Ependymoma

• Circumscribed glioma, Mostly arise next to the ependyma- lined ventricular system, including the central canal of the Spinal cord/ Posterior fossa/ Supratentorial.

• In adults ⟶ spinal cord and supratentorial ependymomas>>> better clinical outcomes.

• In children ⟶ near the 4th ventricle (post. Fossa)>>> worse clinical outcomes.

• There is no grade 1 nor grade 4 .

Ependymoma WHO grade 2, Macroscopic:

• Solid and non-infiltrative mass.

• Moderately well demarcated from adjacent brain.

• The proximity to vital structures often makes complete removal impossible, except in the spinal cord (total resection is more feasible).

Microscopic:

• Uniform small cells with round to oval nuclei and granular chromatin in a fibrillary background.

• low cellularity.

• low mitotic count.

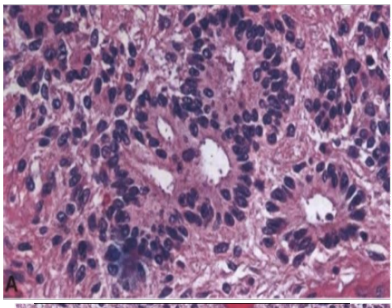
• No necrosis or MVP (microvascular proliferation).

Morphology:

• Tumor cells may form glandlike structures (rosettes) → Rosette formation (Spoked wheels).

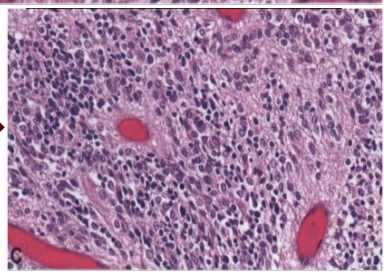
Ependymal rosettes: diagnostic hallmark of ependymoma (specific hallmark, not found in every case)

-Tumor cells arranged around central canal or lumen (made of tumor cells itself).



Perivascular pseudorosettes: not specific (seen in glioblastoma and medulloblastoma) but sensitive (found in the most cases).

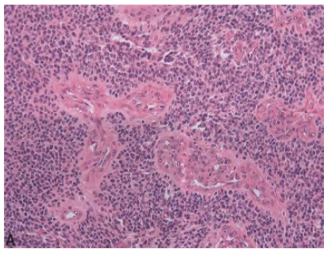
- Tumor cells radially arranged around vessels.
- Called “pseudo” because the central structure is not formed by the tumor itself, but instead represents a native, non-neoplastic element.



Anaplastic ependymomas, WHO grade 3:

• Show less evident ependymal differentiation (less Ependymal rosettes).

• Brisk mitotic rates, and microvascular proliferation carry more prognostic impact than necrosis and atypia.



Neuronal &Glioneuronal tumors

- Less frequent than gliomas
- Lower-grade lesions (grade 1or 2)
- Present with seizures

- Neuronal characteristics and express neuronal markers (synaptophysin and neurofilaments)

Central neurocytoma

WHO grade 2: neuronal tumor within and adjacent to the lateral ventricle(s) and/or the third ventricle affecting young adults.

Gangliоglioma

WHO grade 1: glioneuronal tumor affecting children and young adults. composed of a mixture of neoplastic ganglion and glial cells, most commonly in the temporal lobe.

Dysembryoplastic neuroepithelial tumor (DNT)

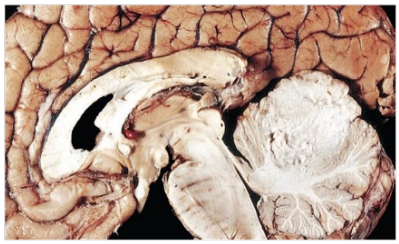
WHO grade 1: glioneuronal tumor affecting the cerebral cortex of children and young adults most commonly in the superficial temporal lobe.

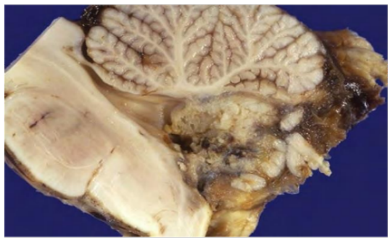
Embryonal (Primitive) Neoplasms

- 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.

Medulloblastoma

- In children (in cerebellum)
- All are highly malignant, WHO grade 4
- radiosensitive.



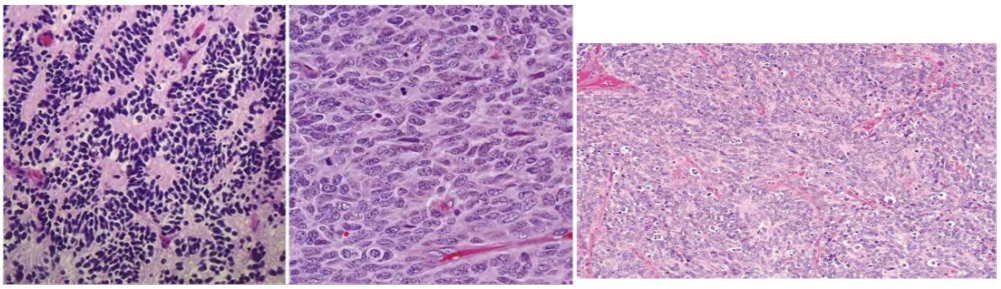


Macroscopic:

- well circumscribed.
- Spread to the subarachnoid space → Dissemination through the CSF.
- +/- Small foci of necrosis, but extensive necrosis is rare.

Morphology:

- Very Cellular.
- Small blue primitive cells (little cytoplasm and hyperchromatic nuclei>>> High N/C ratio).
- Mitoses are abundant.
- Express neuronal markers such as synaptophysin.
- The expression of glial markers (GFAP) is less common.



• Homer Wright Rosettes:

- Primitive tumor cells surrounding central neuropil (delicate pink material formed by neuronal processes) .
- Represents focal neuronal differentiation.
- Not specific (seen in neuroblastoma and pineablastoma).

Oncogenic pathways in Medulloblastoma:

➢ Wnt pathway activation: gain of function mutations in the gene for β-catenin >>> the most favorable prognosis of all the genetic subtypes.

➢ MYC overexpression: due to MYC amplification>>> the poorest prognosis.

➢ Hedgehog pathway activation: associated with loss of function mutations in PTCH1 (a negative regulator of the Hedgehog)>>> intermediate prognosis, but the concomitant presence of P53 mutation >>> very poor prognosis.

• Medulloblastomas are classified according to molecular characteristics in addition to histopathological features into:

➢ Medulloblastoma, WNT activated

➢ Medulloblastoma, SHH activated and P53 wildtype

➢ Medulloblastoma, SHH activated and P53 mutant

➢ Medulloblastoma, non-WNT/non-SHH

Meningiomas

• Tumors that arise from meningothelial cells of the arachnoid matter.

• Age at presentation: adults (women>men)

• Location: intracranial, intraspinal or orbital attached to the dura.

• Express progesterone receptors and may grow more rapidly during pregnancy, only to regress after delivery.

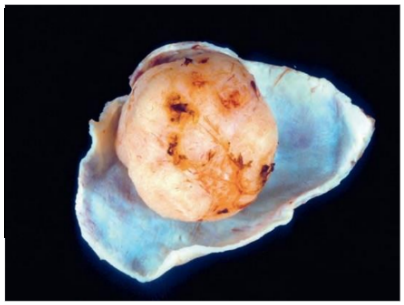
Pathogenesis:

• The most common cytogenetic abnormality is loss of chromosome 22, especially the long arm (22q) >>> include the region that harbors the NF2 gene.

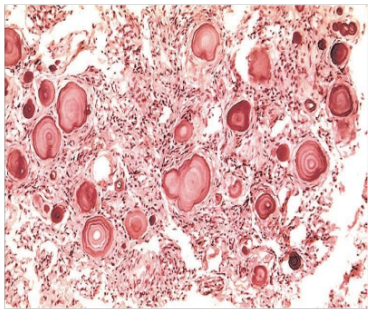
Macroscopic:

• Rubbery, rounded, or bosselated dural masses that compress underlying brain.

• Mostly separable (Circumscribed) from underlying brain, but some tumors are infiltrative.



Meningiomas (WHO grade 1):



- Well-defined dura-based masses.
- Epithelioid cells arranged in whorly (syncytial)pattern
  +/- psammoma bodies (concentric rings of calcification deposited).
- Meningothelial (most common pattern)→clusters of epithelioid cells with fuzzy or indiscernible cell membranes
  (It is hard to differentiate the margins of each cell).
- Other patterns include fibroblastic (collagen deposition), transitional (meningothelial and fibroblastic differentiation at the same tumor) , and psammomatous .

ATYPICAL MENINGIOMAS, WHO grade 2:

•Recurrence and aggressive local growth (require radiation/surgery is not enough)

Diagnostic Criteria :

1) >=4 mitoses/10 HPF.

2) "3 out of 5 characteristics are present": increased cellularity, small cells with a high N/C ratio, prominent nucleoli, patternless growth, or necrosis.

3) Clear cell or chordoid subtypes of meningioma.

ANAPLASTIC MENINGIOMAS, WHO grade 3 (malignant):

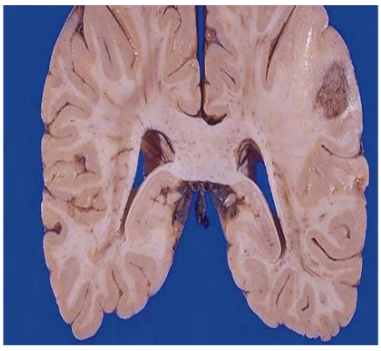
• Highly aggressive, resemble a high-grade sarcoma or carcinoma morphologically.

Diagnostic Criteria :

1) >20 mitoses/ 10HPF.

2) Papillary; or rhabdoid meningioma.

Metastatic Tumors



- Mostly carcinomas.
- The most common primary sites are lung, breast, skin (melanoma), kidney, and gastrointestinal tract
- Sharply demarcated masses, at the grey-white matter junction, and elicit local edema.
- The boundary between tumor and brain parenchyma is sharp at the microscopic level with surrounding reactive gliosis.

Primary Central Nervous System Lymphoma

- The most common CNS neoplasm in immunosuppressed individuals.
- Aggressive disease , poor response to chemotherapy.
- 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 but not as discrete as metastases.

Germ Cell Tumors

- Primary or metastatic
- **Primary brain germ cell tumors:**
  - Locations: along the midline, most commonly in the pineal and the suprasellar regions (post. Pituitary and infundibular stalk).
  - 90% during the first 2 decades of life.
- The most common primary CNS germ cell tumor is germinoma, closely resembles testicular seminoma.
- Other germ cell tumors include: teratoma (mature and immuture), embryonal carcinoma, yolk sac tumor, chriocacinoma and mixed germ cell tumors.