

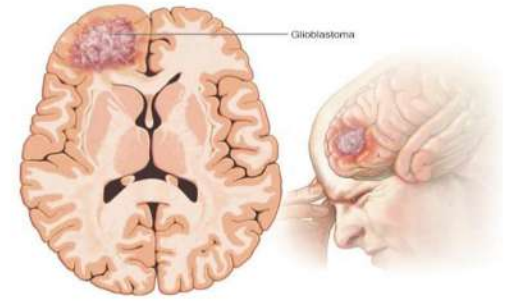
وَقُلْ رَبِّ زِدْنِي عِلْمًا



# PERIPHERAL NERVOUS SYSTEM

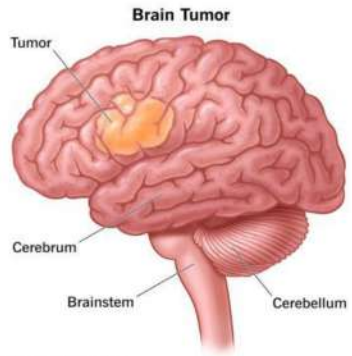
SUBJECT : Pathology  
LEC NO. : 2  
DONE BY : Baraa Al-otaibei  
Mohammed majed

عن أنس قال: كان أكثر دعاء النبي صلى الله عليه وسلم: "اللهم ربنا آتنا  
في الدنيا حسنة، وفي الآخرة حسنة، وقنا عذاب النار" رواه البخاري .



# Neurosciences II Module

## Central Nervous System Tumors



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Dr. Ola Abu Al Karsaneh



# Classification

## 1. Gliomas:

- Astrocytoma and variants
- Oligodendroglioma
- Ependymoma

## 2. Neuronal Tumors

- Central neurocytoma
- Gangliogliomas
- Dysembryoplastic neuroepithelial tumor

## 3. Embryonal (Primitive) Neoplasms

- Medulloblastoma

هذا السلايد من المحاضرة الماضية.  
امس اخذنا ال glioma والحين راح  
نكمل باقي الانواع.  
نقول بسم الله

## 4. Other Parenchymal Tumors

- Primary CNS Lymphoma
- Germ Cell Tumors

## 5. Meningiomas

## 6. Metastatic Tumors

## 2. Neuronal Tumors

- Less frequent than gliomas.
- Composed of cells with neuronal characteristics.
- Present with seizures.

هذا ال category بميزه انه المنشأ تاعه شبه  
ال neuron عشان هيك سميناها neurocytoma  
وهما غالبا بييجينا المريض ومعه  
seizures وكمان انتشارهم قليل جدا فهنحكي عنهم عالسريع

### 1. Central neurocytoma:

- Low-grade.
- Within and adjacent to the ventricular system (**lateral or third ventricle**).
- Composed of evenly spaced, round, uniform nuclei and often islands of neuropil

هذا النوع يمكن لو شفتاه بالامتحان نخربط بينه وبينه  
ال oligo كونه في شبه بالوصف ولكن نميزه انه بكون  
بجوار ال Ventricles

## 2. Gangliogliomas

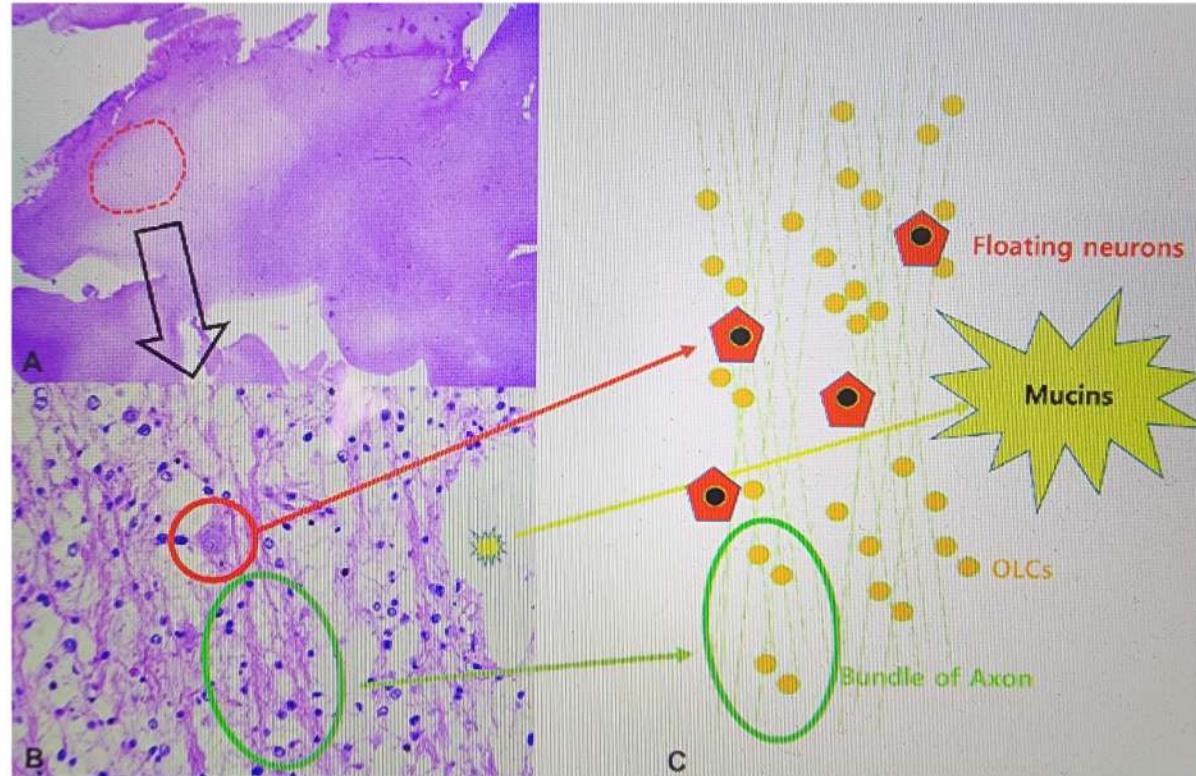
- Mixture of **glial** elements, usually a low-grade astrocytoma and mature appearing **neurons**.
- Most are slow-growing and present with seizures.

## 3. Dysembryoplastic neuroepithelial tumor:

- A low-grade tumor of children and young adults that grows slowly
- In the temporal lobe
- Manifests as a seizure
- **Floating neurons in a myxoid background**

ثالث نوع من اسمه بصير بالاطفال وهو يتميز  
انه بنشوف فيه الـ neuron ويسبحو جوات  
myxoid background

# مافي صورة لل dyembryoplastic فجتلكم هاي الصورة من النت ونلاحظ كيف ال floating neuron



# 3. Embryonal (Primitive) Neoplasms

## 1. Medulloblastoma (WHO grade IV)

- Primitive Neuroectodermal Tumor: **PNET**
- Primitive **small cell (blue cell) tumor**
- Occurs in more **children** and in the **cerebellum**.
  - Children: Midline of the cerebellum
  - Adults: Lateral of the cerebellum
- Presents with Sx & Sx of ICP (headache, nausea, vomiting)
- **Highly malignant**, and the prognosis for untreated patients is dismal; however, it is radiosensitive.
- With treatment, the 5-year survival rate may be as high as 75%.

ال category الثالثة بدنا نذكر بشو المقصود بال pnet  
ال pnet يعني لما يصير cancer بخلايا بتشبه الخلايا  
ال primitive اللي بتتطور عند الجنين  
أشهر نوع منهم هو medulloblastoma  
وهو High grade tumor  
وبميزه انه مكون من خلايا صغيرة بنطاق معينة.  
وكمان هذا ال tumor برغم خطورته اذا ما تعالج  
بقلك اذا تعالج نسبة النجاة منه زينة

ال meduloblastoma لها انواع مهم نميز بينهم  
وهي الانواع احنا بتصنفها حسب ال pathogenesis  
وبدنا نعرف كل نوع وال prognosis ماله

## Pathogenesis

-Oncogenic pathways in these tumors are the following:

- **Wnt pathway activation:** have the most **favorable** prognosis
- **Hedgehog pathway activation:** have an **intermediate** prognosis, but the concomitant presence of TP53 mutation confers a very poor prognosis.
- **MYC overexpression** due to MYC amplification: have the **poorest prognosis**



➤ **Gross:**

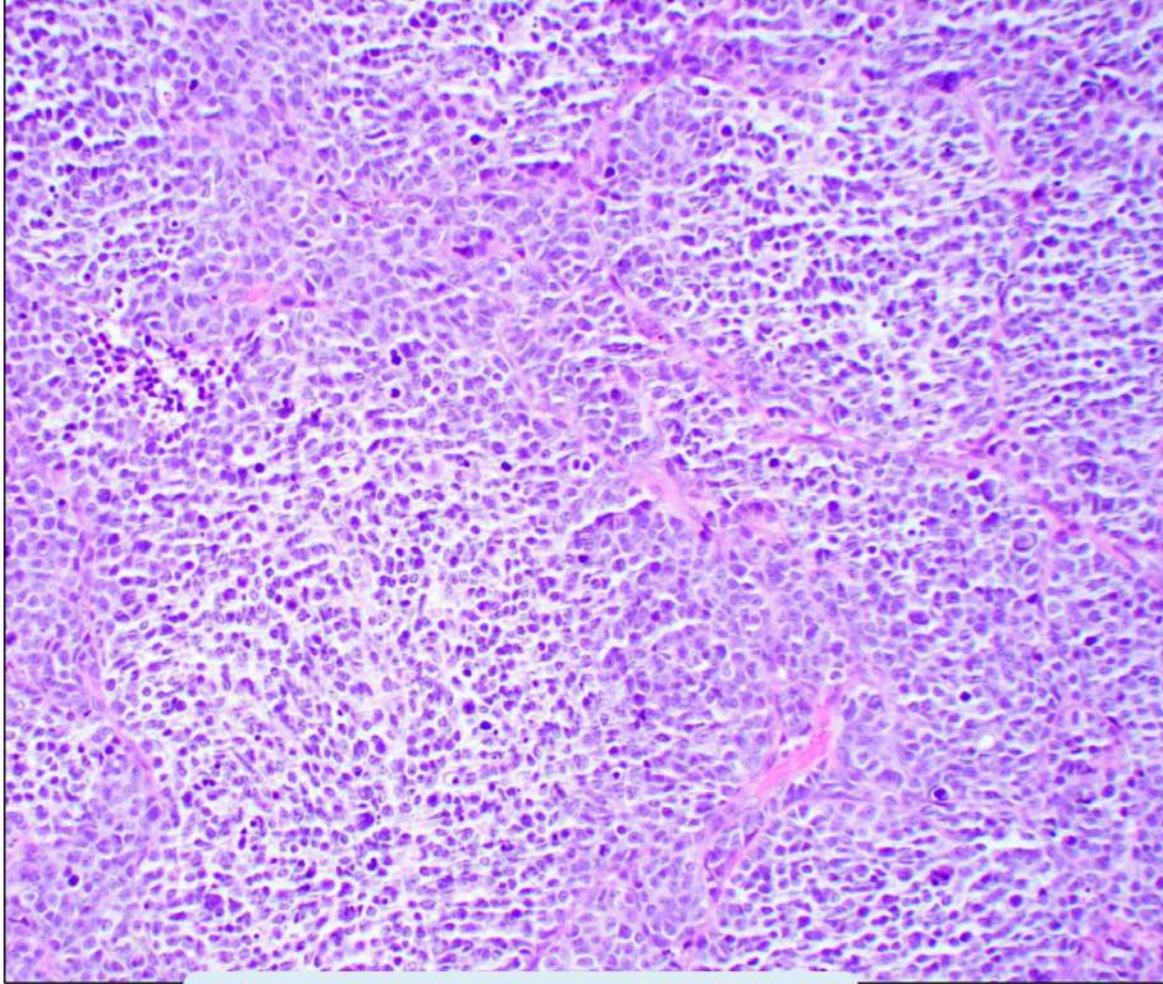
- Well circumscribed, friable and extend to involve the leptomeninges

➤ **Microscopic:**

- Densely cellular, with sheets of anaplastic (“**small blue**”) cells.
- Tumor cells are small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.
- Often, focal neuronal differentiation is seen in the form of **Homer Wright Rosettes** (primitive tumor cells surrounding central neuropil (pink material formed by neuronal processes)).

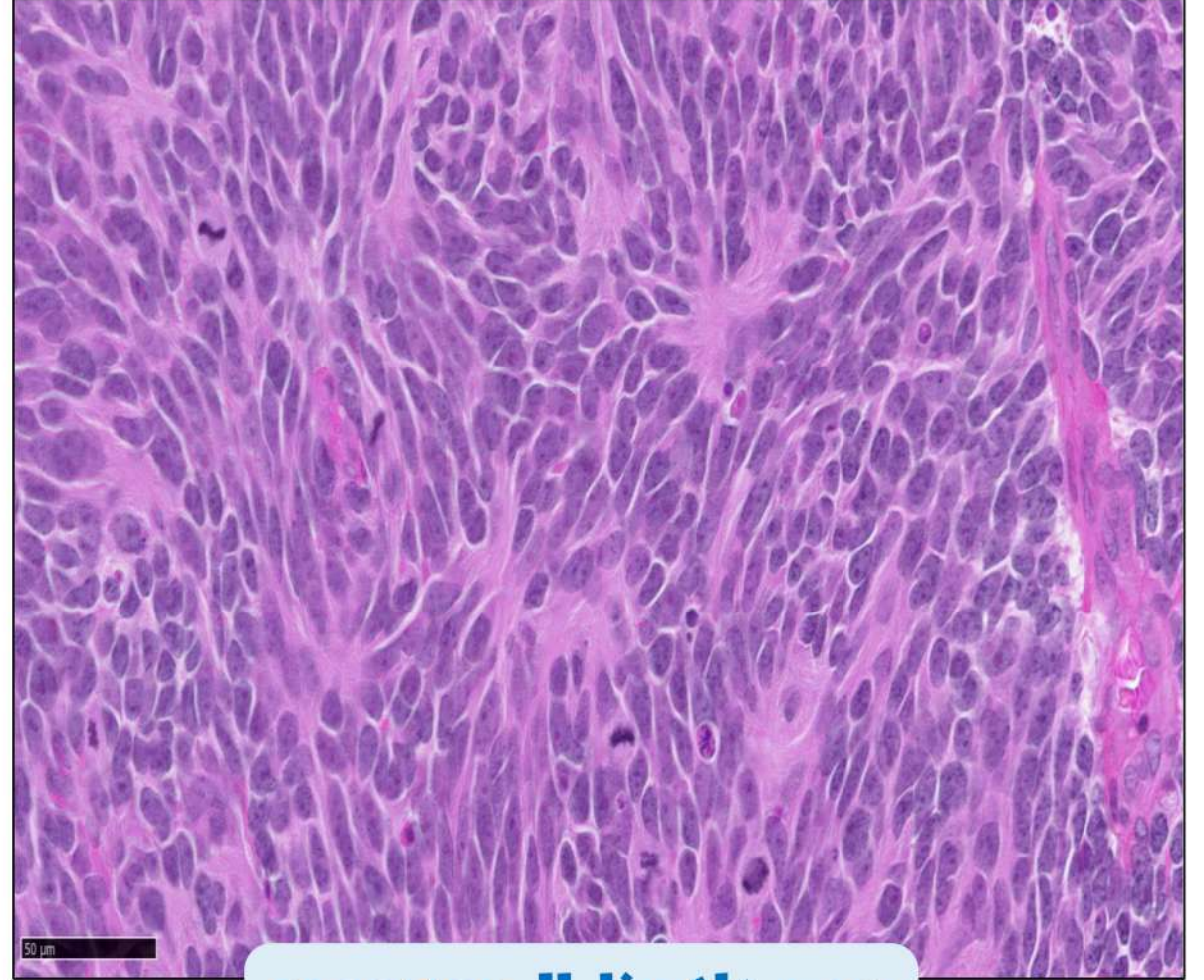
small = meduloblastoma كلشي  
وهون كمان هنشوف نفس ال rossetes اللي حكينا عنهم  
بال neuroblastoma هذول بكونو عاملين دائرة  
حوالين منطقة وردية بنسميهم Homer Wright Rosettes

## Sheets of undifferentiated cells



نلاحظ الخلايا الصغيرة ويا دوب سيتوبلازم

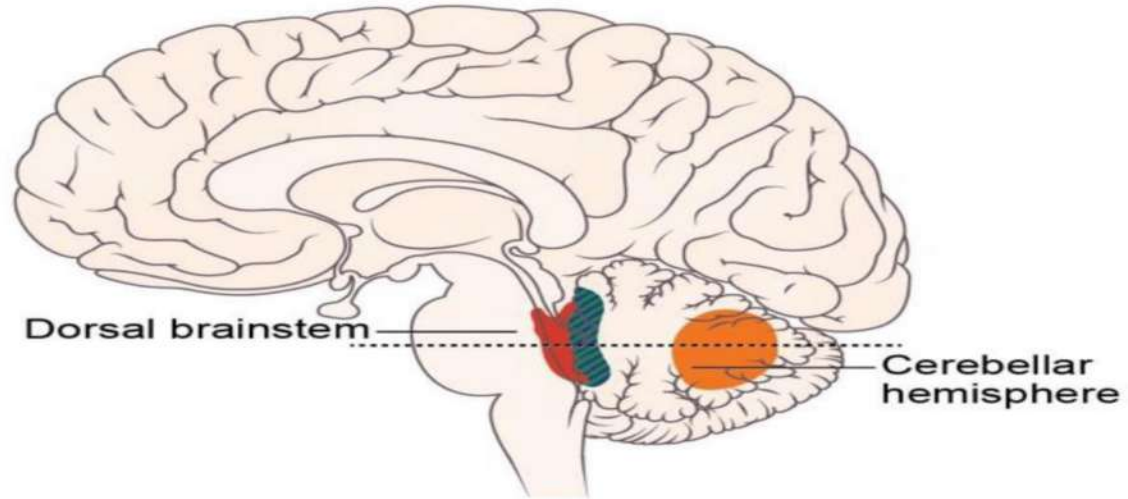
## Homer Wright Rosettes



هون نلاحظ ال rosettes

## Medulloblastoma subtypes

|                      | Wnt  | Shh   | Group 3   | Group 4   |
|----------------------|--|---|---|---|
| Molecular features   | <ul style="list-style-type: none"> <li>• CTNNB1</li> <li>• Monosomy 6</li> </ul> | <ul style="list-style-type: none"> <li>• GL1</li> <li>• PTCH1</li> <li>• SMO</li> <li>• SUFU</li> <li>• TP53</li> </ul> | <ul style="list-style-type: none"> <li>• FSTL5</li> <li>• MYC</li> <li>• VEGFA</li> </ul> | <ul style="list-style-type: none"> <li>• KDM6A</li> <li>• MYC</li> <li>• OTX</li> </ul> |
| 5-year survival rate | 95-100%  | 40% (p53 mutant) & 80% (p53 wildtype)   | ~30-60%   | 75%   |
| Anatomical location  | Dorsal brainstem   | Cerebellar hemisphere   | Midline   | Midline   |



يعني لو كان ال p53 سليم راح يكون ال 80% prognosis  
ولو كان فيه mutation راح يصير 40%

الان بدنا نحكي عن سرطانات ممكن يصيرو  
primary باماكن اخرى غير ال CNS ولكن برضو  
بصيرو primary بال CNS.

## 4. Other Parenchymal Tumors

### 1. Primary Central Nervous System Lymphoma

ال Lymphoma بنميزها بال Cases لما نعرف انه  
المريض في عنده نقص مناعة و EBV virus  
بتشوفها على شكل multiple nodule

- Mostly as diffuse large B-cell lymphomas.
- **It is the most common CNS neoplasm in immunosuppressed individuals** (nearly always positive for EBV).
- It is an aggressive disease with a relatively poor response to chemotherapy as compared with peripheral lymphomas.
- Primary brain lymphoma is often found as **multiple tumor nodules within the brain parenchyma**, yet the involvement of sites outside of the CNS is uncommon.
- Lymphoma originating outside the CNS rarely spreads to the brain parenchyma

# Morphology

بتحب تعمل تجمع حوالين ال BV وبتأكد من  
النوع لما نشوفها CD20 positive

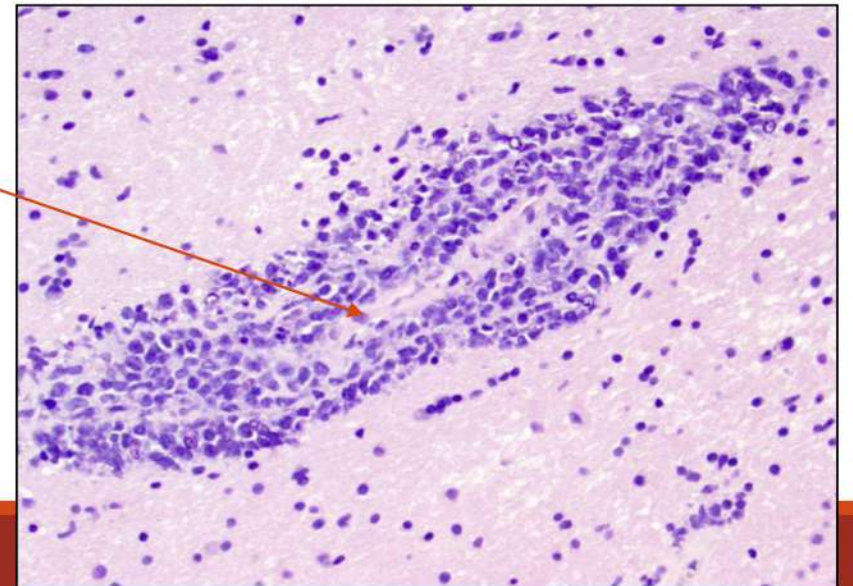
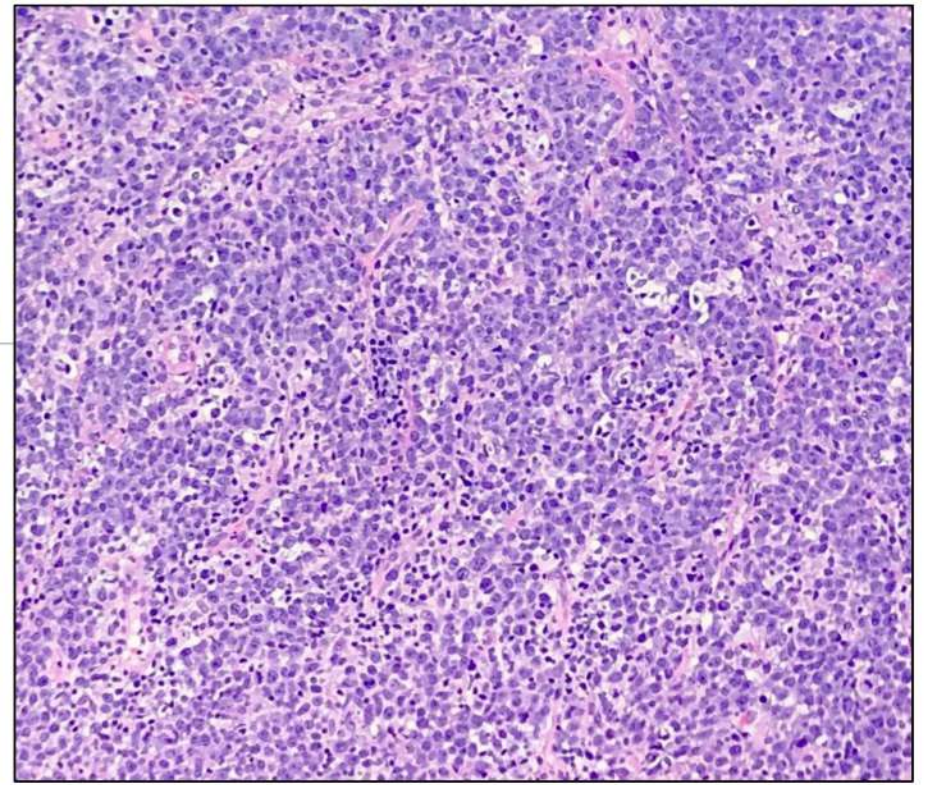
## ➤ Gross:

- Involves deep gray structures, as well as the white matter and the cortex.
- Periventricular spread is common.
- **Well defined** as compared with glial neoplasms.

## ➤ Microscopic:

- Nearly always aggressive large B-cell lymphomas.
- Malignant lymphoid cells **accumulate around blood vessels** and infiltrate the surrounding brain parenchyma.
- Positive for B cell markers such as **CD20**

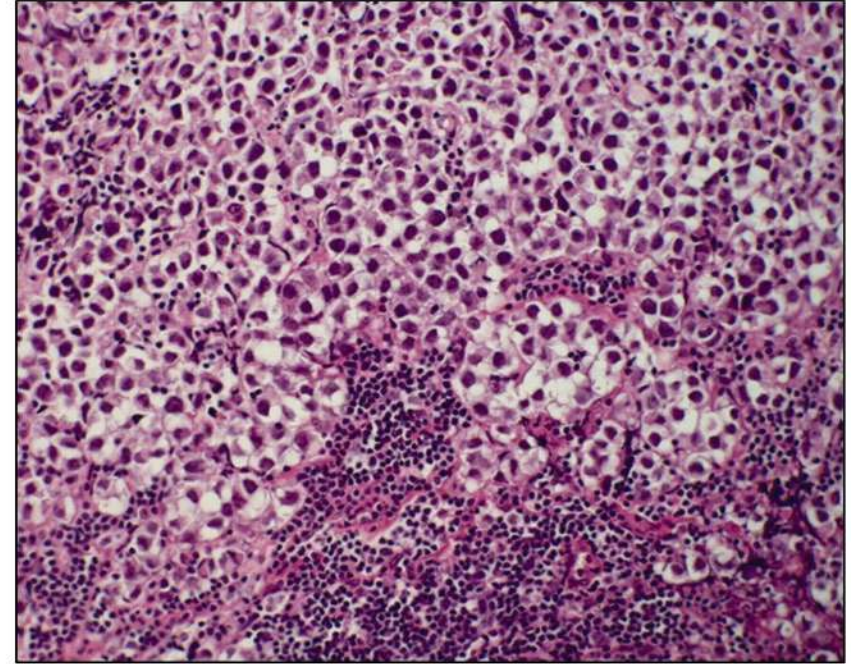
إذا لما يجي كيس لمريض مناعته سيئة وعنده multiple nodule  
وحدود واضحة و CD20 positive وسألنا عن خصائصها؟  
بقدر احكي انها positive for EBV وبتتجمع حول ال BV



## 2. Germ Cell Tumors

اخذنا انواع كثير لل germ cell tumor باماكن  
اخرى لكن لما نحكي عن ال CNS فأكثر نوع  
لل germ بصير بنسميه Germinoma  
ولما اشوفه بالمريض لازم اتأكد انه  
primary ومش واصل من مناطق اخرى بالجسم

- Occurs along the midline ( most commonly in the **pineal** and the **suprasellar regions**)
- They are a tumor of **the young**
- In the pineal region show a strong male predominance.
- **The most common primary CNS germ cell tumor is germinoma** (resembles testicular seminoma)
- Secondary CNS involvement by metastatic gonadal germ cell tumors also occurs.



## 5. Meningiomas (WHO grade I-III)

- **Benign** tumors arise from arachnoid meningotheial cells.
- Usually in adults and are often attached to the dura.
- Most in adult females, Tumor cells contain **PROGESTERON receptors**
- May be found along any of the external surfaces of the brain
- Presents with vague Sx or focal findings due to compression of the adjacent brain.
- Most are easily separable from the underlying brain, but some are infiltrative

الان بنحكي عن نوع بطلع من CNS cover بسميه  
grade 1 meningiomas  
grade 1 يعتبر benign  
بتأكد لما اشوفه progesteron positive receptor  
وبشكل عام بالتشخيص سهل نستأصلها

اكيد ال grade كل ما يزيد هيكون اسوأ  
احيانا بتكون multiple فهشوف عند المريض NF2  
الحالات الغير وراثية برضو هشوف mutation ب NF2

- The overall prognosis is determined by the lesion size and location, surgical accessibility, and histologic grade
- **Multiple** meningiomas are associated with neurofibromatosis type 2 (NF2).
- About half of meningiomas not associated with NF2 have mutations in the NF2 tumor suppressor gene (in all grades).



# □ Morphology

## WHO grade I:

هسا هنشوف كيف نميز بين ال grades  
ال 1 grade لها اشكال مختلفة اللي بجمعهم انهم مو عاملين invasion ولا mitosis بالتالي سهل استئصالهم  
ال meningothelial بنشوف فيها الخلايا بتسبح بالسيتوبلازم وما الهم حدود  
ال fibroblastic يعني شكل الخلايا بكون مثل ال fibroblast  
ال transitional هذا هنشوف فيه خصائص من اول نوعين لانه انتقالي  
ال psammomatous يعني معبي psammoma  
ال secretory من اسمه هنشوف خلايا مليانة gland وبتطلع افرازات

- Grows as dura-based masses that may compress the brain, **but No brain invasion.**
- Extension into the overlying bone may be present.
- Histologic patterns include:
  - **Meningothelial** (whorled clusters of cells without visible cell membranes)
  - **Fibroblastic** (elongated cells and abundant collagen deposition) -
  - Transitional** (features of the meningothelial and fibroblastic types)
  - **Psammomatous** (numerous psammoma bodies) - **Secretory** (glandlike spaces containing PAS-positive eosinophilic material)

هاي بكون الها invasion واخطر وحتى لو  
استئصلناه في احتمال كبير يرجع وهيكون  
فيه mitosis وهذول ما كانو ب grade1  
وبالسلاید كمان في 5 خصائص اذا  
وجدنا منهم 3 راح اتأكد انها grade 3

## Atypical meningiomas (WHO grade II):

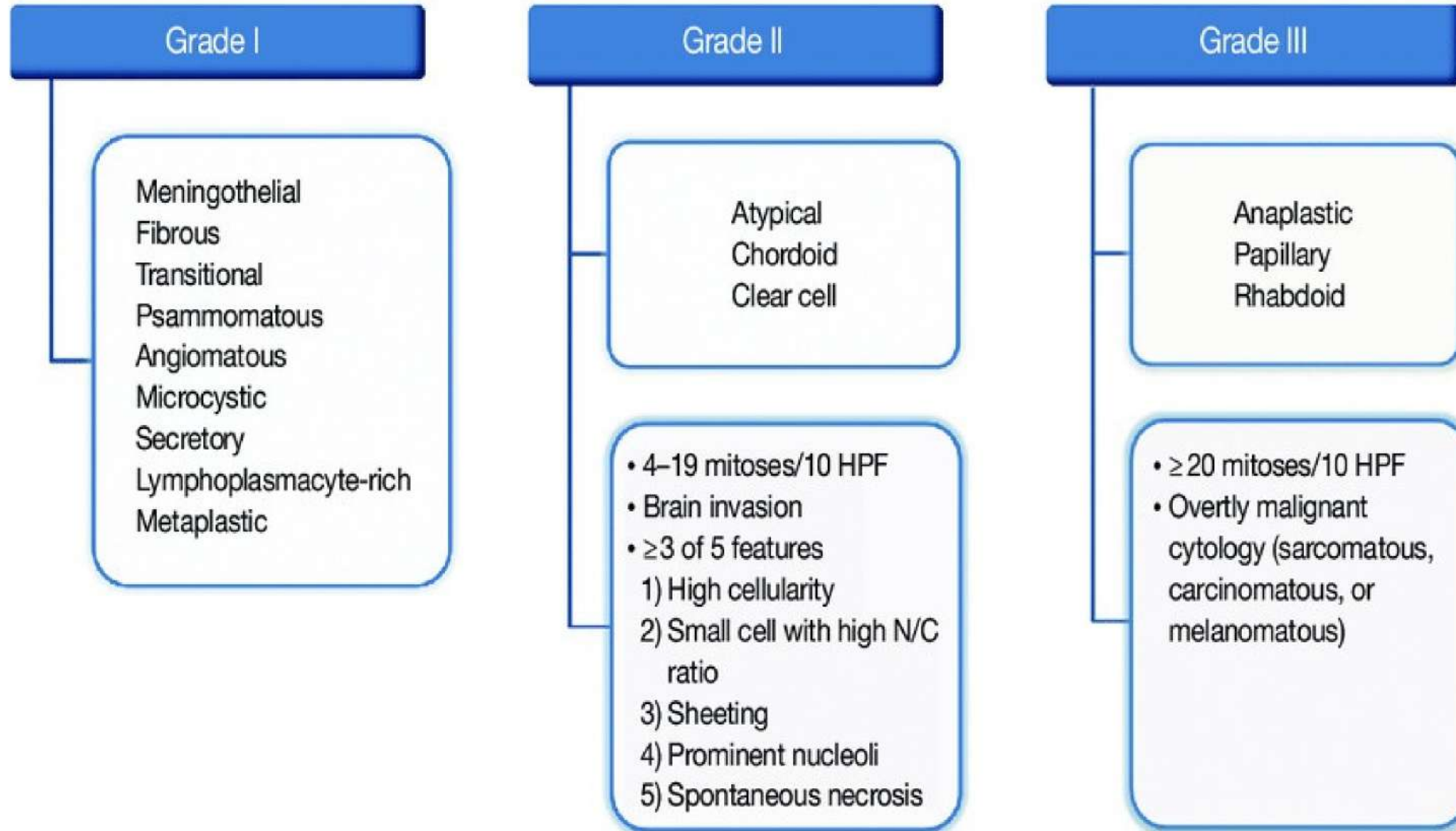
- These tumors demonstrate more aggressive local growth and a higher rate of recurrence.
- The presence of either an **increased mitotic rate OR prominent nucleoli, increased cellularity, patternless growth, high nucleus-to-cytoplasm ratio, or necrosis**
- Some histologic patterns—**clear cell and chordoid**  
تذكرو انه 2C with grade 2
- **The presence of brain invasion.**

## **Anaplastic (malignant) meningiomas (WHO grade III)**

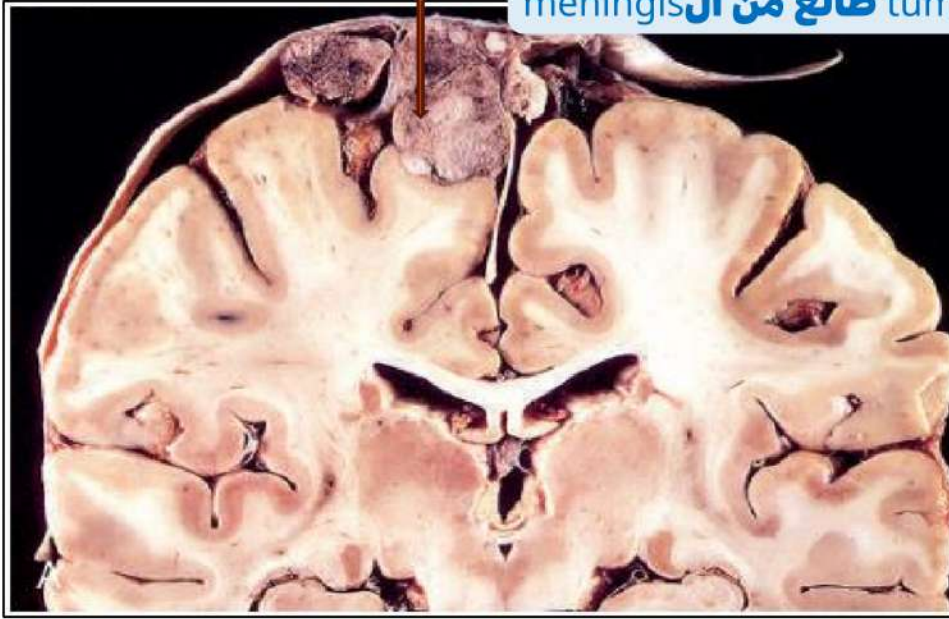
-Highly aggressive tumors that may resemble a high-grade sarcoma or carcinoma morphologically. - **Mitotic rates** are typically much **higher than in atypical meningiomas**. - **Papillary** or **Rhabdoid** morphology

هاي بتكون malignant وعنا كثير mitosis ويمنكن  
تكون papillary او Rhabdoid

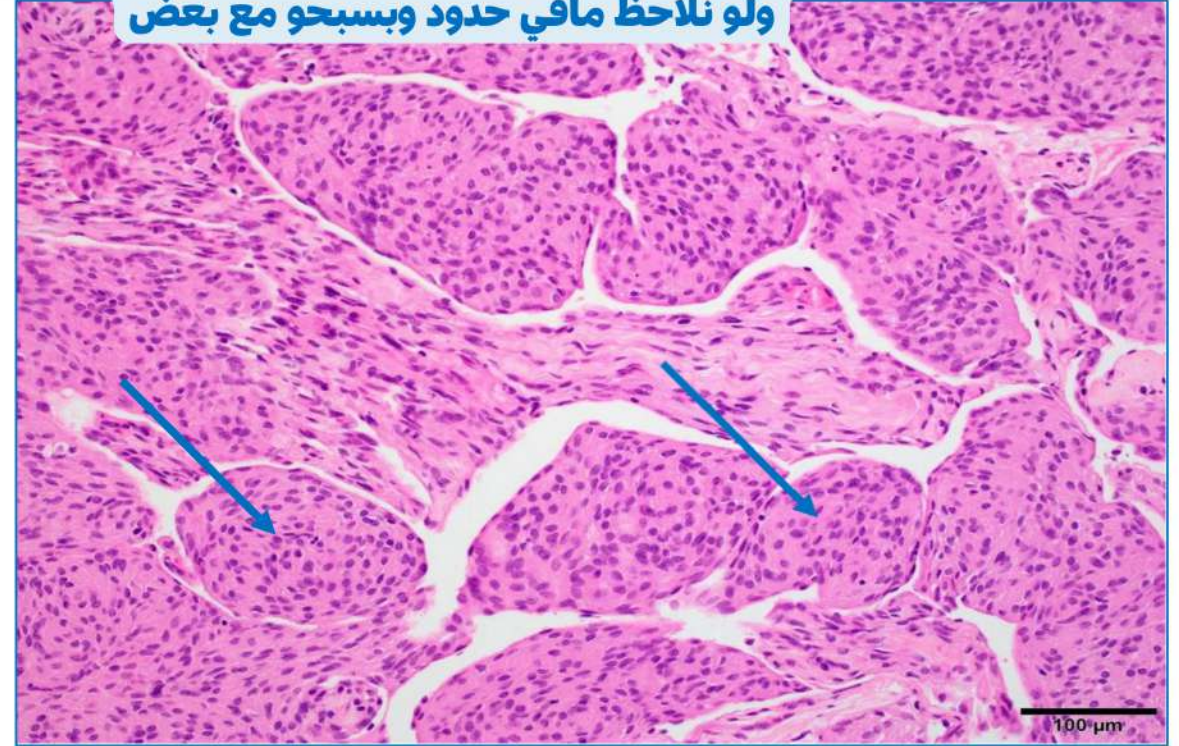
# الكلمات المفتاحية لكل Grade



شوفو كيف ال tumor طالع من ال meninges



هذا النوع الاول اللي حكيينا عنه meningothelial ولو نلاحظ مافي حدود وبسبحو مع بعض



نلاحظ هون psammoma bodies



## 5. Metastatic Tumors

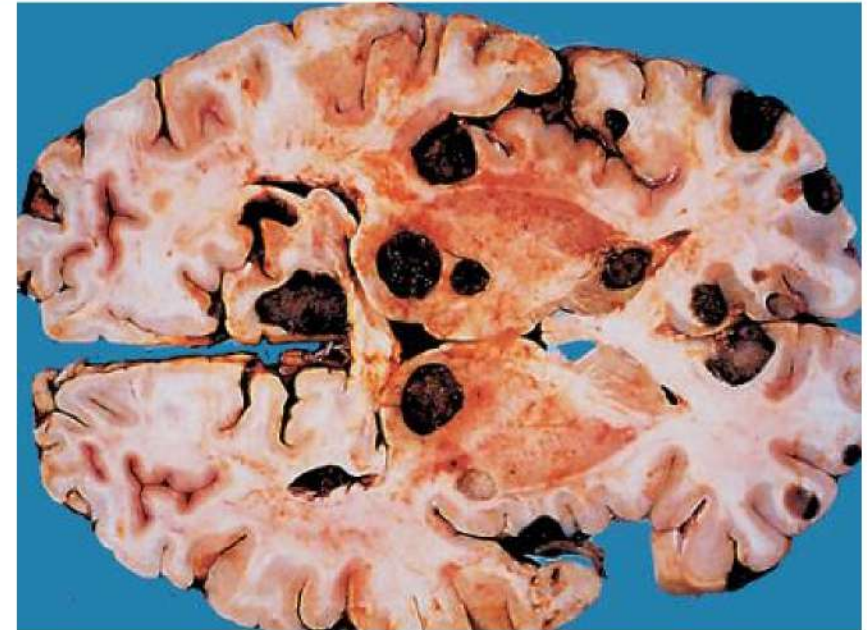
هاي آخر category  
حكينا لو نتذكرو انه في نسبة منيحة من الاورام بكونو  
secondary وجايين من اماكن ثانية غالبا من الرئة  
والصدر والجلد الكبد والجهاز الهضمي  
فلو شفت tumor جاي عال brian هشك بهاي الاماكن

- Mostly carcinomas.
- The most common primary sites are the **lung, breast, skin (melanoma), kidney, and gastrointestinal tract**, which together account for about 80% of cases.

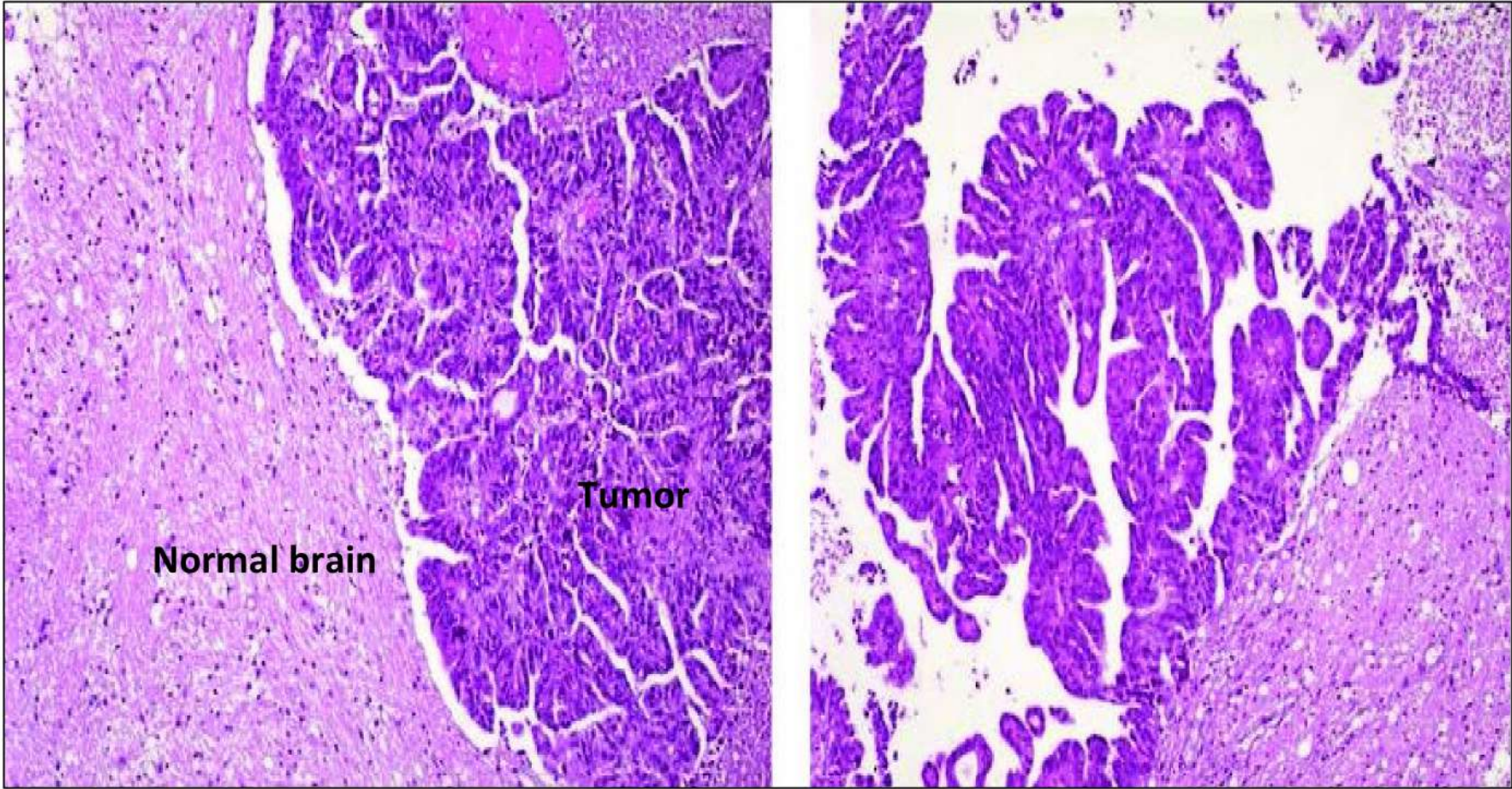
### ➤ Gross:

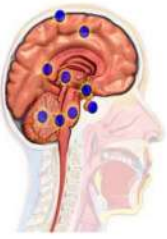
- Form **sharply demarcated masses** (usually **multiple**), often at the grey-white matter junction.
- The boundary between tumor and brain parenchyma is sharp at the microscopic level as well, with surrounding reactive gliosis

الان نلاحظ هاي الصورة ومن هذول ال black pigment  
هيكون واضح انه المنشأ melanoma



# Brain Metastasis





# Familial Tumor Syndromes

## 1. Tuberos Sclerosis:

- An autosomal dominant syndrome
- Results from disruption of **TSC1** tumor suppressor genes, which encodes **hamartin**, or **TSC2**, which encodes **tuberin**. Proteins regulate protein synthesis & cell proliferation.
- Characterized by the development of **hamartomas** and **benign neoplasms** involving the brain and other tissues.

خلصنا السرطانات والان بدنا نحكي عن امراض بتكون مرتبطة بوجود السرطان وزيادة نسبة الاصابة فيه معناها ال Tuberos sclerosis وهذا من اسمه بيحي المريض عنده TSC1 او TSC2 ك Mutation ولازم يكون فيه Hamartoma



الhamartoma هيه مش neoplasm بس بنقدر نحكي abnormal growth  
فهنشوف نفس الشغلات الموجودة بالbrain معها شوية شغلات abnormal  
ممكن يكون خلل بالكمية او ال arrangement  
الhamartoma الهها انواع كلهم benign

## CNS hamartomas:

- Consists of **cortical tubers** and **subependymal hamartomas**, including a larger tumefactive form known as **subependymal giant cell astrocytoma**.
- Because of their proximity to the foramen of Monro, they often present acutely with obstructive hydrocephalus.
- Seizures are associated with cortical tubers.

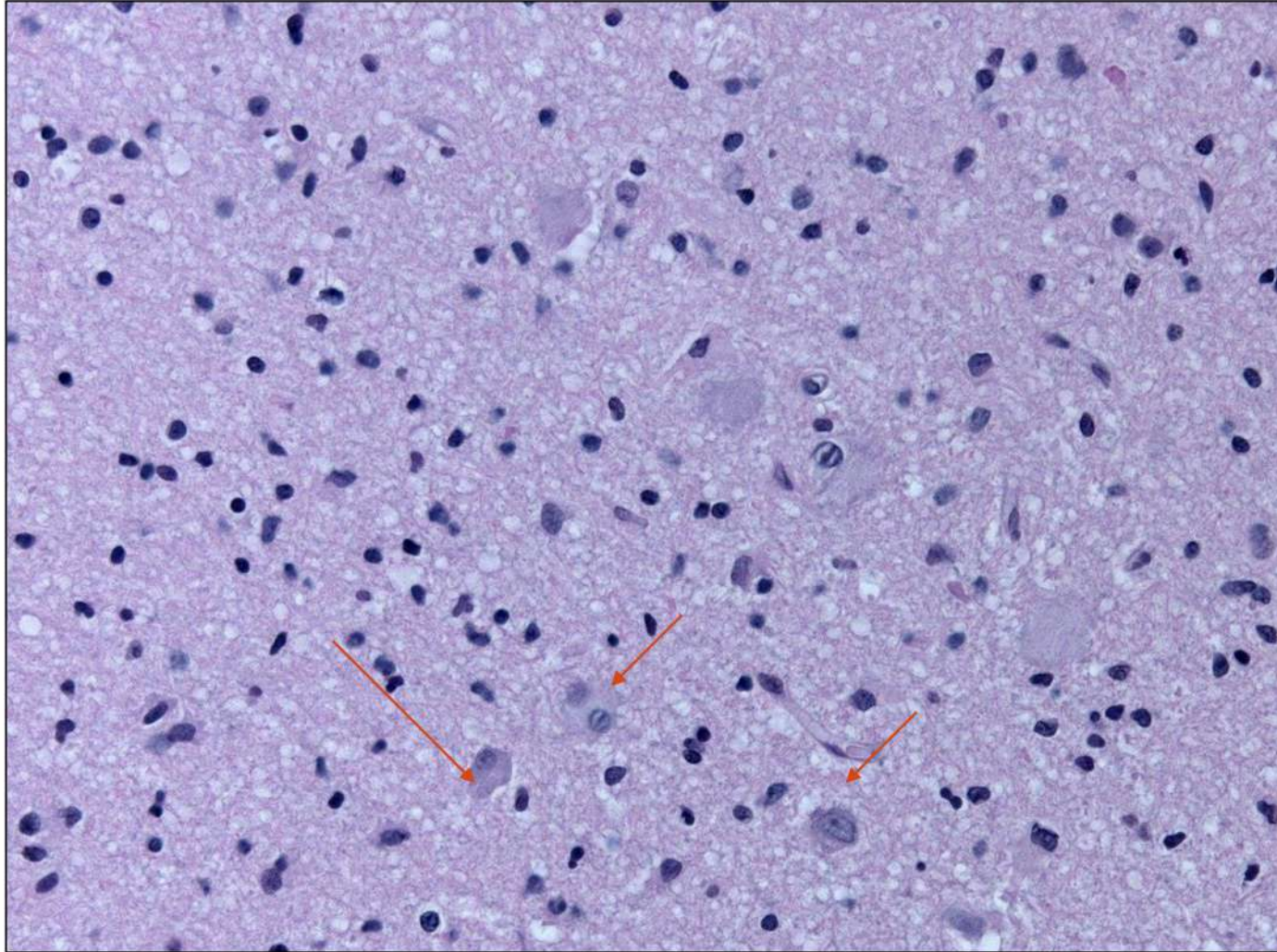
## - MORPHOLOGY

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### Cortical hamartomas

- Firmer than normal cortex and have been likened in appearance to potatoes
- **Composed of haphazardly arranged large neurons that lack the normal cortical laminar architecture.**
- May exhibit a mixture of glial and neuronal features
- Similar abnormal cells are present in subependymal nodules.

## Cortical tuber with dysmorphic neuronal cells



## Extracerebral lesions:

- Renal angiomyolipomas
- Retinal glial hamartomas
- Pulmonary lymphangiomyomatosis
- Cardiac rhabdomyomas.
- Cysts (liver, kidneys, and pancreas)
- Cutaneous lesions include angiofibroma, hypopigmented areas, and sub-ungual fibromas.

هاي بال Tuberous Sclerosis  
ممکن نلاقي lesions برا المخ:

## 2. Von Hippel–Lindau Disease

هذا من اسمه ويتميز ب VHL mutation  
وهذا الجين بالوضع الطبيعي يعمل control  
لل growth factors فلما يصير فيه خلل هييزيد  
ال growth للخلايا جوا ال tumor وهيكون  
في Vascularity عالية

- An autosomal dominant disorder.
- The affected gene, **the tumor suppressor VHL**, encodes a protein that degrades the transcription factor hypoxia-inducible factor (HIF).
- Tumors arising in patients with von Hippel–Lindau disease generally have lost all VHL protein function. As a result, the tumors express high levels of HIF, which drives the expression of VEGF, various growth factors, and sometimes erythropoietin.

Renal cell carcinoma **وال** Cyst **وال** hemangioblastoma **ال**  
VHL disease **بكونو نرتبطين مع ال**

- Individuals develop **hemangioblastomas** within the cerebellar hemispheres, retina, and, less commonly, the brain stem, spinal cord, and nerve roots.
- Patients also may have **cysts** involving the pancreas, liver, and kidneys and have an increased propensity to develop renal cell carcinoma.

Veru Vascular **وبكون cerebellum موجود بال**  
**وخلايا فيها فقاعات ومواد دهنية**

- MORPHOLOGY

**Hemangioblastoma:**

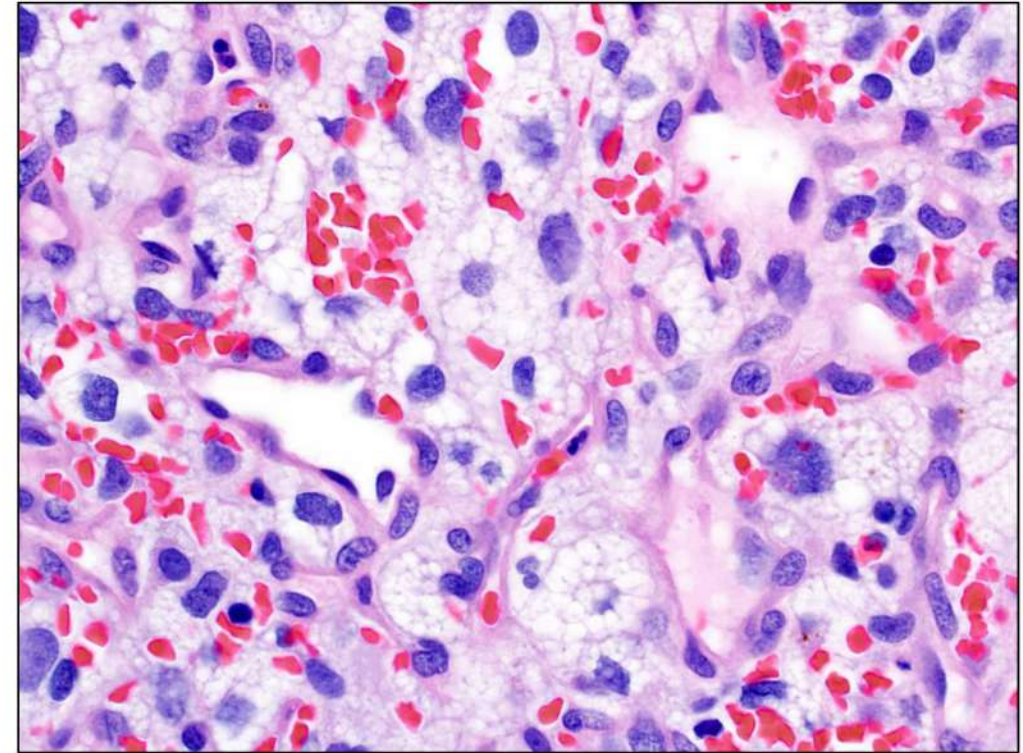
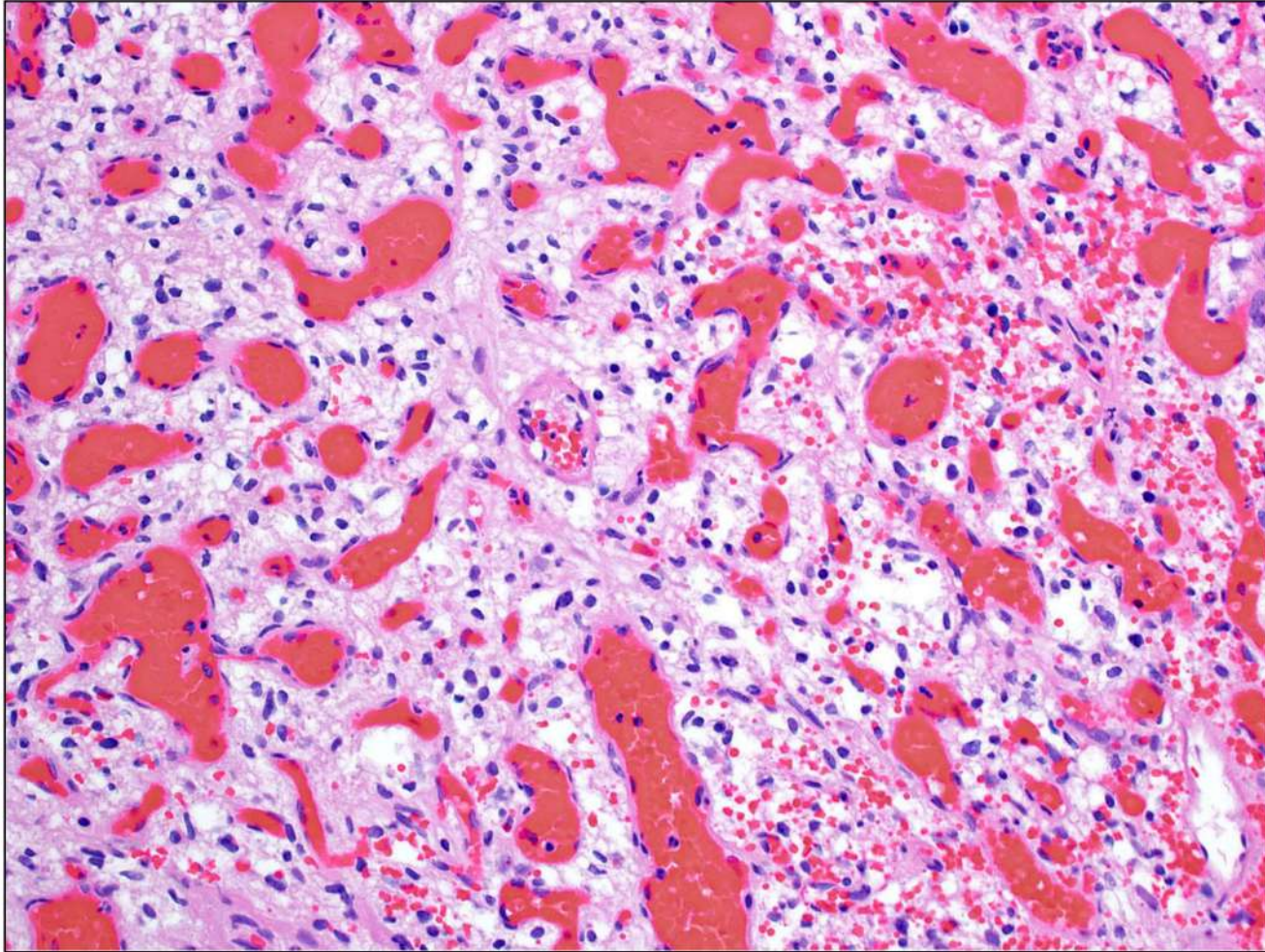
- A highly vascular neoplasm that occurs as a mural nodule associated with a large, fluid-filled cyst.
- Occurs most commonly in the **cerebellum**.

➤ **Microscopically:**

- Consists of numerous **capillary-sized or larger thin-walled vessels** separated by intervening stromal cells with a **vacuolated**, lightly PAS-positive, lipid-rich cytoplasm.
- The stromal cells **express inhibin**.

Classic hemangioblastoma features include numerous vessels and vacuolated stromal cells

شوفو كيف معبا BV وأكو Vacuole





Which of the following neuronal tumors is characterized by evenly spaced, round, uniform nuclei and islands of neuropil?

- a) Gangliogliomas
- b) Medulloblastoma
- c) Central neurocytoma
- d) Dysembryoplastic neuroepithelial tumor

Correct answer: c) Central neurocytoma



Which embryonal neoplasm primarily affects the cerebellum and presents with symptoms of increased intracranial pressure?

- a) Central neurocytoma
- b) Medulloblastoma
- c) Gangliogliomas
- d) Dysembryoplastic neuroepithelial tumor

Correct answer: b) Medulloblastoma

Primary Central Nervous System Lymphoma is most commonly associated with which type of lymphoma?

- a) Diffuse large B-cell lymphoma
- b) Hodgkin lymphoma
- c) Burkitt lymphoma
- d) T-cell lymphoma

Correct answer: a) Diffuse large B-cell lymphoma



**QUIZ TIME**

Which pathway activation in medulloblastoma is associated with the most favorable prognosis?

- a) Hedgehog pathway activation
- b) MYC overexpression
- c) Wnt pathway activation
- d) TP53 mutation

Correct answer: c) Wnt pathway activation

What histological feature is typically seen in medulloblastoma indicating focal neuronal differentiation?

- a) Rosettes
- b) Islands of neuropil
- c) Sheets of undifferentiated cells
- d) Homer Wright Rosettes

Correct answer: a) Rosettes



Which germ cell tumor most commonly resembles testicular seminoma and occurs along the midline in the pineal and suprasellar regions?

- a) Teratoma
- b) Choriocarcinoma
- c) Germinoma
- d) Embryonal carcinoma

Correct answer: c) Germinoma

Which grade of meningioma demonstrates aggressive local growth, a higher rate of recurrence, and may show brain invasion?

- a) Grade I
- b) Grade II
- c) Grade III
- d) Grade IV

Correct answer: b) Grade II



What is the most common primary site for metastatic tumors to the central nervous system?

- a) Liver
- b) Lung
- c) Colon
- d) Prostate

Correct answer: b) Lung

A 30-year-old female with a history of breast cancer presents with new-onset seizures. Brain MRI shows a solitary enhancing mass in the temporal lobe. Biopsy reveals sheets of small blue cells with scant cytoplasm and hyperchromatic nuclei. What is the most likely diagnosis?

- a) Germinoma
- b) Glioblastoma
- c) Medulloblastoma
- d) Metastatic carcinoma

Correct answer: c) Medulloblastoma

عن أبي بكر الصديق رضي الله عنه أنه قال لرسول الله صلى الله عليه وسلم: علمني دعاء أدعوه به في صلاتي قال: "قل: اللهم إني ظلمت نفسي ظلما كثيرا، ولا يغفر الذنوب إلا أنت فاغفر لي مغفرة من عندك، وارحمني إنك أنت الغفور الرحيم" متفق عليه

**Thank you**