even if it is malignant
- Cerebrospinal dissemination → Brain tumors are very infiltrative and cannot be localized
- Grading → In brain tumors we use four-tier system → Grade 1, 2, 3 & 4 → Benign grade 1 هو تقريباً للكيسة لا تكون جديده متدائمة ولكن ما زاد الـ grade تزايد Aggressiveness
→ In brain tumors ما ينجح في حاد Benign أو Malignant بنسبة الـ grade ببل حاد

Brain tumors لها تصنيف خاص، يعني بعض النظر عن تصنيف الـ Tumor بناءً على تصنيف الـ Pathology هل هو malignant أو Benign بناءً على خصائصه التي ينتجها على المريض. وجود الـ Tumor يمكن أن يكون في الـ Brain هو بذاته خاصية Malignant لأنه في المنطقة ما يستعمل أي زيادة بالحجم رأي الـ Tumor حتى لو Benign هي أعراض symptoms سيئة ويمكن يؤدي لـ death.



Gliomas

→ Tumors of neuroglial 'Supporting' cells

- The most common of primary tumors
- Derived from multipotent progenitor cell → Stem cells
- Within particular age groups → Each type of glioma prefer particular age group
- Predilection for specific regions



Astrocytoma; grade II-IV

- 80% of primary brain tumors in adults *→ most common*
- Usually in cerebral hemispheres
- May occur also in the cerebellum, brain stem and spinal cord
- 4-6 decades
- Morphologic classification
 - Grade 2* → Diffuse Astrocytoma
 - Grade 3* → Anaplastic Astrocytoma
 - Grade 4* → Glioblastoma



Astrocytoma; grade II-IV

→ New classification of tumors

- Molecular classification

- IDH mutant
 - Better prognosis
- IDH wild type → Normal

Isocitrate
dehydrogenase
metabolic up
activity of cells

Astrocytoma; grade II-IV

■ Pathogenesis of Glioblastoma

→ Grade 4

Starts de novo ← ■ Primary

↳ No preceding other tumor

- In older individual new onset
- Most are wild type IDH
- Gains of chromosome 7
- Loss of chromosome 10
- ✓ ■ TERT promoter mutations
- ✓ ■ EGFR amplification

■ Secondary

من يعني مني glioma
تأنت موجودة قبل
(grade 2 or 3)
دها progression

- In younger patients, progression of lower grade astrocytoma
- Driver mutations of IDH1 or IDH2



Astrocytoma; grade II-IV

- Most gliomas have genetic aberrations that lead to
 - Evasion of senescence
 - Telomeres/telomerase
 - Escape normal growth control
 - CDKN2A deletion ~> *Tumor suppressor gene*
 - Activation of growth signaling
 - EGFR or PDGFR
 - Evasion of apoptosis
 - TP53 mutation

Astrocytoma; grade II-IV

■ Morphology

■ Diffuse astrocytoma

- Gross, size and texture
- Microscopy
- IHC; GFAP, IDH1 (90%)

Gross → Not well-demarcated
 Size → Start from 1cm and may involve the entire brain tissue.
 Texture → Soft, Solid

Type of intermediate filaments

لے عبا عن جز من Cytoskeleton تبع cells
 صا او IF بتختلف من نوع cell لاف
 صا د بغيرنا ما يكون ما در من فميز
 نوع او Tumor عن فرجه morphology

Muscle → Desmin
 Epithelial cells → Cytokeratin
 Neuroglial cells → GFAP

↳ Glial fibrillary acidic protein

■ Anaplastic astrocytoma

■ Glioblastoma

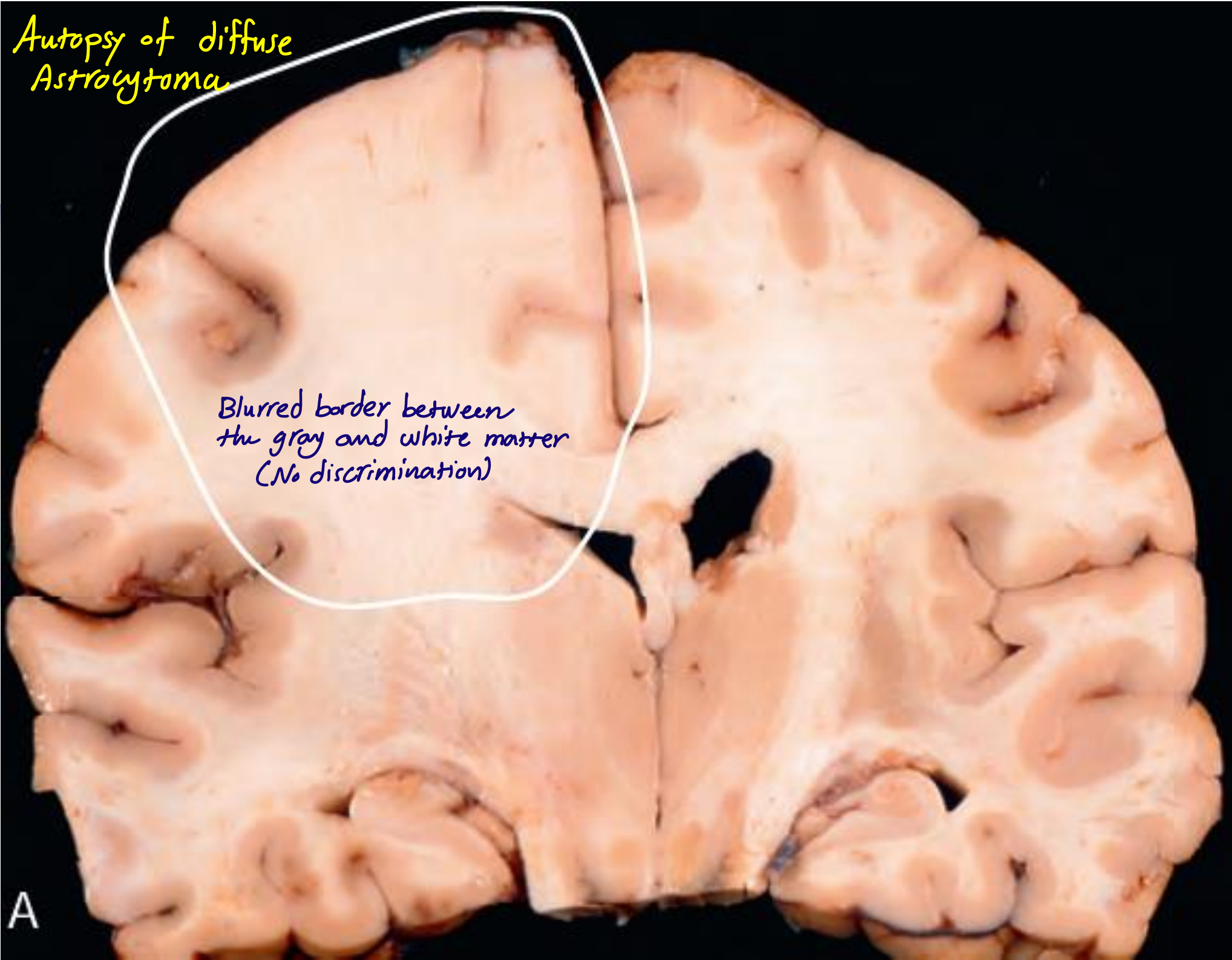
- ↳ Most aggressive
- ↳ Poor prognosis (<Year)
- Gross
- Microscopy

The same of
 diffuse astrocytoma
 but with increased
 cellularity with increased
 nuclear atypia and mitosis

Autopsy of diffuse Astrocytoma

Blurred border between
the gray and white matter
(No discrimination)

A



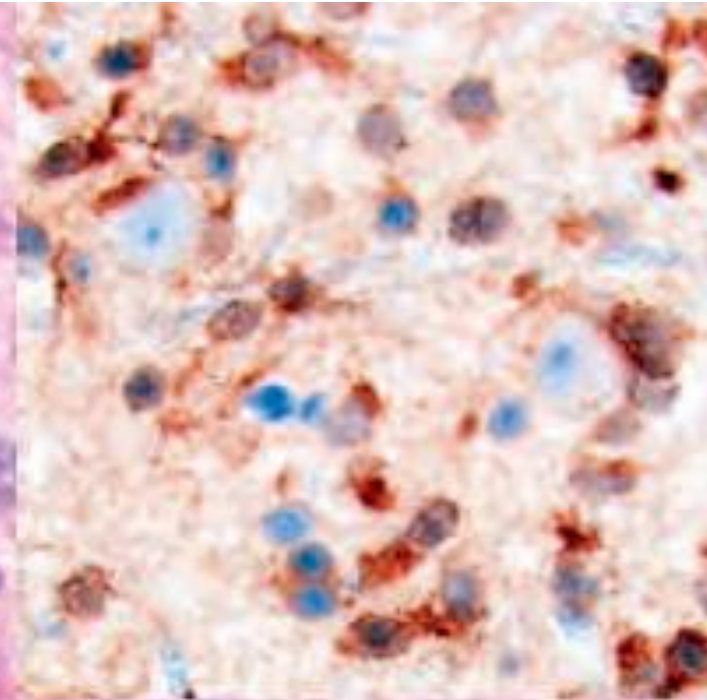
Diffuse

Astrocytoma

*limited changes normal ^{بـنـاء} astrocytes

*Nuclei of astrocytes are closely adjacent to each other

*Satellitosis → Aggregations of astrocytes around the neurons



Glioblastoma

Dense area, the center is radiolucent due to center necrosis as a result of ischemia resulting from the fast developing tumor

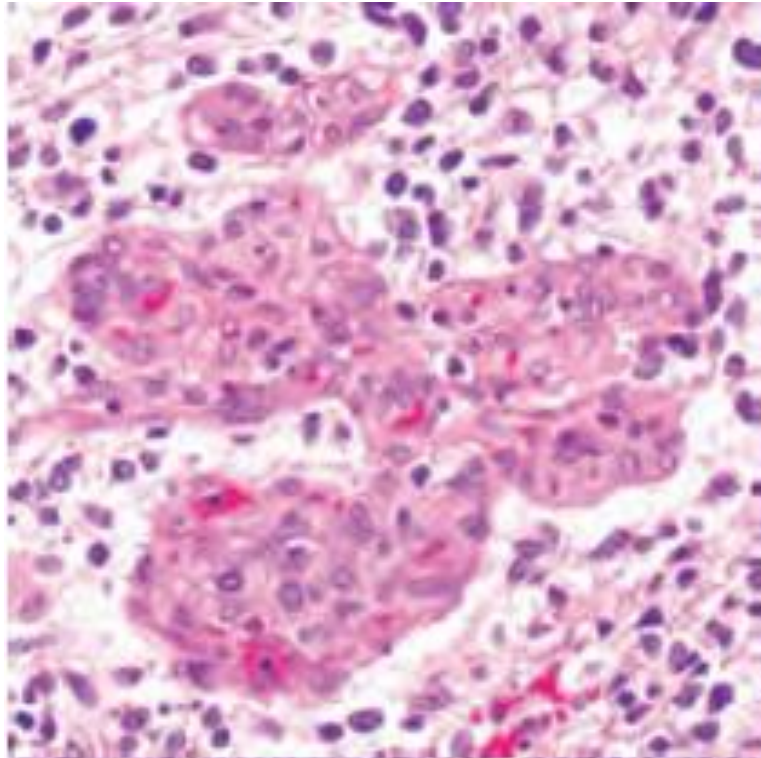
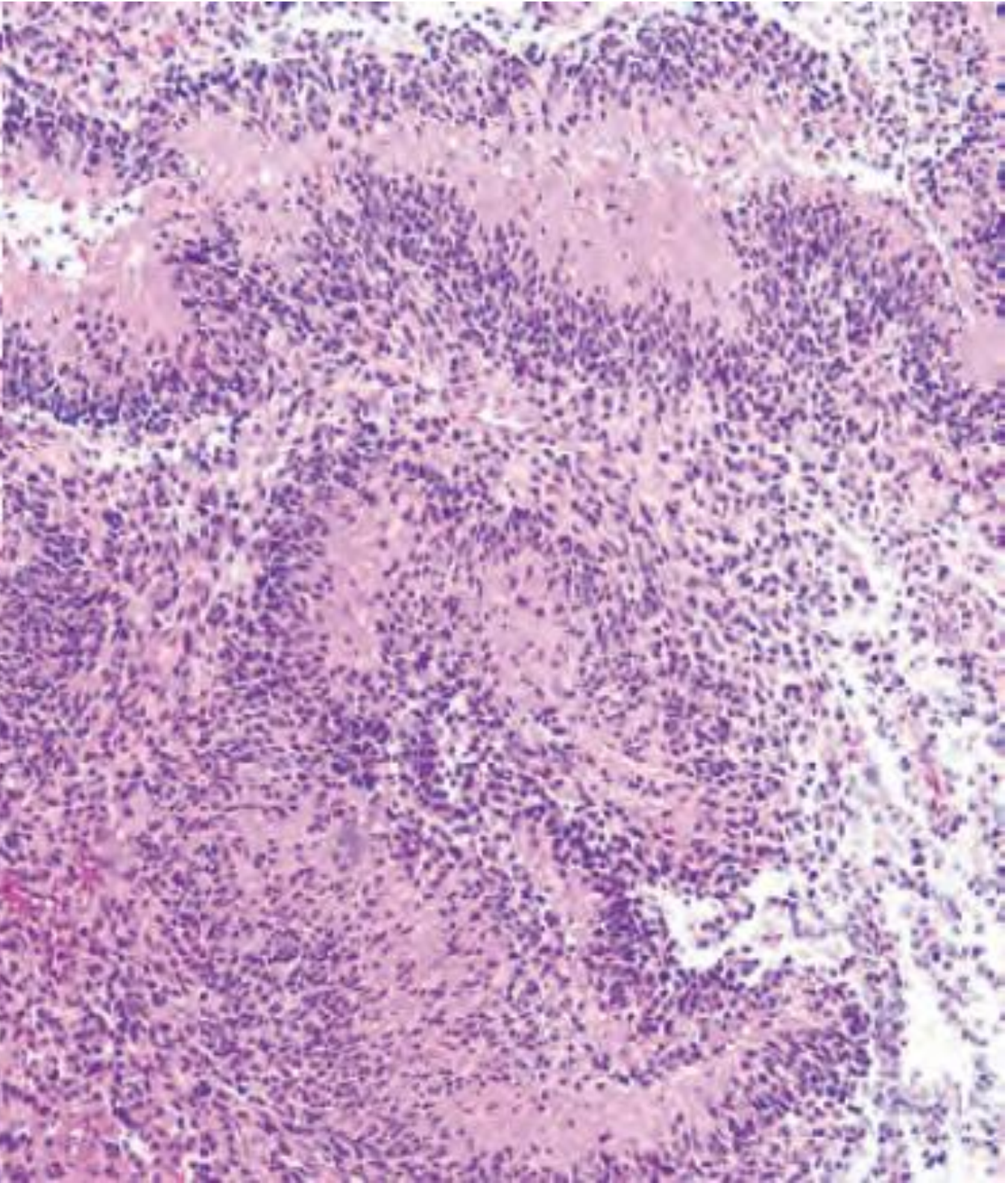
A



Glioblastoma

- Well-demarcated grade 2 ~~size~~
- Also it may pass to the other hemisphere through the C. callosum (Butterfly-like)
- Hemorrhage





Glio

blastoma

- Necrosis
- Palisading → Alignment of tumor cells around the necrosis
- BVs proliferation



Oligodendroglioma

- Best prognosis of glial tumors
- 5-15% of gliomas
- 4-5 decade
- White matter of cerebral hemispheres



*Astrocytoma is near
the cortex
(near the gray matter)*

Oligodendroglioma

grade 2 → Oligodendroglioma
grade 3 → Anaplastic oligo...
grade 4 → Glioblastoma

end result of all types
of glioma

■ Pathogenesis

- IDH mutation and whole arm chromosomal codeletion 1p and 19q
- With progression to anaplastic form loss of CDKN2A
- No EGFR amplification (in contrast to high grade astrocytoma) → Glioblastoma
- TERT promoter mutation (as in glioblastoma)



Oligodendroglioma

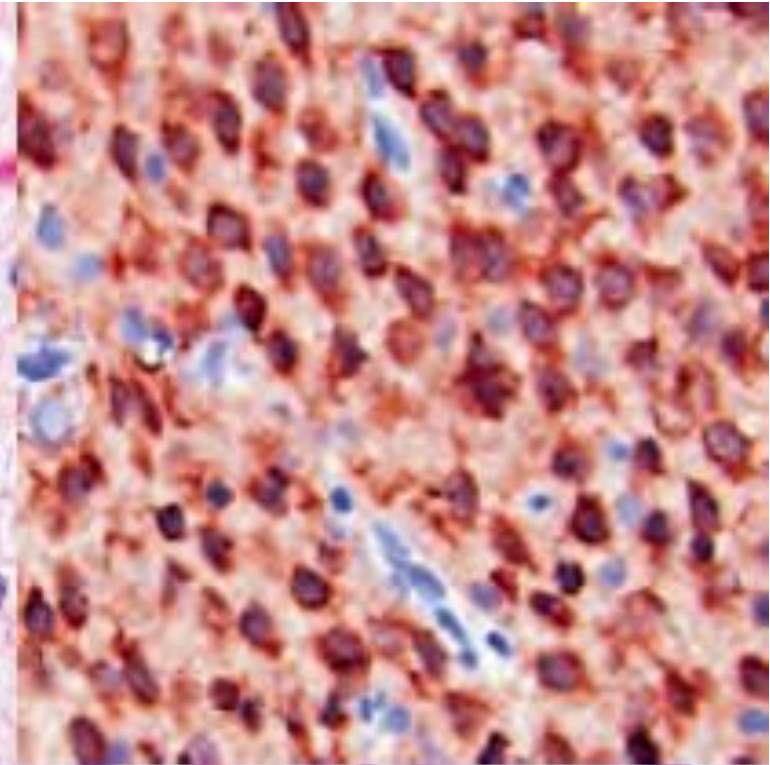
→ Dystrophic calcification

- Morphology
 - Often with cyst
 - Microscopy
- Anaplastic oligodendroglioma → Increased cellularity, atypia...

Oligodendro

glioma

- Rounded oval nucleus
- Bland innocent nucleus (بريئة)
(يعني أقرب إلى normal)
- No prominent nuclei
- Clear 'halo' around the nucleus
مميز





Pilocytic astrocytoma

→ Grade 1 astrocytoma

→ easier surgical removal

- More discrete borders
- Relatively benign behavior
- Children and young adults
- Cerebellum and around III. Ventricle
- KIAA1549-BRAF gene fusion/duplication



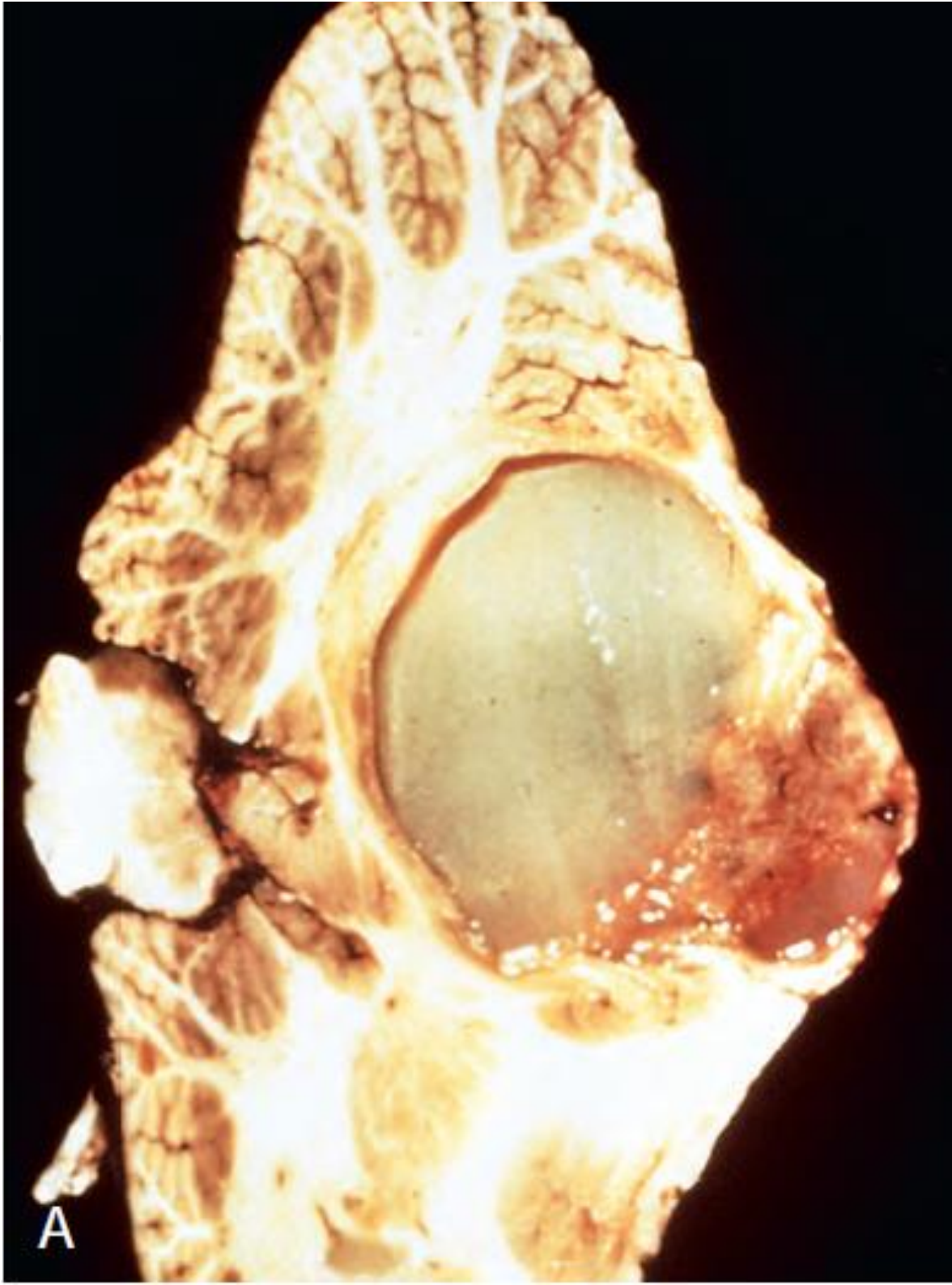
Pilocytic astrocytoma

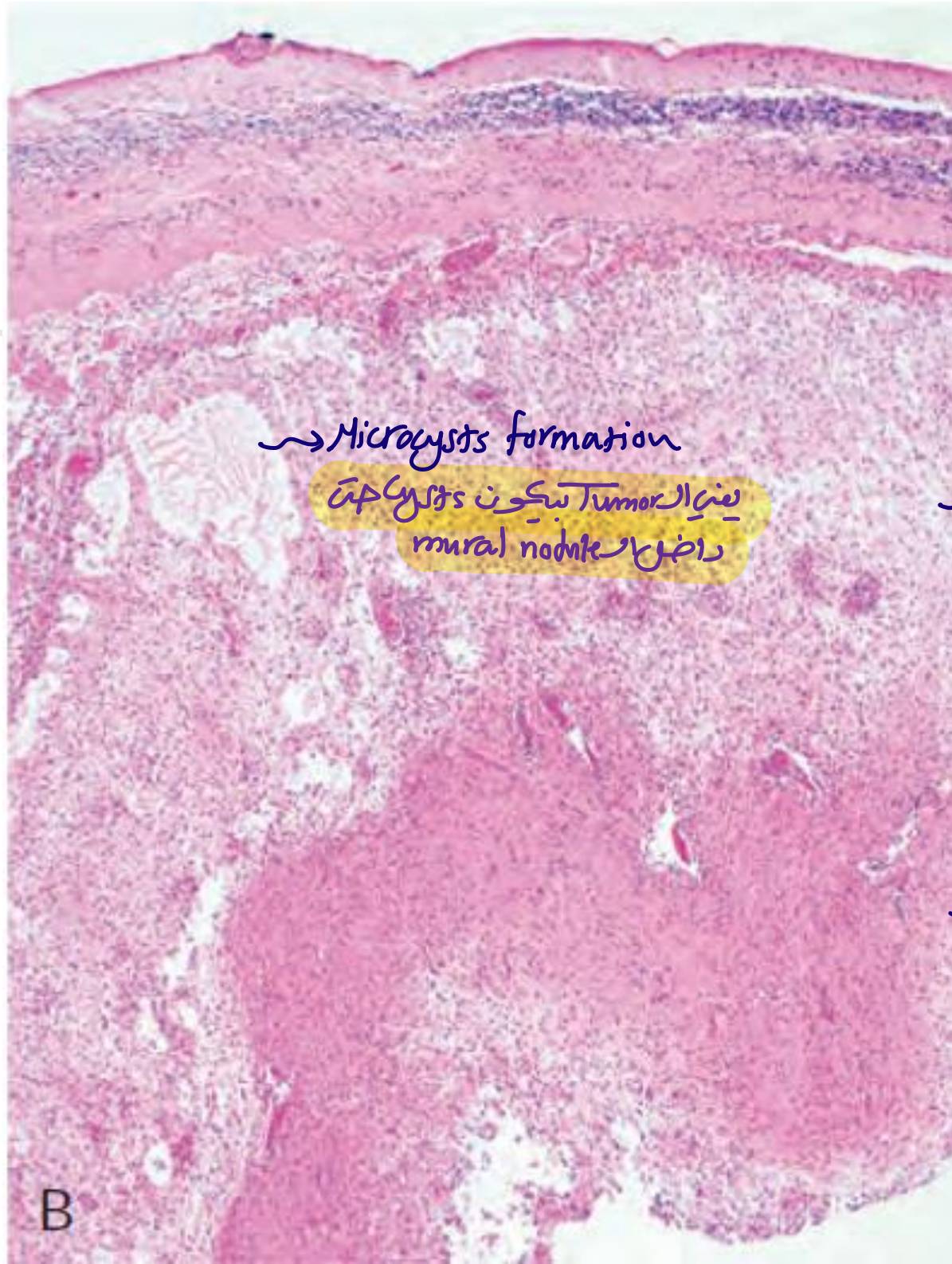
- Morphology

- Well demarcated and cystic with mural nodule
- Limited brain invasion
- Loose microcystic and dense fibrillar areas
- Other microscopic features

مميز →

→ 2 areas under microscope





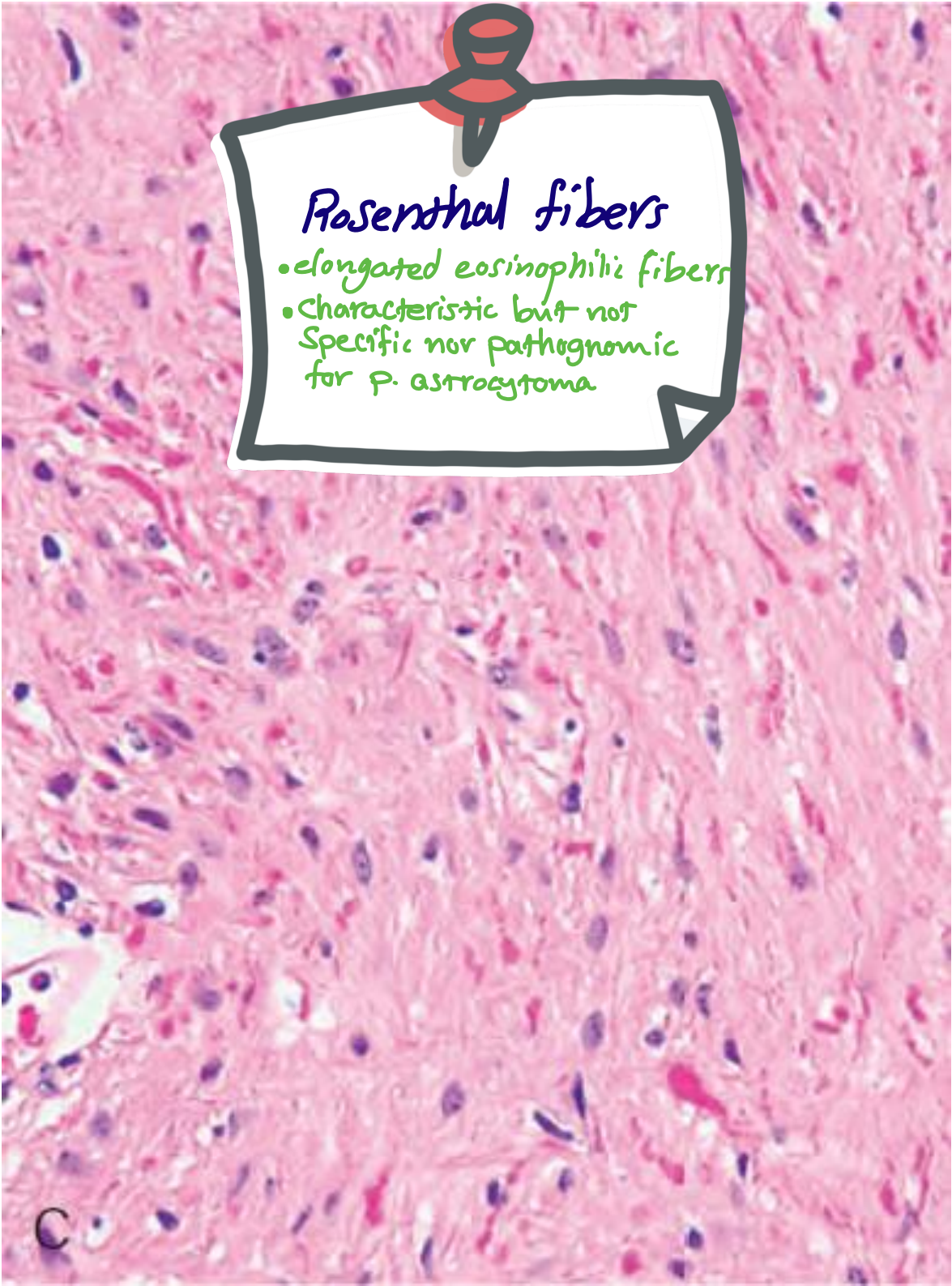
→ Microcysts formation

تكون الكيسات الصغيرة
Tumor
داخل العقدة الجدارية
mural nodules

→ loose area
(microcystic)

→ Compact area
(dense fibrillar)

B



A high-magnification histological image of brain tissue, likely from a pilocytic astrocytoma, stained with hematoxylin and eosin (H&E). The tissue shows numerous elongated, eosinophilic (pink) fibers, which are Rosenthal fibers, interspersed among the nuclei of glial cells. A red pushpin is at the top of the image, and a white note with a black border is pinned to it. The note contains the title 'Rosenthal fibers' and two bullet points. In the bottom left corner of the image, there is a small black letter 'C'.

Rosenthal fibers

- elongated eosinophilic fibers
- characteristic but not specific nor pathognomic for p. astrocytoma



Ependymoma

→ Ventricles, central canal

- Close to ependymal cells lined spaces
- 1-2 decades
 - Near the IV ventricle
 - 5-10% in the primary brain tumors in this group
- In adults
 - The spinal cord is the most common location
 - Frequently in the setting of NF2 ✓✓



Ependymoma

- Pathogenesis
 - NF2 gene mutated in spinal cord tumors
 - Distinct sets of driver mutations not shared with those of astrocytoma
- Morphology
 - Solid non infiltrative
 - Cerebrum, cerebellum and spinal → everywhere
 - Micro

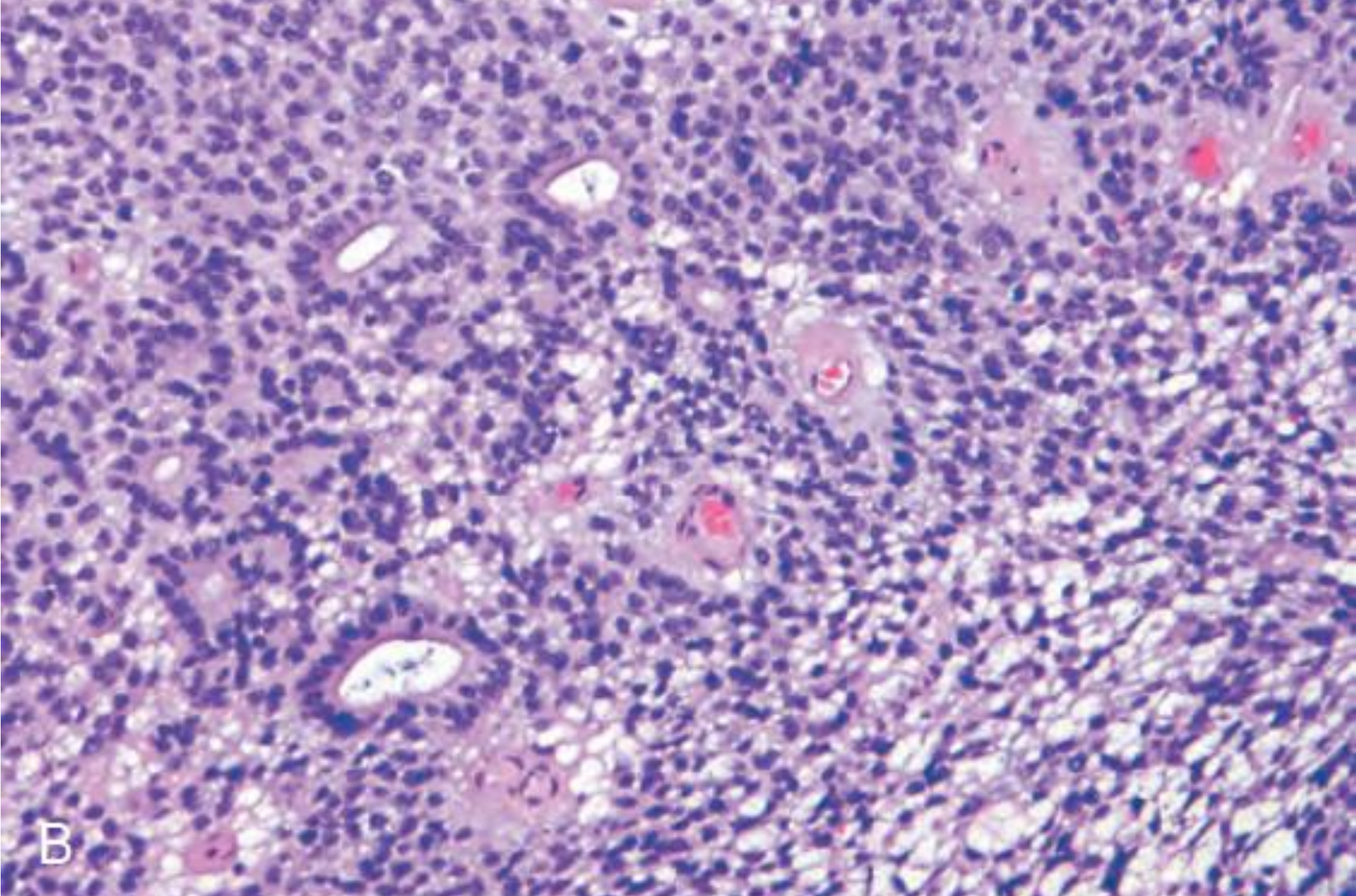
- well-demarcated
- spots of hemorrhage
- Amenable for surgery (يسهل الجراحون علىه)
- The danger comes from its location beside the brainstem, not from its biologic behavior (malignant or benign)



Rounded innocent nuclei (looking benign 'bland')

Rosette formation → True → lumen ↓
→ Pseudo → Bv ↓

B



This histological micrograph shows a dense population of cells with small, round, darkly stained nuclei. Several rosette formations are visible, which are clusters of cells arranged around a central point. Some of these rosettes have a central clear space (lumen), while others have a central area of eosinophilic (pink) staining, likely representing a blood vessel. The overall appearance is that of a benign, low-grade neoplasm.



Ependymoma

- variants ←
- Myxopapillary ependymoma → Distal part of spinal cord
 - Subependymoma

→ ependymal cells rich in capillary network that produce the CSF

→ Modified part of the ependymal layers

Choroid plexus tumors

- Rare → Mostly
- Benign or malignant
- Choroid plexus papilloma
 - Most common in children; lateral ventricles
 - In adults IV ventricle
 - Hydrocephalus → increased amount of CSF

Glial Tumors Are Finished

Neuronal and glioneuronal tumors

- 
- cell bodies of neurons (neuronal cells)
- glial cells
- **Gangliogliomas** → Ganglioneuronal tumor
 - Dysembryoplastic neuroepithelial tumor

Medulloblastoma

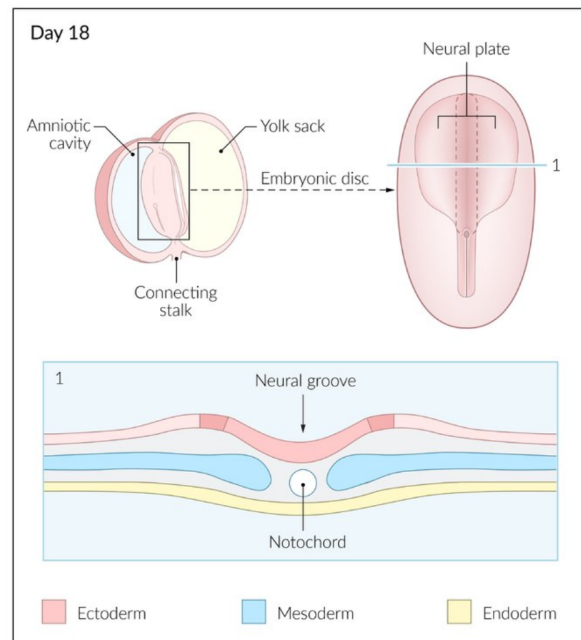
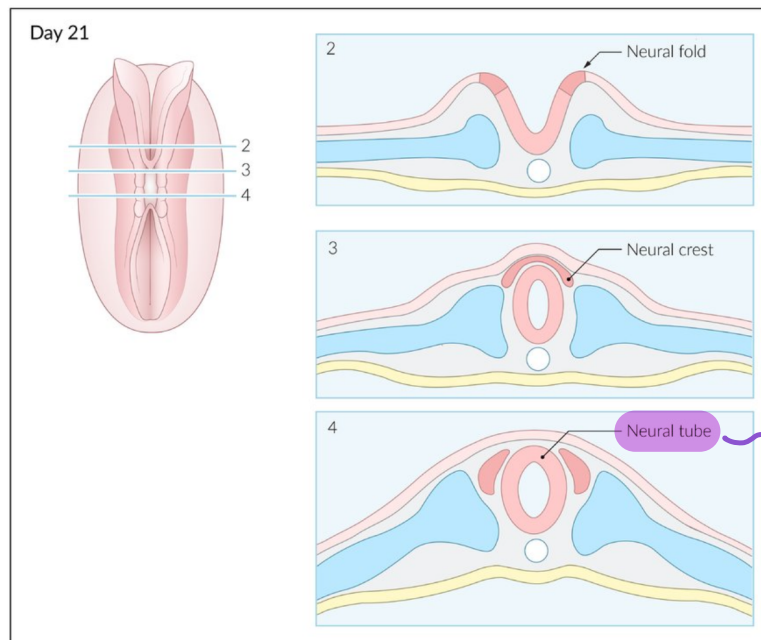
✓✓

→ Cells resemble that of embryonal cells

- Embryonal primitive neoplasm
- 20% of pediatric brain tumors
- Exclusively in the cerebellum ✓✓
- Predominantly in children

→ Infratentorial نَبَطِي

→ جِثْلُو كِنَا tumor مكانه
 رِطَابِه سَكَن اَر Medulloblastoma
 بَنَفْع نَخِي اَنه MB



→ lined by primitive nervous system cells
 → large nucleus
 → large N/C ratio
 → high mitosis



Medulloblastoma

- Pathogenesis
 - SHH pathway
 - The vermis or lateral cerebellum
 - WNT pathway → *β-catenin, APC* تبع
 - Around the anterior IV ventricle
 - Or middle cerebellar peduncle



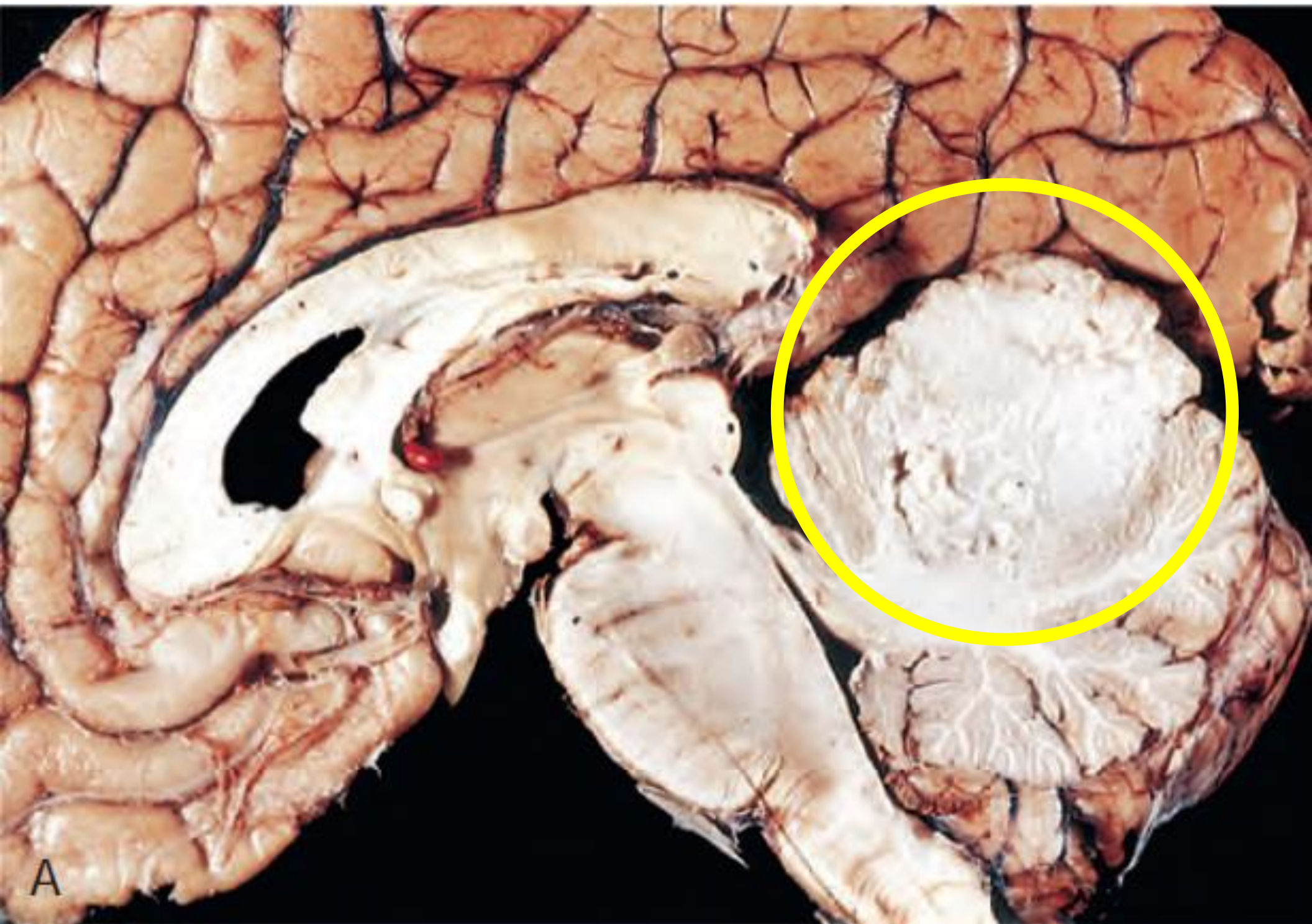
Medulloblastoma

→ High grade aggressive tumor (grade 4)
grade 1, 2... نسيجه

■ Morphology

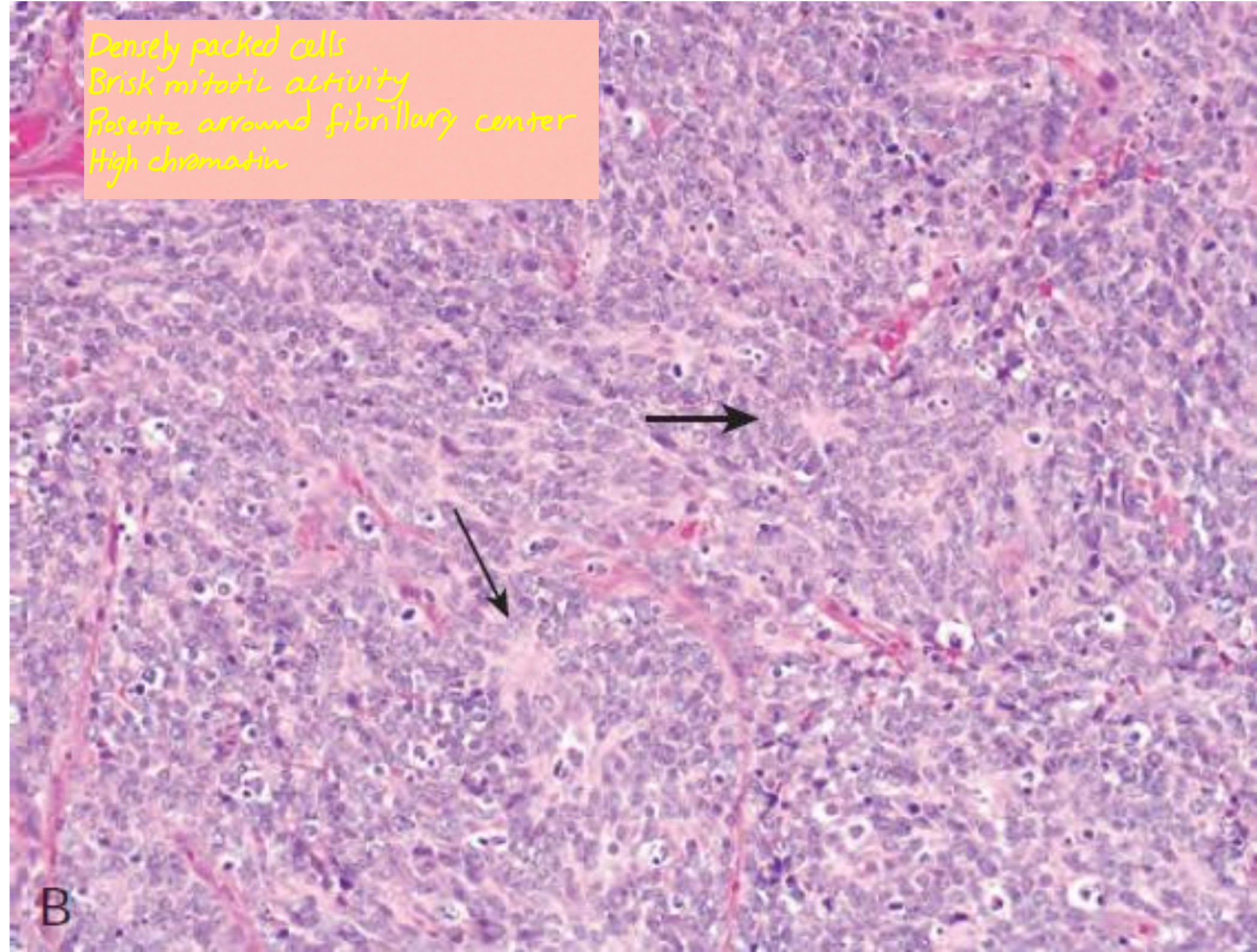
- Often well circumscribed
- May involve the leptomeninges
- Microscopy
- Mitosis → Crazy mitosis (very very high) → If not treated → Rapid deterioration
- Homer Wright rosettes
- Desmoplastic nodular variant → In adults
 - Almost always SHH activated
- Large cell anaplastic variant
- Subarachnoid/CSF dissemination

حوائط
fibrillary center



A

Densely packed cells
Brisk mitotic activity
Rosette around fibrillary center
High chromatin



B



Meningiomas

- Tumors of adults
 - Arise from the arachnoid
 - Usually attached to the dura
 - Along any point of the external surface
 - Or within the ventricular system (from the choroid plexus)
 - Previous radiotherapy is a risk factor
- Meningioma grade 1*
→ No invasion, easily separated from brain tissue
- Include some arachnoid cells*

Meningiomas

■ Pathogenesis

- Common lesion in NF2
- ✓ ■ 50-60% of sporadic cases show mutant NF2 gene

■ Morphology

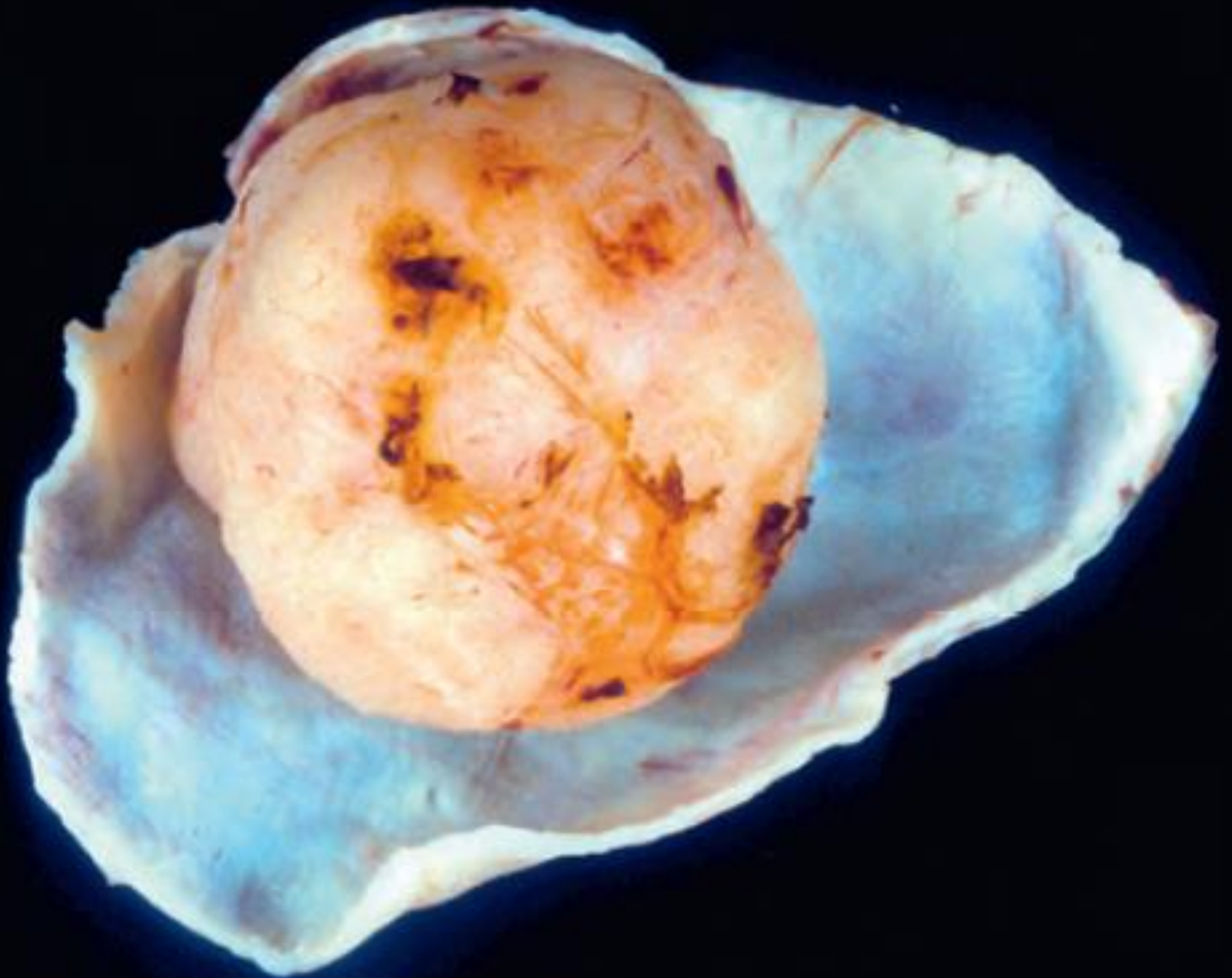
■ Gross

- En plaque growth → grow under the dura without forming a mass (only thickening of dura)
- Firm to gritty (psammoma)

↳ concentric layer of calcification
'union skin appearance'

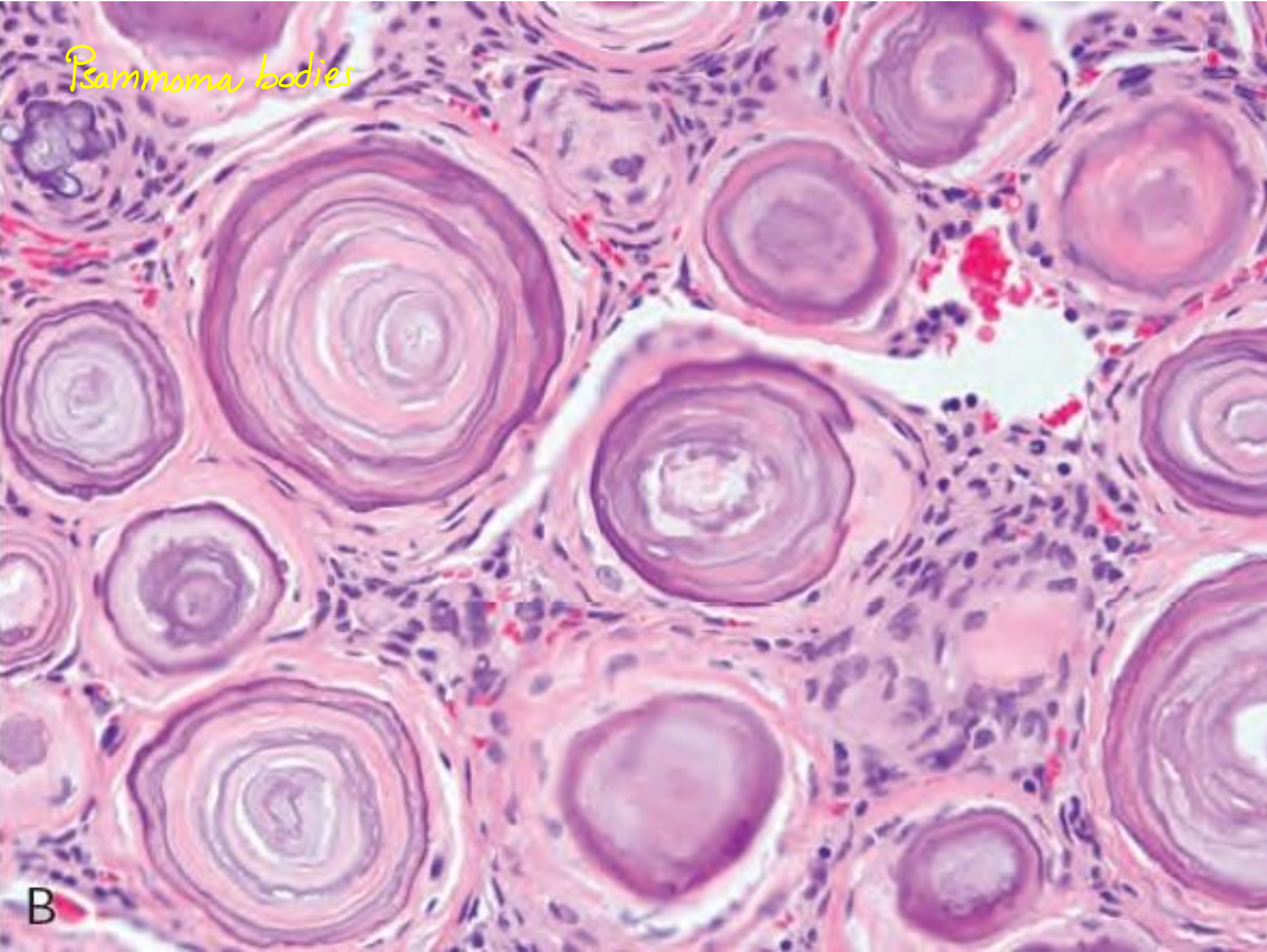
← إذا كان عدداً كبيراً كثيراً ينحكي عنها
Psammomatous meningioma

The mass must be removed
with the dura



A

Rammoma bodies



B



Meningiomas

- Morphology
 - Microscopy
 - Meningothelial
 - Fibroblastic
 - Transitional
 - ✓ ■ Concentric wrapping (whorls)
 - Psammomatous
- } *No important*

Meningiomas

ما از کجای حال آنها بقیه grade 1
نیستند grade 2,3 پس ما نشانی

■ Atypical meningioma → Grade 2

- One fourth of the cases
- Higher recurrence rate
- RT in addition to surgery
- Aggressive features

Radiotherapy ←

■ Anaplastic meningioma → Grade 3

- 1-3%
- Carcinomatous/sarcomatous features

من الصعب تفرقة عليها انها
meningioma
و يمكن تفرقة metastatic
tumor