FINAL

Lecture 3

بسم الله الرحمن الرحيم

Pathology Mind Maps

CNS Tumors-3

Done by:Nour Elzogheir

This file contains the lecture material presented through mind maps to make the information clearer, more organized, and easier to follow. It is designed to simplify studying and make revision more effective.

We truly hope you find it beneficial.
If it helps you in any way, please remember us in your prayers.

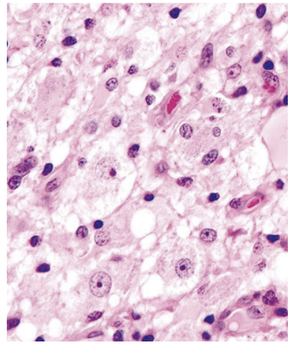
Best of luck in your studies !

Neuronal Tumors

رَبِّ اشْرَحْ لِي صَدْرِي وَيَسِّرْ لِي أَمْرِي وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي يَفْقَهُوا قَوْلِي

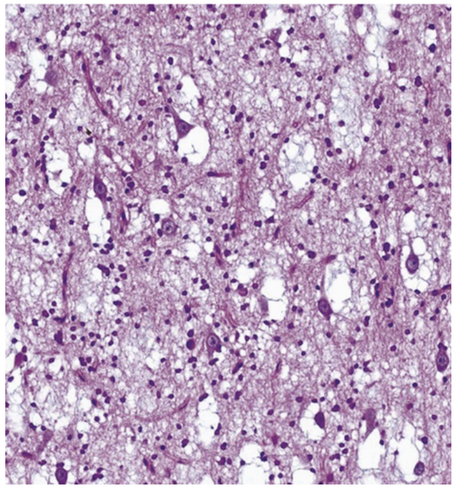
Characteristics

1. They are less common than gliomas.
2. Composed of cells with **neuronal characteristics** and **express neuronal immunohistochemical markers**: synaptophysin, NeuN, and neurofilaments.
3. Typically low grade with indolent biological behavior.
4. Often present with seizures, especially in **children and young adults.**



Gangliogliomas (grade 1)

- **Age of onset** → most commonly in **children or young adults**
- **Morphology** → a glioneuronal tumor composed of a mix of **neoplastic glial and ganglion cells**
- **Location** → can arise anywhere but **most commonly in the temporal lobe** (>70%)
- **Genotype** → Include genetic alterations that lead to **MAPK pathway activation**, which is associated with 20-50% of **BRAF gene mutations**



Dysembryoplastic neuroepithelial tumor (DNT) WHO grade 1 (glioneuronal tumor)

- **Age of onset** → most commonly in **children or young adults**
- **Location** → **most commonly in the superficila temporal lobe**
- **Presentation** → Slow-growing, indolent tumor; often presents with chronic, **drug-resistant seizures.**

Embryonal Primitive Neoplasms

Definition/Origin:
1. They are primitive small round cell tumors of neuroectodermal origin that resemble CNS progenitor cells.
2. They show **very limited differentiation** and might show partial differentiation (to neuronal, glial, or other neural lineages).

presentation:
1. Mainly in **children** (medulloblastomas account for 20% of brain tumor cases in children).
2. Mainly in the **cerebellum** but can also be diagnosed in the brainstem.
3. They are highly malignant (grade 4) but radiosensitive, so treatment with total excision followed by chemotherapy and irradiation gives a 5-year survival rate as high as 75%; however, **prognosis in untreated patients is poor (dismal).**

Examples include medulloblastoma, embryonal tumors with multilayered rosettes, CNS neuroblastoma, and AT/RT.

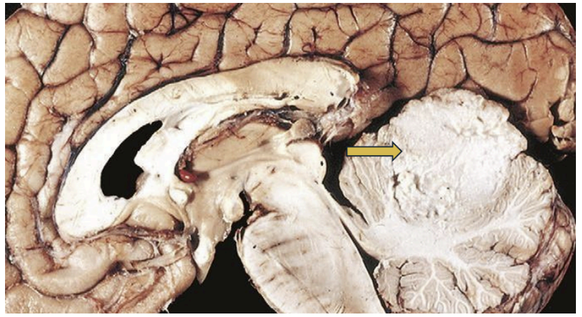
Medulloplastoma

Gross presentation:
- Appear as a **friable, pink, well-circumscribed mass** with occasional macroscopic foci of necrosis (extensive necrosis is rare).
- In children, it appears in the midline; in adults, it appears laterally.

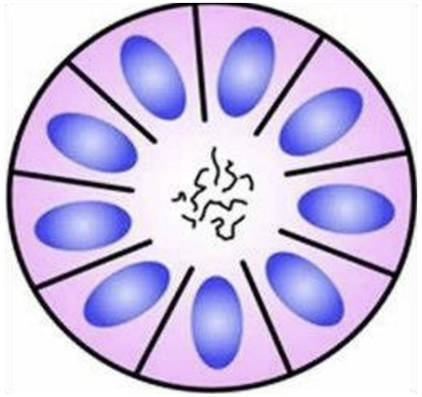
Complications:
- Can extend to the surface of the cerebellum and **involve the leptomeninges.**
- They have a tendency to spread to the subarachnoid space and disseminate through the CSF, forming discrete tumor nodules in other locations.

Microscopic presentation:
- Very **cellular** under the microscope, forming sheets of small primitive cells **("small blue")** with a hyperchromatic, elongated, crescent-shaped nucleus and scant cytoplasm.
- Mitosis is abundant → **can see apoptotic bodies.**
- Cells might surround a pink central eosinophilic mass called **neuropil**, forming **Homer Wright rosettes**, which indicate focal neuronal differentiation → this is not specific to medulloblastoma and can be seen in other neuroectodermal tumors (neuroblastoma and pineoblastoma).

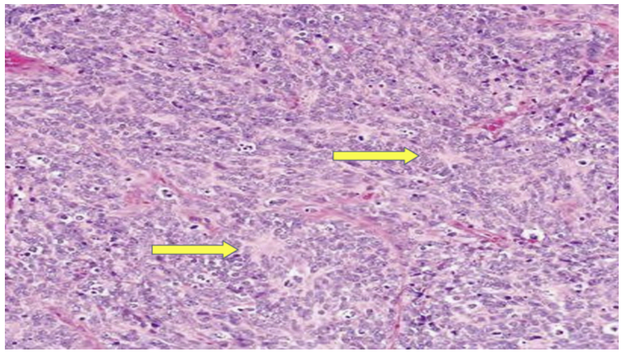
Embryonal Primitive Neoplasms



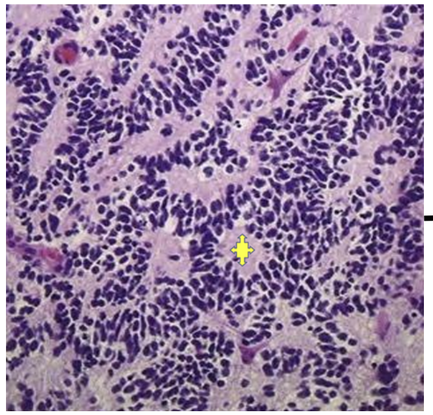
- well-circumscribed tumor representing medulloblastoma, seen here destroying the superior midline cerebellum.



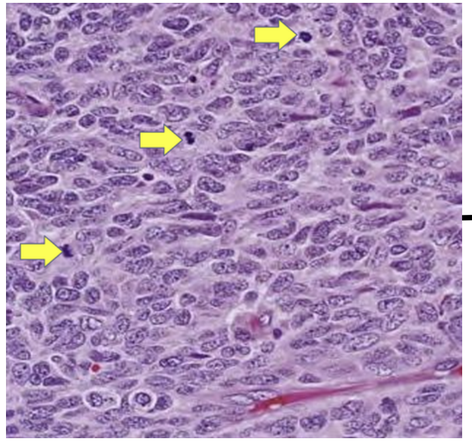
- Homer Wright Rosettes



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



The yellow arrows in the figure indicate Homer Wright rosettes, where tumor cells surround eosinophilic material (neuropil)



This figure shows frequent mitotic figures, as indicated by the arrows pointing to three mitotic figures in this field

Meningiomas, WHO grades 1–3 they are the most common extra axial tumors of the CNS

Origin/Clinical features:

- **Origin** → They arise from **meningothelial cells** of the **arachnoid** mater and attach to the dura.
- **Age of onset** → **Adults**, and more common in women.
- **Location** → Can occur on any external surface of the brain, spinal cord, within the ventricular system, and from the stromal arachnoid cells in the choroid plexus.
- **Presentation** → Depends on the location. Common symptoms are headaches, weakness, and seizures.
  - Most meningiomas are separable from the underlying brain, but some are infiltrative (higher chances of recurrence).
- **Prognosis** → Depends on the location, lesion size, surgical accessibility, and histological grade.
  - They **express progesterone receptors**, **so they may grow rapidly during pregnancy and regress after delivery.**

Genetic basis/pathogenesis:

- Most common → loss of the long arm of chromosome 22 **(22q)** → leads to deletion of the region that harbors the NF2 gene → **mutations in NF2 occur in 50%–60% of sporadic cases.**
- If multiple meningiomas + CN8 schwannoma or glial tumor → this is a sign of **inherited NF2 syndrome.**

Macroscopic:

Rubbery, rounded dural mass that compresses the underlying brain and is usually separable.

Grade 1

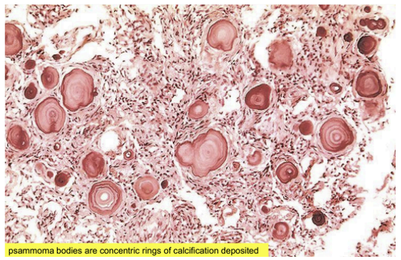
Morphology:

- Well-defined masses that attach to dura and compress the brain with no invasion and might include overlying bone extension.
- Epithelioid cells are arranged in a **whorled (syncytial) pattern** and **might include psammoma bodies.**

Histological subtypes:

There are no prognostic differences between them.

1. **Meningothelial** → most common subtype; has clusters of epithelioid cells with indistinct cell membranes.
2. **Fibrous meningiomas (Fibroblastic)** → has spindle cells with a lot of collagen.
3. **Transitional (Mixed)** → meningothelial + fibrous features.
4. **Angiomatous** → rich in blood vessels.
5. **Lymphoplasmacytic-rich** → filled with immune cells (lymphocytes + plasma cells).
6. **Psammomatous** → abundant psammoma bodies.
7. **Secretory**
8. **Metaplastic.**



Grade 2

Higher risk of recurrence and more aggressive local growth compared to grade 1 and might require radiation in addition to surgery.

Diagnosis:

Has to meet ONE of the following:

- Mitotic count **(9-14 per 10 HPF)**
- 3 or more of the following atypical features: increased cellularity, small cells with high N/C ratio, prominent nucleoli, patternless growth, or necrosis
- Clear cell meningioma or choroid meningioma (**grade 2 regardless of other features)**
- Brain invasion

Grade 3

Rare, highly aggressive, resemble a high grade sarcoma or carcinoma

Diagnosis:

Has to meet ONE of the following:

- High mitotic count **(≥ 20 per 10 HPF**)
- Frank anaplasia
- TERT promoter mutation
- Homozygous deletion of CDKN2A/B
- Either papillary or rhabdoid meningioma

Primary Nervous System Lymphoma

"Primary" → it starts in the brain (distinguish it from secondary CNS lymphoma

Epidemiology

- Make up **~2%** of extranodal lymphomas and **~1%** of intracranial tumors.
- **The most common CNS neoplasm in immunosuppressed individuals**, such as AIDS patients and organ transplant recipients.
- In non-immunosuppressed populations, the frequency increases **after 60 years of**

Prognosis

- **Aggressive** disease + **poor response to chemotherapy** (especially compared to the same lymphoma type outside the CNS).

Morphology

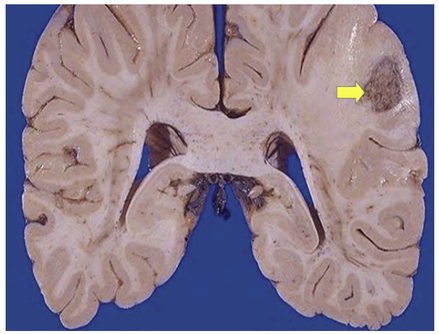
- often multifocal
- relatively well defined **(Metastatic > PCNSL > gliomas)**

Spread Pattern

- Spread outside the nervous system is **rare**.
- Lymphomas that start outside the CNS **rarely spread to brain parenchyma** (but can involve the leptomeninges).

Metastatic Tumors:

- Make up more than 50% of adult intracranial tumors, mostly carcinomas (lung, kidneys, breast, colon) and melanoma.
- They are sharply demarcated, often seen at the white-gray matter junction, and elicit local edema + reactive gliosis.



Red-brown mass at the gray-white matter junction from a metastatic renal cell carcinoma.

Familial Tumor Syndromes

→ **Inherited syndromes caused by mutations in tumor suppressor genes and associated with increased risk of neoplasms.**
→ **Very likely to develop CNS tumors.**

Tuberous Sclerosis

Genetics/Incidence:

- Autosomal Dominant
- 1 in 6000 births

Definition/Origin:

- A neuroectodermal syndrome characterized by multiple hamartomas and benign neoplasms.

→ **Hamartomas:** benign disorganized outgrowths of mature cells that belong in the tissue.

- Includes two main types here:
  - **Cortical Tubers:** they are epileptogenic + surgical resection might be beneficial.
  - **Subependymal Nodules :** might grow larger and turn into **Subependymal Giant Cell Astrocytoma (SEGA)** (characteristic here).
- Histologically, they are subependymal hamartomas and glioneuronal hamartomas.

Extracerebral manifestation:

- Renal angiomyolipomas, retinal glial hamartomas, pulmonary lymphangioleiomyomatosis, and cardiac rhabdomyomas → many of these develop **during childhood and adolescence.**
- Cysts (in liver, kidneys, and pancreas).
- Cutaneous lesions → angiofibromas (in central face), localized leathery thickenings (shagreen patches), ash-leaf patches (hypopigmented macules), and subungual fibromas (beneath the nails, appearing later in the disease course).

Von Hippel-Lindau Disease

A syndrome characterized by multiple tumors and cystic lesions in different organs

Genetics/Incidence:

- Autosomal Dominant
- 1 in 30,000 to 40,000 births

Manifestations:

- In the CNS: **Hemangioblastomas** → highly vascular neoplasms consisting of numerous capillary-size or larger thin-walled vessels with intervening neoplastic **stromal cells (the actual tumor cells).**
  - Stromal cells have vacuolated, lipid-rich cytoplasm → appear clear and foamy.
  - Stromal cells **express inhibin**, which distinguishes hemangioblastomas from other highly vascular tumors, such as metastatic clear cell renal cell carcinoma.
  - Most common in the **cerebellum and retina**, but may occur in the brainstem, spinal cord, and nerve roots.
- (Usually benign) Cysts in the pancreas and liver.
- Cysts in the kidneys + **increased risk of clear cell renal cell carcinoma.**
- **Pheochromocytomas** arising from the adrenal medulla.

الحمد لله حتى يرضى، والحمد لله إذا رضي، والحمد لله بعد الرضا

اللهم اجعل أجر هذا العمل صدقة جارية عن روح **عمر عطيه عوده المرابي**

- اللَّهُمَّ اغْفِرْ له وَارْحَمْهُ، وَاعْفُ عنْه وَعَافِهِ، وَأَكْرِمْ نُزُلَهُ، وَوَسِّعْ مُدْخَلَهُ، وَ اغْسِلْهُ بمَاءٍ وَثَلْجٍ وَبَرَدٍ، وَنَقِهِ مِنَ الخَطَايَا كما يُنَقّى الثَّوْبُ الأبْيَضُ مِنَ الدَّنَسِ.
- اللَّهُمَّ أبدله داراً خيراً من داره، وأهلاً خيراً من أهله، وأدخله الجنّة، وأعذه من عذاب القبر ومن عذاب النّار.
- اللهمّ يمّن كتابه، ويسّر حسابه، وثقل بالحسنات ميزانه، وثبّت على الصراط أقدامه، وأسكنه في أعلى الجنات، بجوار حبيبك محمد صلّى الله عليه وسلم.
- اللهم اغفر لحينا وميتنا وشاهدنا وغائبنا وصغيرنا وكبيرنا وذكرِنا وأنثانا اللهم من أحييته منا فأحيِه على الإسلام ومن توفيته منا فتوفه على الإيمان اللهم لا تحرمنا أجره ولا تضلنا بعده.
- اللهم اغفر له وارفع درجته في المهديين، واخلفه في عقبه في الغابرين، واغفر لنا وله يا رب العالمين، وافسح له في قبره، ونوّر له فيه.
- اللَّهُمَّ أنزل على أهله الصّبر والسلوان وارضهم بقضائك.

اللهم لا تفجعنا بأنفسنا ولا أهلنا ولا أحبتنا، اللهم أعوذ بك من فواجع الأقدار ومن مصائب الدنيا وتقلب حوادثها، اللهم إنا نخاف الفقد فلا تحملنا ما لا طاقة لنا به.