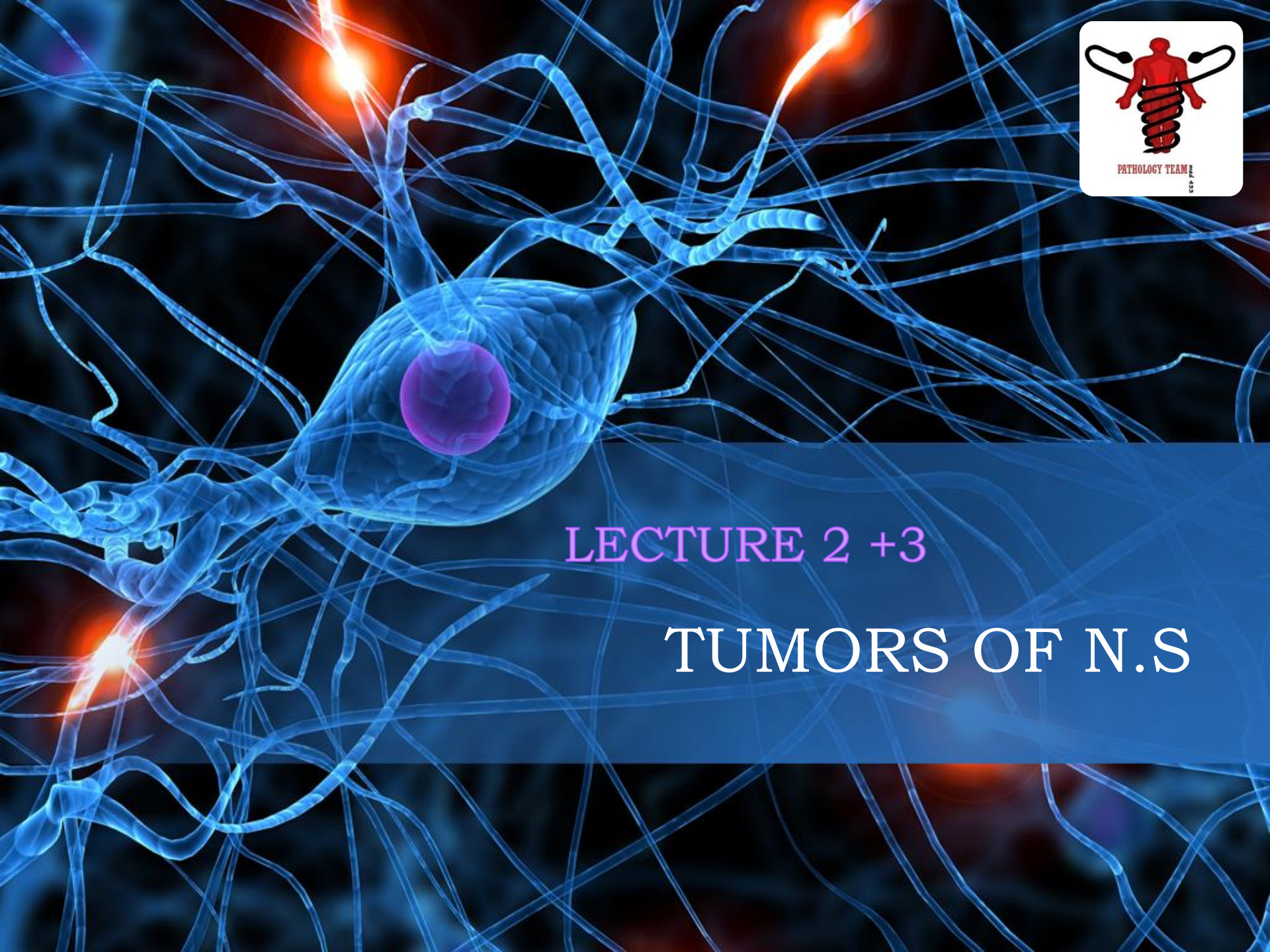


LECTURE 2 +3

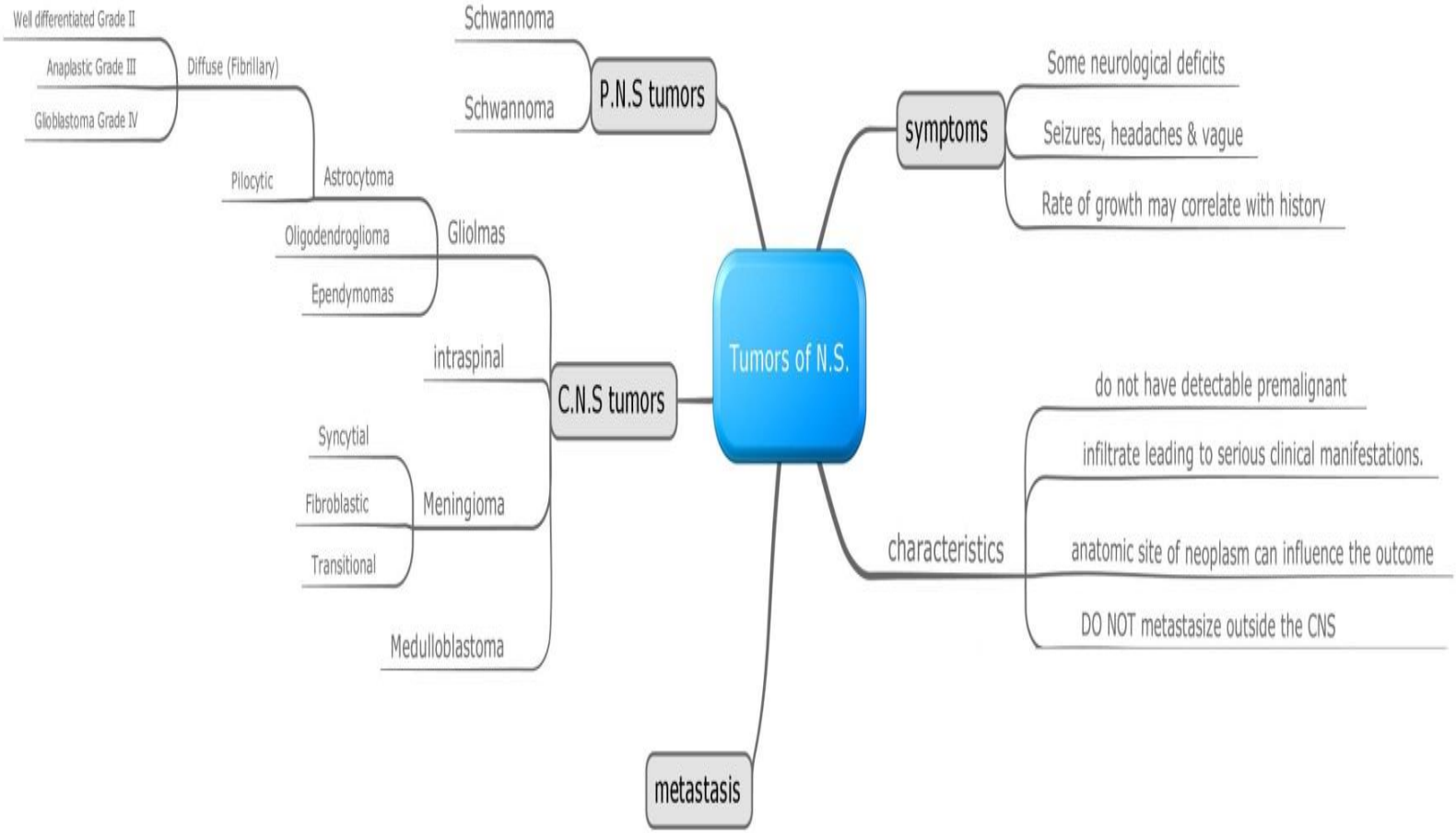
TUMORS OF N.S

Objectives:

- Appreciate how the anatomy of the skull and the spinal column influences the prognosis of both benign and malignant primary CNS tumors.

- List the principal clinicopathological features of some of the main types of tumors that can arise within the central and the peripheral nervous systems.

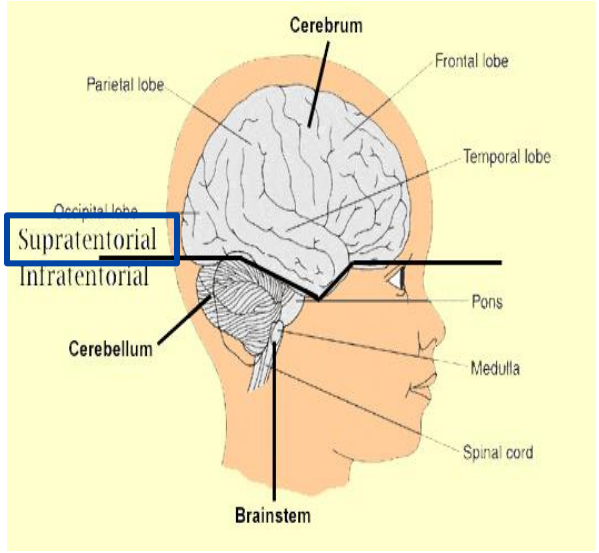
Mind Map


Tumors of N.S.
P.N.S tumors
Schwannoma
Schwannoma
C.N.S tumors
Gliolmas
Astrocytoma
Pilocytic
Diffuse (Fibrillary)
Well differentiated Grade II
Anaplastic Grade III
Glioblastoma Grade IV
Oligodendroglioma
Ependymomas
intraspinal
Meningioma
Syncytial
Fibroblastic
Transitional
Medulloblastoma
symptoms
Some neurological deficits
Seizures, headaches & vague
Rate of growth may correlate with history
characteristics
do not have detectable premalignant
infiltrate leading to serious clinical manifestations.
anatomic site of neoplasm can influence the outcome
DO NOT metastasize outside the CNS
metastasis

TUMORS

- Intracranial tumors are more than intraspinal tumors.
- About three-quarters are primary tumors, and the rest are metastatic.
- accounting for 20% of all pediatric tumors.

- CNS tumors in childhood and adult tumors **are not the same** in histologic subtypes and locations (In childhood, tumors are likely to arise in the posterior fossa, while in adults they are mostly supratentorial fig.).



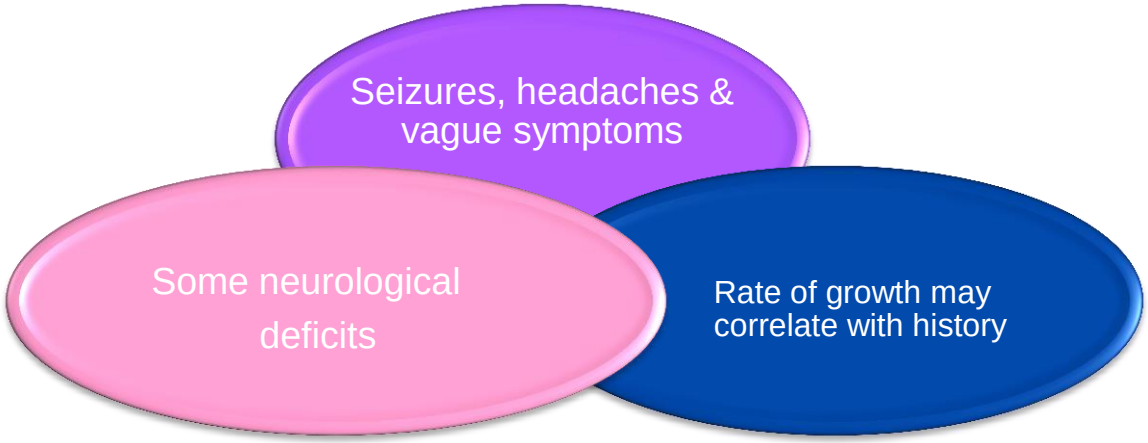
figure

- General characteristics of C.N.S tumors:

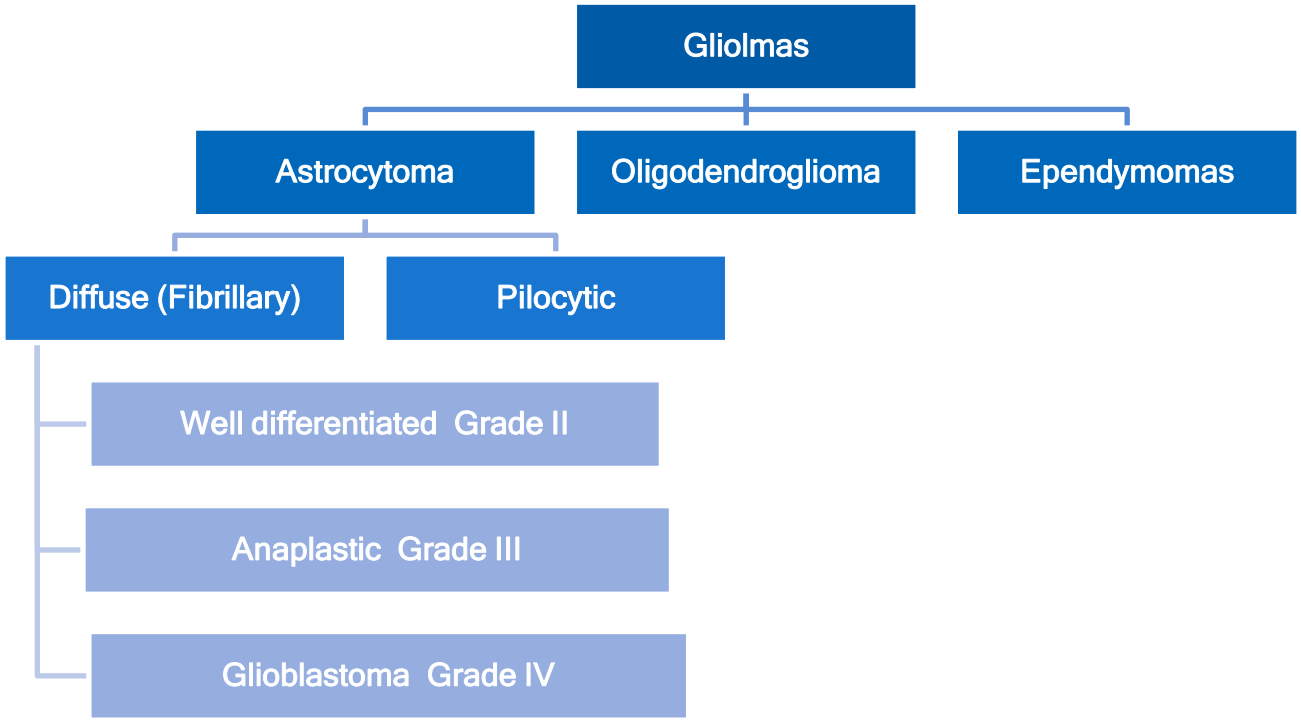
- These tumors do not have detectable premalignant or in situ stage (original position) comparable to other carcinomas.
- Low-grade lesions may infiltrate to many regions of the brain leading to serious clinical manifestations.
- Unrelated to histological classification, anatomic site of neoplasm can influence the outcome due to:
  - Local effect (i.e. a benign meningioma may cause cardiorespiratory arrest from compression of medulla).
  - Non resectable means not able to be removed (i.e. brain stem gliomas)

- The tumors of the CNS **DO NOT** metastasize outside the CNS usually even it is highly malignant.

- General manifestations and symptoms :



- **GLIOMAS :** tumor of the brain parenchyma



Astrocytoma

1- Fibrillary astrocytoma

- **Effected site :** Cerebral hemisphere.
- **Common age:** older people (40-60 years).

It has 3 grades:

- Grade II (Diffused astrocytoma)

- Well differentiated
- Malignant
- Can be static for several years, but at some point they progress
- Moderate cellularity & Variable pleomorphism
- caused by acquired mutation: in the 2 metabolic isoenzymes isocetirate dehydrogenase (IDH1 & IDH2) *

* This becomes important diagnostic tool.

- Grade III (Anaplastic astrocytoma)

- Less differentiated
- Malignant
- More cellularity & greater pleomorphism and mitotic.
- Rapid growth lead to clinical deterioration.

- Grade IV (Glioblastoma astrocytoma) :

- most common and most malignant primary brain tumor
- Poor prognosis ,with treatment mean survival 15 months (Fast progression)
- Malignant
- More cellularity & greatest pleomorphism
- Pseudopalisading necrosis & vascular proliferation.
- secondary glioblastoma caused by acquired mutation: in p53 (suppressor gene) while the primary is characterized by amplification of epidermal growth factor receptor gene(EGFR).
- Benign Astrocytoma may transforms after a while to secondary Glioblastoma

Astrocytoma

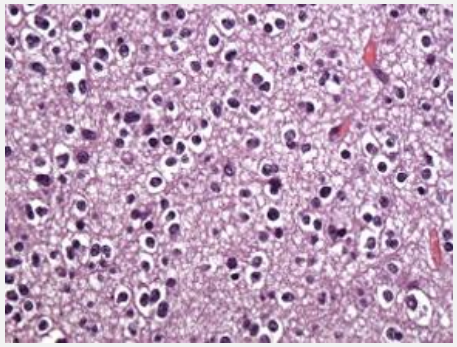
2- Pilocytic astrocytoma

- **Effected site :** cerebellum (but may involve other sites)
- **Common age:** children and young adults
- Relatively it is **benign**
- **Histologically:**
- Cystic appearance.
- Well circumscribed
- Rosenthal fibers & hyaline granular bodies .
- No necrosis and mitosis.
- it has bipolar cells with elongated hairlike processes because **(GFAP is positive)***

*GFAP = Glial fibrillary acidic protein. This protein is found in the CNS gives fibrillary appearance

Oligodendroglioma (fried egg appearance)

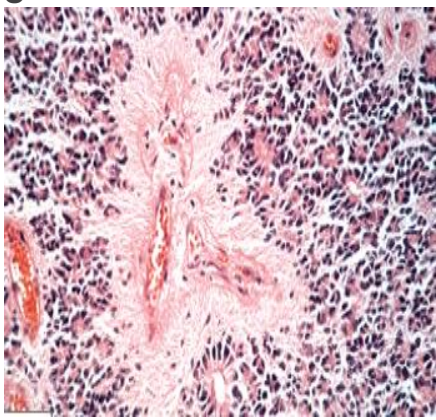
- Common age: (40-50 years)
- Effected site : mostly in cerebral hemispheres especially frontal and temporal.
- Better prognosis than astrocytoma. it responses to treatment (surgery, chemotherapy and radiation).
- Genetic findings : deletion of chromosome 1p and q19 (this type responses to chemotherapy + radiotherapy).



- **Histologically:**
  - Nuclei is rounded with cytoplasmic halo + Blood vessels are thin and they form an interlacing pattern + focal hemorrhage and calcification.

Ependymoma

- Often, it arises from ependymal-lined ventricle system, including the central canal of the spinal cord.



Age	Site
First two decades	4th ventricle
Adult	Spinal cord

- Histologically:

- Cells form round or elongated structures (rosette, canals) same embryological ependymal canal .
- More frequently appears as Perivascular pseudo-rosettes (tumor cells surround blood vessels)

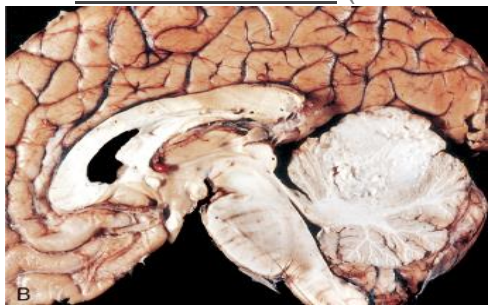
Medulloblastoma (embryological primitive neoplasms)

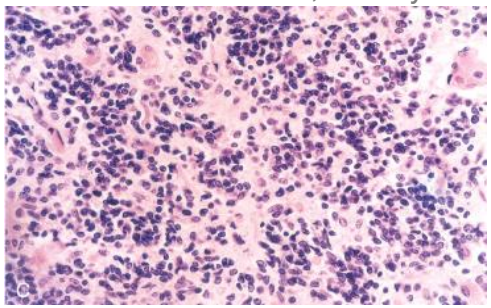
✓ Age : children

✓ Site : crebellum.

✓ the tumor is often largely undifferentiated

✓ highly malignant, and the prognosis for untreated patients is dismal, but in other hand it is radiosensitive.(With total excision and radiation, the 5-year survival rate may be as high as 75%.)





*anaplastic ("small blue") cells

*little cytoplasm and hyperchromatic nuclei

*mitosis

Meningioma

✓ Benign tumor of adult.
✓ Originate from meningothelial cell of the arachnoid.

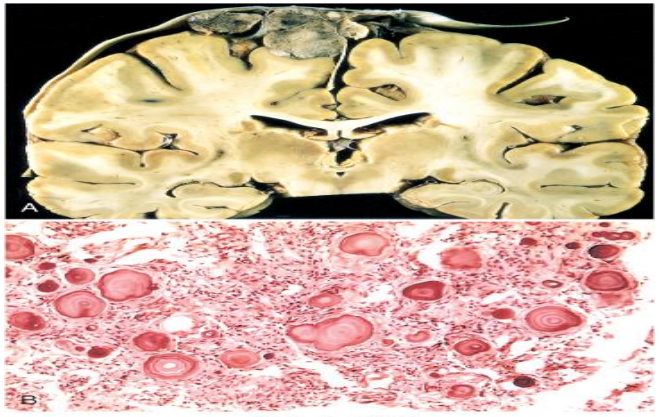
Main subtypes:

- Syncytial — cluster of cells without visible cell membrane
- Fibroblastic — elongated cells with collagen deposition between them
- Transitional — share features of the syncytial and fibroblastic type

- Notice:

✓ there is atypical meningioma and anaplastic (malignant) meningioma.
✓most meningiomas are easily separable from underlying brain, but some tumors infiltrate the brain (presence of invasion increase risk of recurrence).
✓Histological features:

- Atypical meningiomas > (pleomorphism, mitosis, increas cellularity)
- Anaplastic (malignant) meningiomas > necrosis



*Well demarcated
*Attached to the dura with compression of underlying brain
***Whorled** pattern of cell growth and **psammoma** bodies*

*A **psammoma body** is a round collection of calcium, seen microscopically.

Schwannoma

- ✓ Benign tumor
- ✓ In the CNS, they are often encountered within the cranial vault in the cerebellopontine angle (fig2), where they are attached to the vestibular branch of the eighth nerve (tinnitus* and hearing loss).
- ✓ schwannomas are Sporadic but Bilateral acoustic schwannoma is associated with Neurofibromatosis type 2 mutation.
- ✓ Attached to the nerve but can be separated from it.

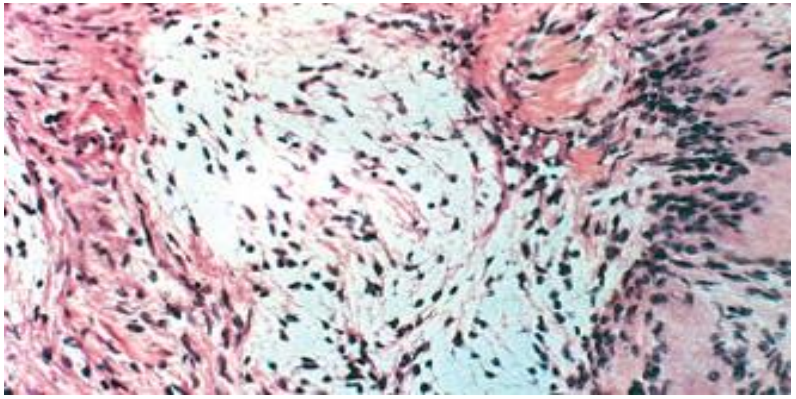


Figure 1

- Histological features:
*MultiCellular Antoni A pattern
*lesscellular Antoni B
*Verocay bodies(nuclear-free zones of processes that lie between the regions of nuclear palisading)

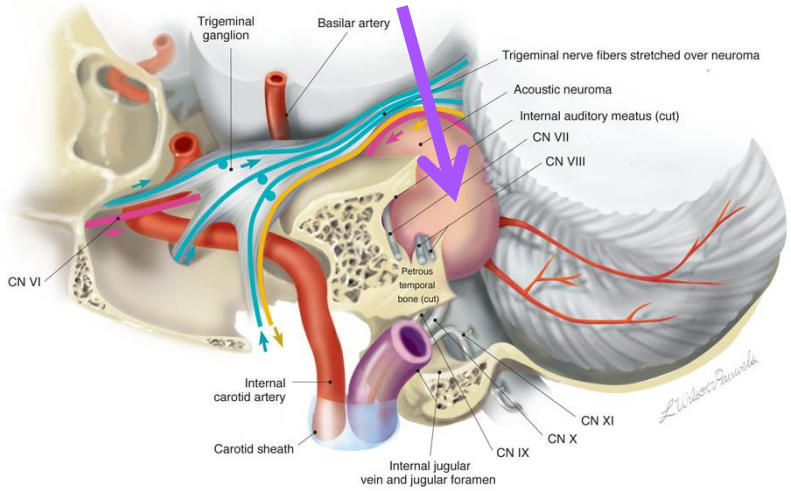


Figure V–17 Schwannoma: an enlarged tumor in the cerebellopontine angle compressing the root of the trigeminal nerve (sagittal section through the jugular foramen).

Figure 2

*Tinnitus: is the perception of sound in the ears or head where no external source is present. Some call it "ringing in the ears" or "head noise".

Neurofibromas

- ✓ Arise sporadically or in association with type 1 neurofibromatosis, rarely malignant, Examples: (cutaneous neurofibroma) or in peripheral nerve (solitary neurofibroma)
- ✓ Neurofibromas cannot be separated from nerve trunk (in comparison to shcwannoma)
- ✓ plexiform neurofibroma, mostly arising in individuals with Neurofibromatosis type 1, potential malignancy.

Metastatic tumors

✓About half to three-quarters of brain tumors are primary tumors, and the rest are metastatic.

✓ Lung, breast, skin (melanoma), kidney, and gastrointestinal tract are the commonest primary organs that metastasize to N.S.

Homework

Q1/ Describe the inheritance pattern and the main features of Type 1, and 2 Neurofibromatosis

	Type 1 Neurofibromatosis	Type 2 Neurofibromatosis
Inheritance pattern	Autosomal dominant pattern	
Main features	Changes in skin colour (pigmentation).The signs and symptoms of this condition vary widely among affected people	- Bilateral vestibular schwannoma is a hallmark of NF2. - loss of function mutation of the merlin gene in chromosome 22. (Merlin is cytoskeletal protein that function as a tumor suppressor) The most common tumors associated with are vestibular schwannomas or acoustic neuromas(These growths develop along the auditory nerve)

Q2/ Which one of these two syndromes, has a propensity for the neurofibromas to undergo malignant transformation at a higher rate than that observed for comparable tumors in the general population?

Plexiform Neurofibroma associated with small but real risk of malignant transformation

Summary from Robbins

SUMMARY

Tumors of the Central Nervous System

- Tumors of the CNS may arise from the cells of the coverings (meningiomas), the brain (gliomas, neuronal tumors, choroid plexus tumors), or other CNS cell populations (primary CNS lymphoma, germ cell tumors), or they may originate elsewhere in the body (metastases).
- Even low-grade or benign tumors can have poor clinical outcomes, depending on where they occur in the brain.
- Distinct types of tumors affect specific brain regions (e.g., cerebellum for medulloblastoma, an intraventricular location for central neurocytoma) and specific age populations (medulloblastoma and pilocytic astrocytomas in pediatric age groups, and glioblastoma and lymphoma in older patients).
- Glial tumors are broadly classified into astrocytomas, oligodendrogliomas, and ependymomas. Increasing tumor malignancy is associated with more cytologic anaplasia, increased cell density, necrosis, and mitotic activity.
- Metastatic spread of brain tumors to other regions of the body is rare, but the brain is not comparably protected against spread of distant tumors. Carcinomas are the dominant type of systemic tumors that metastasize to the nervous system.

SUMMARY

Peripheral Nerve Sheath Tumors

- In most peripheral nerve sheath tumors, the neoplastic cells show evidence of Schwann cell differentiation.
- Peripheral nerve sheath tumors are important features of the familial tumor syndromes neurofibromatosis type 1 (NF1) and type 2 (NF2).
- Schwannomas and neurofibromas are benign nerve sheath tumors.
- Schwannomas are circumscribed, usually encapsulated tumors that abut the nerve of origin and are a feature of NF2.
- Neurofibromas may manifest as a sporadic subcutaneous nodule, as a large, poorly defined soft tissue lesion, or as a growth within a nerve. Neurofibromas are associated with NF1.
- About 50% of malignant peripheral nerve sheath tumors occur de novo in otherwise normal persons, while the remainder arise from the malignant transformation of a preexisting NF1-associated neurofibroma.

Challenge yourself

1-The neoplasm that most frequently occurs in the fourth ventricle is:

A- Oligodendroglioma

B- Ependymoma

C- Medulloblastoma

D- Neuroblastoma

2- Loss of heterozygosity for chromosomes 1p and 19q is the most common genetic finding in:

A- Medulloblastoma

B- Astrocytoma

C- Meningioma

D- Oligodendroglioma

3- A biopsy was taken from a patient and it showed whorled pattern of growth and psammoma bodies. What is the most likely diagnosis:

A- Medulloblastoma

B- Glioblastoma

C- Meningioma

D- Pilocytic astrocytoma

4- Bilateral acoustic schwannoma is associated with :

A- V600E

B- NE2

C- NF2

D- IDH1

5- In meningioma presence of brain invasion is associated with :

A- Decreased risk of recurrence

B- Increased risk of recurrence

C- It has no effect

3-psammoma bodies are found in:

A-meningioma

B-glioblastoma

C-schwannoma

D-neurofibroma

1- B 2- D 3-C 4- C 5- B 6-A

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