وقل رب زدني علماً

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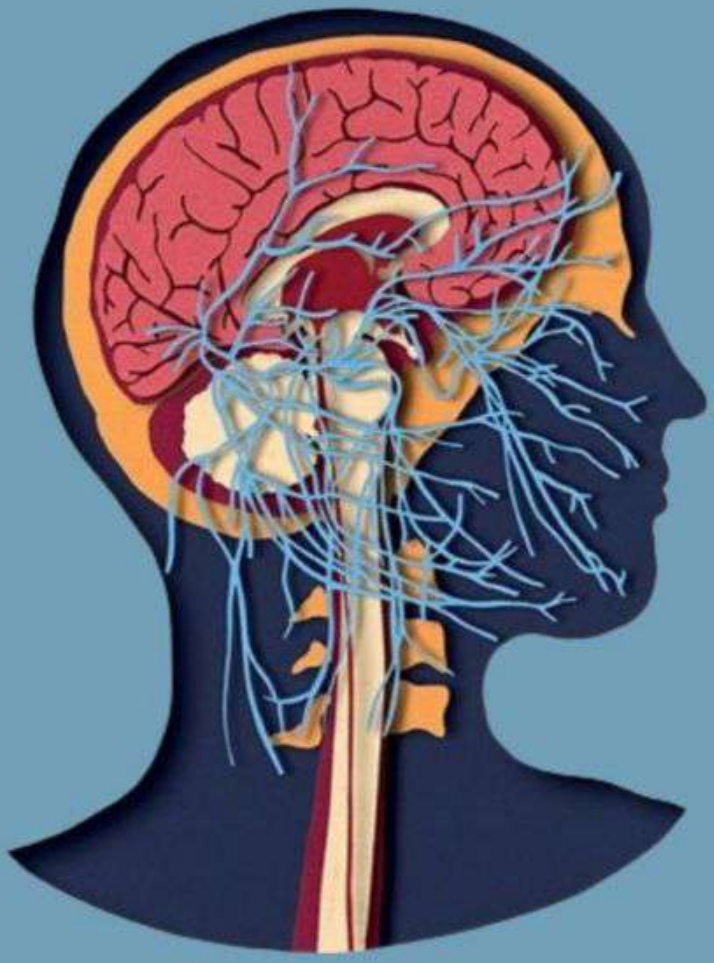
# PERIPHERAL NERVOUS SYSTEM



SUBJECT : Pathology-TABLE

LEC NO. : 2

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# PNS

# Pathology Lecture 2

# Central Nervous System Tumors

## 2) Neuronal Tumors

| 1.Central neurocytoma: | 2.Gangliogliomas | 3.Dysembryoplastic neuroepithelial tumor |
|---|---|---|
| GENERAL FEATURES | GENERAL FEATURES | GENERAL FEATURES |
| -Low-grade<br><br>-Within and adjacent to the ventricular system (Lateral or third ventricle)<br><br>-Composed of evenly spaced, round, uniform nuclei and often islands of neuropil | - Mixture of glial elements, usually a low-grade astrocytoma and mature appearing neurons<br><br>- Most are slow-growing and present with seizures. | - A low-grade tumor of children and young adults that grows slowly<br><br>- In the temporal lobe<br><br>- Manifests as a seizure<br><br>- Floating neurons in a myxoid background |

## 3) Embryonal (Primitive) Neoplasms

### Medulloblastoma (WHO grade IV)

| ANATOMICAL SITE & AGE | GENERAL INFORMATION | PATHOGENESIS | GROSS | MICROSCOPIC |
|---|---|---|---|---|
| - Occurs in more children and in the cerebellum<br>- Children: Midline of the cerebellum<br>- Adults: Lateral of the cerebellum | - Primitive Neuroectodermal Tumor: PNET<br><br>- Primitive small cell (blue cell) tumor<br>BLUE: DARK CELLS<br><br>- Presents with Sx &Sx of ICP (headache, nausea, vomiting)<br><br>-Highly malignant, and the prognosis for untreated patients is dismal; however, it is radiosensitive.<br><br>- With treatment, the 5-year survival rate may be as high as 75%. | -*Oncogenic pathways* in these tumors are the following:<br><br>•Wnt pathway activation: have the most favorable prognosis<br><br>•Hedgehog pathway activation: have an intermediate prognosis, but the concomitant presence of TP53 mutation confers a very poor prognosis.<br><br>•MYC overexpression due to MYC amplification: have the poorest prognosis | - Well circumscribed, friable and extend to involve the leptomeninges | - Densely cellular, with sheets of anaplastic ("small blue") cells<br><br>-Tumor cells are small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.<br><br>- 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" |
| Medulloblastoma subtypes | 1. WNT<br>MOLECULAR FEATURES: CTNNB1, Monosomy 6<br><br>5-YEAR SURVIVAL: 95%-100% GOOD PROGNOSIS<br><br>ANATOMICAL SITE: Dorsal Brainstem | 2. Shh<br>MOLECULAR FEATURES: GL1, PTCH1, SMO, SUFU, TP53<br><br>5-YEAR SURVIVAL: 40% (P53 MUTANT), 80% (P53 WILDTYPE) INTERMEDIATE PROGNOSIS<br><br>ANATOMICAL SITE: Cerebellar Hemisphere | 3. Group 3<br>MOLECULAR FEATURES: FSTL5, MYC, VEGFA<br><br>5-YEAR SURVIVAL: 30-60% POOR PROGNOSIS<br><br>ANATOMICAL SITE: Midline | 4. Group 4<br>MOLECULAR FEATURES: KDM6A, MYC, OTX<br><br>5-YEAR SURVIVAL: 75%<br><br>ANATOMICAL SITE: Midline |

# 4) Other Parenchymal Tumors

## 1. Primary Central Nervous System Lymphoma

| GENERAL FEATURES | GROSS | MICROSCOPIC |
|---|---|---|
| - Mostly as diffuse large B-cell lymphomas<br><br>- It is the most common CNS neoplasm in immunosuppressed individuals (Nearly always positive for EBV)<br><br>- It is an aggressive disease with a relatively poor response to chemotherapy as compared with peripheral lymphomas<br><br>- 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<br><br>- Lymphoma originating outside the CNS rarely spreads to the brain parenchyma | -Involves deep gray structures, as well as the white matter and the cortex<br><br>- Periventricular spread is common<br><br>- Well defined as compared with glial neoplasms. | - Nearly always aggressive large B-cell lymphomas<br><br>- Malignant lymphoid cells accumulate around blood vessels and infiltrate the surrounding brain parenchyma.<br><br>- Positive for B cell markers such as CD20 |

## 2. Germ Cell Tumors

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

# 5) Meningiomas (WHO grade I-III)

## Meningiomas

| GENERAL FEATURES | MORPHOLOGY | | |
|---|---|---|---|
| | GRADE I | GRADE II | GRADE III |
| - Benign tumors arise from arachnoid meningothelial cells.<br><br>- Usually in adults and are often attached to the dura<br><br>- Most in adult females, Tumor cells contain PROGESTERON receptors<br><br>- May be found along any of the external surfaces of the brain<br><br>- Presents with vague Sx or focal findings due to compression of the adjacent brain<br><br>- Most are easily separable from the underlying brain, but some are infiltrative<br><br>- The overall prognosis is determined by the lesion size and location, surgical accessibility, and histologic grade<br><br>- Multiple meningiomas are associated with neurofibromatosis type 2 (NF2)<br><br>- About half of meningiomas not associated with NF2 have mutations in the NF2 tumor suppressor gene (in all grades) | - Grows as dura-based masses that may compress the brain, but No brain invasion<br><br>- Extension into the overlying bone may be present<br><br>***Histologic patterns:***<br>- Meningothelial (whorled clusters of cells without visible cell membranes)<br><br>- Fibroblastic (elongated cells and abundant collagen deposition)<br><br>- Transitional (features of the meningothelial and fibroblastic types)<br><br>- Psammomatous (numerous psammoma bodies)<br><br>- Secretory (glandlike spaces containing PAS-positive eosinophilic material) | - These tumors demonstrate more aggressive local growth and a higher rate of recurrence<br><br>- The presence of either an increased mitotic rate OR prominent nucleoli, increased cellularity, patternless growth, high nucleus-to-cytoplasm ratio, or necrosis<br><br>- ***Histologic patterns—*** clear cell and chordoid<br><br>- The presence of brain invasion | -Highly aggressive tumors that may resemble a high-grade sarcoma or carcinoma morphologically<br><br>- Mitotic rates are typically much higher than in atypical meningiomas<br><br>- Papillary or Rhabdoid morphology |

# 6)Metastatic Tumors

## Metastatic Tumors

| GENERAL FEATURES | GROSS |
|---|---|
| - Mostly carcinomas<br><br>- The most common primary sites are the lung, breast, skin (melanoma), kidney, and gastrointestinal tract, which together account for about 80% of cases | - Form sharply demarcated masses (usually multiple), often at the grey-white matter junction<br><br>- The boundary between tumor and brain parenchyma is sharp at the microscopic level as well, with surrounding reactive gliosis |

# 7) Familial Tumor Syndromes

## Familial Tumor Syndromes

### 1. Tuberous 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

### 2. Von Hippel-Lindau Disease

- 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

- 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

## Cortical hamartomas

**MORPHOLOGY**

-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

## Hemangioblastoma

**MORPHOLOGY**

- 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.

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.