Lecture Two & Three

Tumors

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes

Objectives:

Upon completion of this lecture, students should be able to:

- 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.

Background:

CNS tumors exhibit unique characteristics that make them different from tumors of the other body sites. Also childhood CNS tumors differ from those in adults, both in histologic subtypes and locations. Although histological classification and grading play a major rule in predicting the outcome a CNS tumor, the anatomic site of the neoplasm can have lethal consequences irrespective of histologic classification.

Key principles to be discussed:

- CNS tumors incidence and classification, with special consideration of the general differences between the pediatric and the adult population
- The unique characteristics that set CNS tumors apart from neoplastic processes elsewhere in the body
- The incidence, common clinical presentation, location, macroscopic appearances, microscopic features, pattern of spread and prognosis of the following neoplasms will be explained and discussed (within the context of the recommended textbook):
    - Astrocytic neoplasms: Pilocytic astrocytoma, diffuse astrocytoma, anaplastic astrocytoma and gliobastoma
    - Oligodendroglioma
    - Ependymoma
    - Medulloblastoma
    - Meningioma
    - Metastatic tumours
    - Peripheral nerve sheath tumours: schwannoma and neurofibroma

Key principles to be covered by self-directed learning:

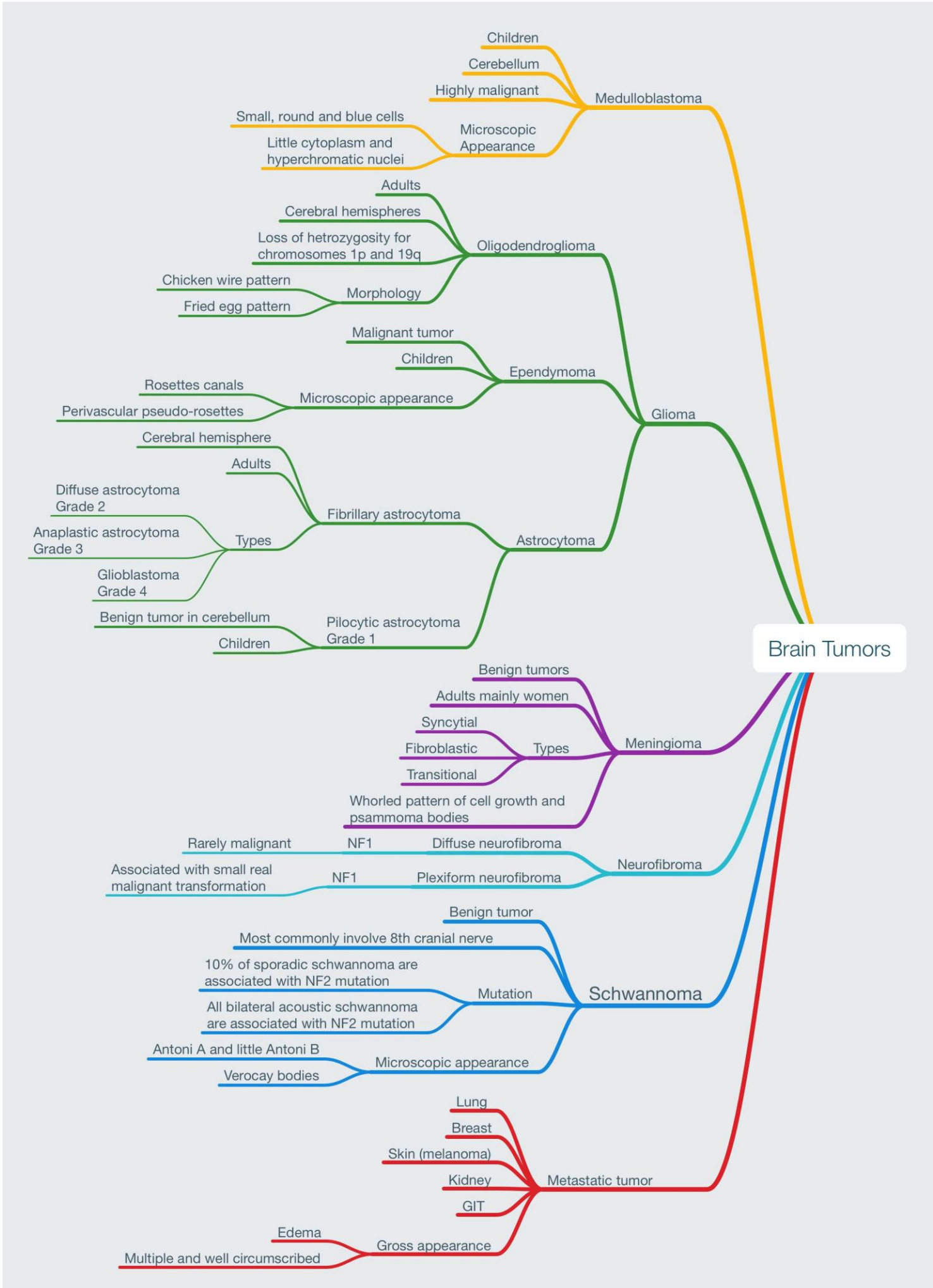
- The inheritance pattern and the main features of:
    - Type 1 Neurofibromatosis
    - Type 2 Neurofibromatosis

Take home messages:

- Histologic distinction between benign and malignant lesions may be more subtle in comparison to other body systems.
- Even low-grade or benign tumors can have a poor clinical outcome depending on their location.
- The most aggressive and poorly differentiated glial tumor is glioblastoma; it contains anaplastic astrocytes and shows striking vascular abnormalities.
- Metastatic spread of brain tumors to other regions of the body is rare, but the brain is not comparably protected against spread of tumors from elsewhere.

Key words:

CNS tumors, astrocytoma, glioblastoma, oligodendroglioma, ependymoma, medulloblastoma, meningioma, metastatic tumours, peripheral nerve sheath tumours, schwannoma, neurofibroma and neurofibromatosis.


Brain Tumors
Medulloblastoma
Children
Cerebellum
Highly malignant
Microscopic Appearance
Small, round and blue cells
Little cytoplasm and hyperchromatic nuclei
Glioma
Oligodendroglioma
Adults
Cerebral hemispheres
Loss of hetrozygosity for chromosomes 1p and 19q
Morphology
Chicken wire pattern
Fried egg pattern
Ependymoma
Malignant tumor
Children
Microscopic appearance
Rosettes canals
Perivascular pseudo-rosettes
Astrocytoma
Fibrillary astrocytoma
Cerebral hemisphere
Adults
Types
Diffuse astrocytoma Grade 2
Anaplastic astrocytoma Grade 3
Glioblastoma Grade 4
Pilocytic astrocytoma Grade 1
Benign tumor in cerebellum
Children
Meningioma
Benign tumors
Adults mainly women
Types
Syncytial
Fibroblastic
Transitional
Whorled pattern of cell growth and psammoma bodies
Neurofibroma
NF1
Diffuse neurofibroma
Rarely malignant
NF1
Plexiform neurofibroma
Associated with small real malignant transformation
Schwannoma
Benign tumor
Most commonly involve 8th cranial nerve
Mutation
10% of sporadic schwannoma are associated with NF2 mutation
All bilateral acoustic schwannoma are associated with NF2 mutation
Microscopic appearance
Antoni A and little Antoni B
Verocay bodies
Metastatic tumor
Lung
Breast
Skin (melanoma)
Kidney
GIT
Gross appearance
Edema
Multiple and well circumscribed

Incidence:

The annual incidence of tumors of the CNS ranges from:

- 10 to 17 per 100,000 persons for intracranial tumors.
- 1 to 2 per 100,000 persons for intraspinal tumors.
- About half to three-quarters are primary tumors, and the rest are metastatic.

CNS tumors are distinct from other tumors, they differ among children and the brain cannot expand (i.e. enclosed with the skull).

Note: These statistics are based on west populations.

Childhood:

- Tumors of the CNS are a large proportion of cancers of childhood, accounting for as many of 20% of all tumors
- CNS tumors in childhood differ from those in adults both in histologic subtype and location
- In childhood, tumors are likely to arise in the posterior fossa (infratentorial/ cerebellum), while in adults they are mostly supratentorial (cerebrum)

Supratentorial region of the brain is the area located above the tentorium cerebelli. Infratentorial below tentorium cerebelli.

- Most common solid tumor in children: primary CNS tumors
- Most common childhood tumor: leukemia

Classification:

May arise from:

- Cells of the coverings (Meningiomas)
- Cells intrinsic to the brain (Gliomas, Neuronal Tumors, Choroid Plexus Tumors)
- Other cell populations within the skull (Primary CNS Lymphoma, Germ-Cell Tumors)
- They may spread from elsewhere in the body (metastases)

- NO staging in CNS tumors. (Since we usually can't tell the boarders/ can't demarcate)
- Grading: depends on differentiating of cells
- Staging: more about invasion, infiltration
- There are always exceptions.

Staging: (pathologists + clinicians)
Metastasis
Lymph nodes
MRI and other tests
Grading: (pathologists)
Proliferation: using the proliferating index (the KI67 test to access mitosis)
Differentiation
Microscope

- High doses of chemotherapy are required to cross the blood brain barrier and eradicate CNS tumors.
- The risk of radiotherapy on low-grade tumors on the long run is progression to high-grade tumors.

General Manifestations:

- Seizures, headaches, vague symptoms
- Focal neurologic deficits related to the anatomic site of involvement
- Rate of growth may correlate with history

General characteristics:

– The anatomic site of the neoplasm can have lethal consequences irrespective of histological classification (i.e. benign tumors can be fatal in certain locations)

→ *Examples on such locations:*

Could be due to local effects (e.g., a benign meningioma may cause cardiorespiratory arrest from compression of the medulla) or nonresectability[1] (e.g., brain stem gliomas).

An example of the locations:
- Brain stem.
- Surgeons cannot reach it.
- In addition, cardiovascular and respiratory centers are located there.

– These tumors do not have detectable premalignant or in situ stages (malignant cells within the basement membrane; treatable) comparable to those of carcinomas.

Meaning, they're usually found as tumors whether they're benign or malignant, especially that their tests aren't as easily/regularly performed as other tumors (like pap smears for cervical tumors)

– The pattern of spread of primary CNS neoplasms differs from that of other tumors:

- Rarely metastasize outside the CNS
- The subarachnoid space does provide a pathway for spread ~1% metastasizes in the spinal cord.

- But the brain is one of the commonest sights of metastasis (from other organs)
- Rarely metastasize due to the BBB.

→ *What Are The Layers That Surround Subarachnoid Space?* Pia mater (inferiorly), Arachnoid mater (superiorly), Dura mater

- Even Low-Grade lesions may infiltrate large regions of the brain, leading to serious clinical deficits, nonresectability, and poor prognosis.

[1] An **unresectable** tumor is **defined** as one that cannot be removed completely through surgery. Since surgery often offers the best chance for a cure with solid tumors, this can be discouraging news to hear.

Very benign tumors in brainstem can kill; since the surgeon can't reach such an area.

Gliomas:

Gliomas are tumors of the brain parenchyma that are classified histologically on the basis of their resemblance to different types of glial cells. The major types of glial tumors are:

- Astrocytomas.
- Oligodendrogliomas.
- Ependymomas.

Astrocytoma is the prototype of gliomas.
There is nothing called Microglioma. Why? Because they're from the bone marrow

Astrocytomas:

Originates from astrocytes.

- The most common types are diffuse and pilocytic astrocytomas.
- Mutations that alter the enzymatic activity of two isoforms of the metabolic enzyme isocitrate dehydrogenase (IDH1 and IDH2) are common in lower-grade astrocytomas.
- **Fibrillary:** Not benign because recurrence is possible.
  - Account for about 80% of adult gliomas
  - 4th to 6th decade
  - Commonly found in the cerebral hemispheres of adults and the brainstem of children.
  - Variable grades: There is no grade I in fibrillary astrocytoma.
    - Diffuse astrocytoma (Grade II)

      II is a subtype of 4
    - Anaplastic astrocytoma (Grade III)
    - Glioblastoma (Grade IV)
  - IDH1 (immunostain) is positive.

You cannot completely excise diffuse astrocytoma, because infiltration beyond the grossly evident margins is always present.

Grade 4 (glioblastoma):

- Glioblastoma is the most common malignant CNS tumor in adults.
- There must be necrosis or microvascular proliferation.
- Microvascular proliferation: the proliferation is not in the number of vessels rather it is in the thickness of endothelium.
- P53 is a marker for low-grade gliomas, but if you saw it in a high-grade glioma, it tells you that it was low grade.
- Secondary glioblastomas develop slowly through progression from low-grade diffuse astrocytoma (WHO grade II) or anaplastic astrocytoma (WHO grade III).

– **On the basis of histologic features, they are stratified into three groups:**

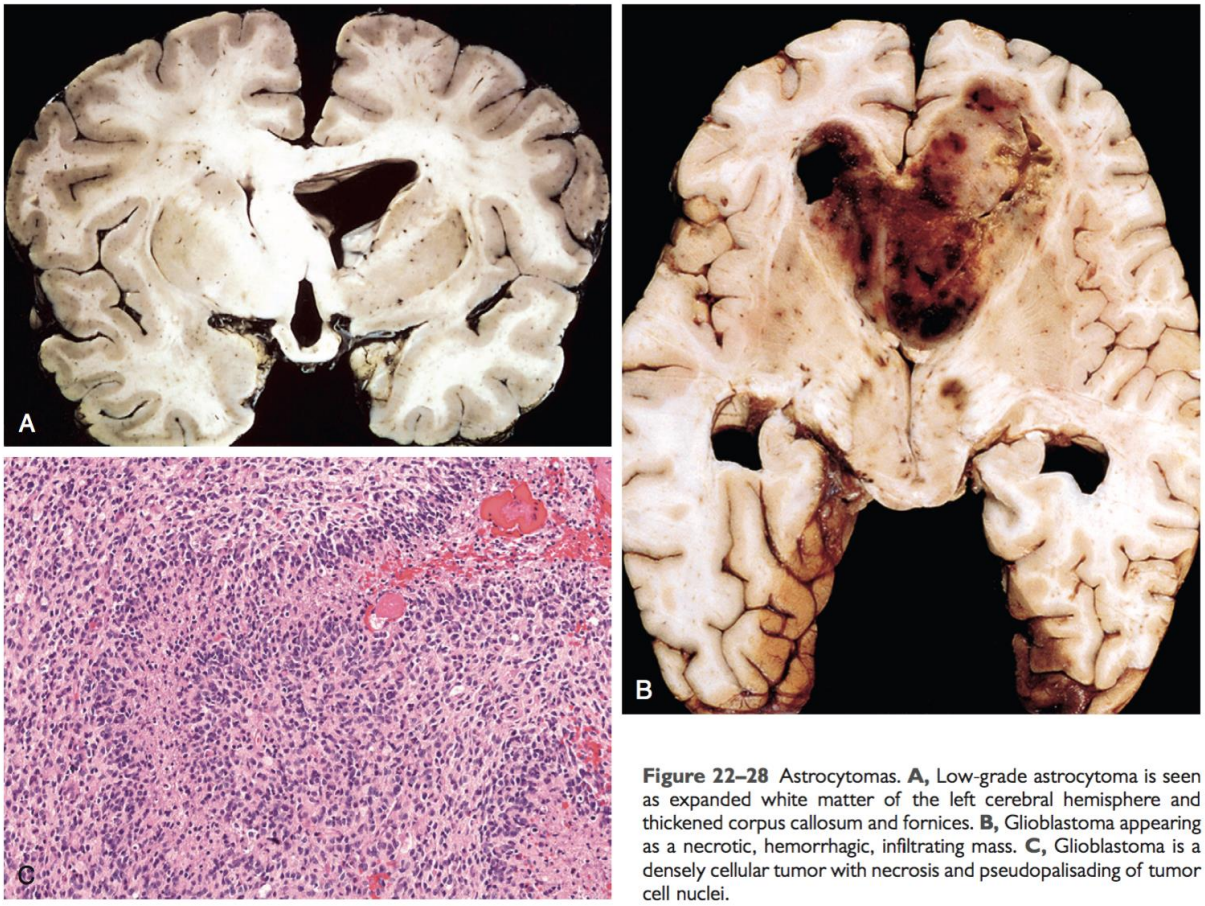


Figure 22–28 Astrocytomas. **A,** Low-grade astrocytoma is seen as expanded white matter of the left cerebral hemisphere and thickened corpus callosum and fornices. **B,** Glioblastoma appearing as a necrotic, hemorrhagic, infiltrating mass. **C,** Glioblastoma is a densely cellular tumor with necrosis and pseudopalisading of tumor cell nuclei.

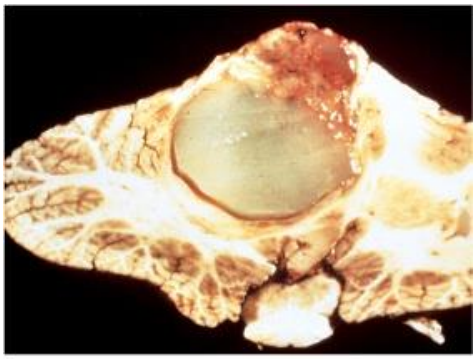
Glioblastoma used to be called glioblastoma multiform (GBM) because it has various forms. It is also important to know that glioblastoma is characterized by necrosis and hemorrhage which cross the midline with butterfly appearance (picture B).

Some benign tumors might be lethal in certain anatomical sites, e.g. meningiomas, and colloid cysts. A colloid cyst is a cyst containing gelatinous material in the brain. It is almost always found just posterior to the foramen of Monro in the anterior aspect of the third ventricle, originating from the roof of the ventricle. Colloid cysts are potentially dangerous tumors, because they often generate nonlocalizing symptoms but are associated with sudden death, even in children. They are histologically benign, but their midline location may lead to obstruction of the foramen of Monro and to hydrocephalus. Read more

Group	Morphology	Characteristics
Well differentiated "diffuse astrocytoma" (WHO grade II)	▪ Mild to moderate increase in the number of glial cell nuclei ▪ Variable nuclear pleomorphism ▪ Glial fibrillary acidic protein (GFAP)-positive astrocytic cell processes (that give the background a fibrillary appearance.)	• Static or progress slowly (mean survival of more than 5 years). • Moderate cellularity.
Less differentiated (higher-grade)	▪ More cellular. ▪ Greater nuclear pleomorphism. ▪ Mitosis.	Anaplastic astrocytoma (WHO grade III)
Glioblastoma (WHO grade IV):	▪ All the features of anaplastic astrocytoma, plus: ▪ ***Necrosis* and/or *vascular or endothelial cell proliferation*** ▪ Grim prognosis as the grade increases.	▪ It is the most common CNS primary malignancy of adults. ▪ **Secondary** glioblastomas share *p53* mutations that characterized low-grade gliomas. ▪ **Primary** glioblastomas are characterized by amplification of the epidermal growth factor receptor ***(EGFR)*** gene. ▪ With treatment, mean survival of 8-10 months.

- **Pilocytic (Grade I):**
  - Typically affects children and young adults
  - Commonly located in the cerebellum
  - Relatively benign

Hairy projections (thick processes coming from the tumor)



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Morphology:

- Often cystic, with a mural nodule.
- Cyst enlargement often causes symptomatic recurrence.
- If it's solid, it's usually well circumscribed.
- Composed of bipolar cells with long, thin "hair- like" processes that are GFAP[2]-positive.
- Rosenthal fibers & hyaline granular bodies are often present.
- Necrosis and mitoses are typically absent.
- Mutations in IDH1 and IDH2 (common in low-grade diffuse astrocytomas) are not found in pilocytic tumors.

There are 2 cases where rosenthal fibers are seen, for example:

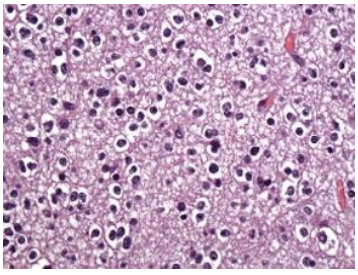
- Child comes with headache, has cystic infratentorial mass → most likely polycystic astrocytoma.
- Adult male comes with abscess and fever, with supratentorial lesions and fibrillary astrocytes → reactive gliosis rather than neoplasm.
  What is Reactive Gliosis? A nonspecific **reactive** change of glial cells in response to damage to the central nervous system (CNS). In most cases, **gliosis** involves the proliferation or hypertrophy of several different types of glial cells, including astrocytes, microglia, and oligodendrocytes.

Oligodendroglioma:

- The most common genetic findings are loss of heterozygosity for chromosomes 1p and 19q
- Detected in Fourth and fifth decades.
- Commonly found in cerebral hemispheres, mainly in the frontal or temporal lobes, with a predilection[3] for white matter.

- Only grade II and III (anaplastic). (No grade 4)
- Even if you see necrosis in oligodendroglioma it is not grade 4 (possibly 3).

- **Morphology:**
  - In oligodendroglioma tumor cells have round nuclei, often with a cytoplasmic halo.
  - Blood vessels in the background are thin and can form an interlacing pattern.



[2] Glial fibrillary acidic protein
[3] A preference or special liking for something; a bias in favor of something.

Very important microscopic characteristics of oligodendroglioma:

- Fried egg shape (nucleus in the middle and white cytoplasm around it)
- Chicken wire in the background (a meshwork of very thin capillaries)

- **Has two types:**

Type	Grade	Average Survival	Morphology	Prognosis
Well-differentiated	(WHO grade II)	10 to 20 years	Infiltrative tumors that form gelatinous, gray masses and may show cysts, focal hemorrhage, and calcification. Mitotic activity is hard to detect.	Better than patients with astrocytomas (5 to 10 years with Rx)
Anaplastic	(WHO grade III)	5 to 10 years	A more aggressive subtype with higher cell density, nuclear anaplasia and mitotic activity.	Worse

Ependymoma:

No grade 4 / grade 2: Ependymoma /grade 3: Anaplastic ependymoma

- Most often arise next to the ependyma-lined ventricular system, including the central canal of the spinal cord.
- Occurs in the first two decades of life, they typically occur near the fourth ventricle.
- **Morphology:**
  - In the fourth ventricle, they are solid or papillary masses extending from the ventricular floor.
  - Tumor cells may form round or elongated structures (rosettes, canals) that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen.

    → *What is a rosette?* *Read*

    - If the tumor cells are surrounding a lumen: true rosettes
    - No true lumen: pseudorosettes (tumor cells surrounding a blood vessel)

  - Anaplastic ependymomas show **increased** cell density, **high** mitotic rates, necrosis and less evident ependymal differentiation = less apparent rosettes.

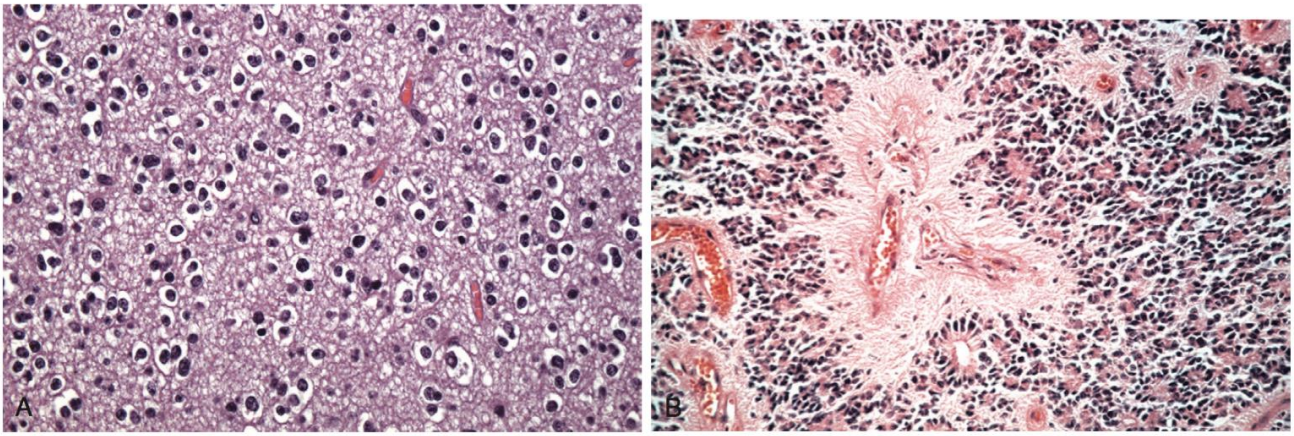


Figure 22–29 Other gliomas. **A,** In oligodendroglioma tumor cells have round nuclei, often with a cytoplasmic halo. Blood vessels in the background are thin and can form an interlacing pattern. **B,** Microscopic appearance of ependymoma.

Meningioma:

- Predominantly benign tumors of adults.
- Origin: meningothelial cell of the arachnoid.
- Well demarcated.
- Attached to the dura with compression of underlying brain.
- Whorled pattern of cell growth and psammoma bodies. Abnormalities of chromosome 22 are sometimes present.
- Multiple meningiomas occur in NF2 patients[4].
- It has varied clinical features but commonly presents with headache, seizures, and neurological deficits.
- The prognosis of meningioma is good.

Grades:
I: has many patterns, which are all benign
II: more mitosis
III: malignant

Psammoma bodies are unique concentric lamellated calcified structures.

With meningiomas, it is important to examine all slides to look for normal brain tissue within the tumor. If brain tissue is found this means that the tumor is infiltrating, has irregular shape making it difficult to excise, and has higher recurrence. If there is no brain tissue in the slides, this means that the meningioma is pushing and not infiltrating, which has better prognosis and can be taken out.

– Morphology:

Meningiomas (WHO grade I/IV) grow as well-defined dura-based masses that may compress the brain but do not invade it (in some cases they do invade it).

If a grade I meningioma invades the brain → then it is not grade I anymore.

[4] Will be explained in the Homework page.

Main subtypes (Histologic Patterns):

Subtype	Description
Syncytial	Named for whorled clusters of cells without visible cell membranes that sit in tight groups
Fibroblastic	Elongated cells and abundant collagen deposition between them
Transitional (classical)	Shares features of the syncytial and fibroblastic types
Psammomatous	Numerous psammoma bodies
Secretory	Gland-like PAS[5]-positive eosinophilic secretions known as pseudopsammoma bodies

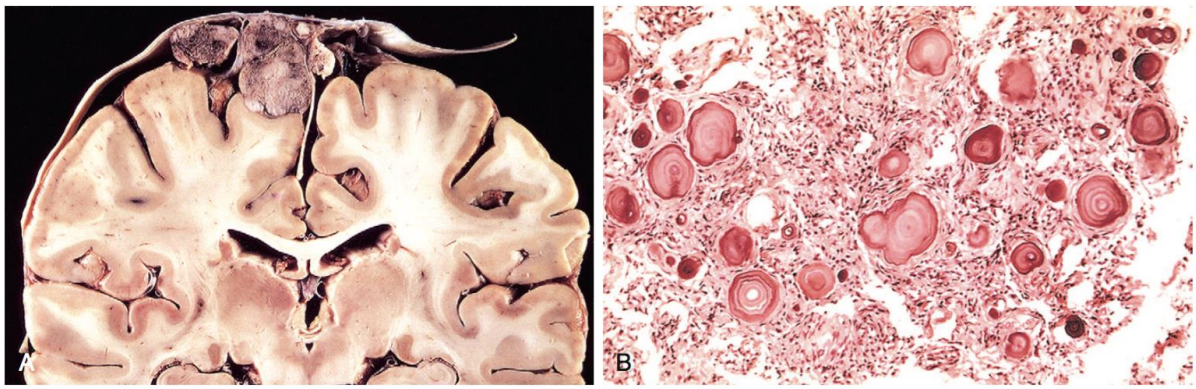


Figure 22–31 Meningioma. **A,** Parasagittal multilobular meningioma attached to the dura with compression of underlying brain. **B,** Meningioma with a whorled pattern of cell growth and psammoma bodies.

Type	Grade	Morphology	Characteristics
Atypical meningiomas	(WHO grade II)	Prominent nucleoli, increased cellularity, pattern-less growth and often have a higher mitotic rate.	More aggressive local growth and a higher rate of recurrence.
Anaplastic	(WHO grade III)	There usually is some histologic evidence of a meningothelial cell origin.	Highly aggressive tumors that may resemble a high-grade sarcoma or carcinoma.

[5] Periodic Acid-Schiff (medical technology: stain used to detect carbohydrates in tissue)

It is important to read about the molecular basis of tumors and their mutations. A lot of studies are being done on targeted therapy of meningiomas to customize specific treatments for particular mutations, in order to avoid the harmful effects of chemotherapy.

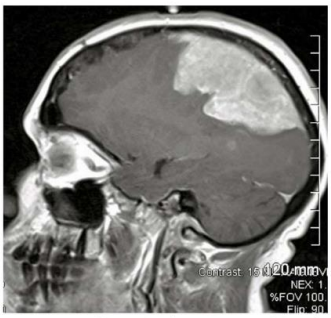


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Figure 20-8. Large Meningioma Pushing into the Cerebral Cort

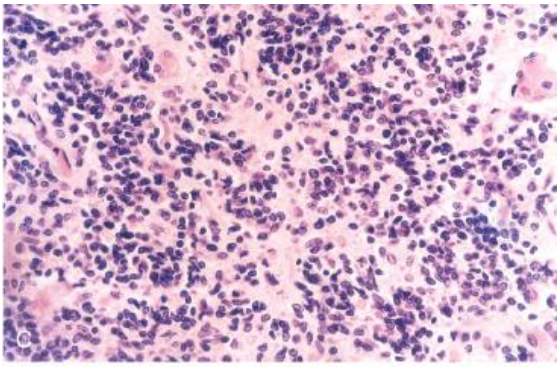
Note the thin dark shadow around the lesion which occurs because the tumor is not actually invading the brain.

Medulloblastoma:

- Primitive "small round cell" appearance (cells still didn't differentiate)
- Grade IV

- Commonly affects children.
- Exclusively in the cerebellum (midline), lateral tumors occur more often in adults.
- Neuronal and glial markers may be expressed, but the tumor is often largely undifferentiated.
- Highly malignant.
- Prognosis for untreated patients is dismal; however, it is exquisitely radiosensitive.
- With total excision and radiation, the 5-year survival rate may be as high as 75%
- **Morphology:**
  - Extremely cellular, with sheets of anaplastic ("small blue") cells
  - Small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.

They have hyperchromatic small round dark nuclei slightly elongated like a carrot.



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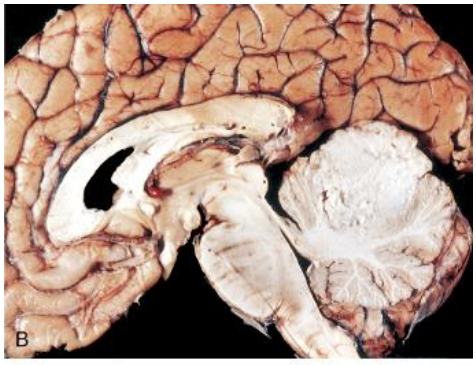

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The small round cell tumors (in children): lymphoma, neuroblastoma, nephroblastoma, Wilms' tumor, medulloblastoma.

Schwannoma:

You can have PNS tumors in cranial nerves

- Benign, encapsulated tumor.
- In the CNS, they are often encountered within the cranial vault in the cerebellopontine angle, where they are attached to the vestibular branch of the eighth nerve (symptoms relate to nerve root compression, which are tinnitus and hearing loss) but can be separated from it.
- Type I: Sporadic schwannomas are associated with mutations in the *NF2* gene.
- Type II: Bilateral acoustic schwannoma is associated with NF2.

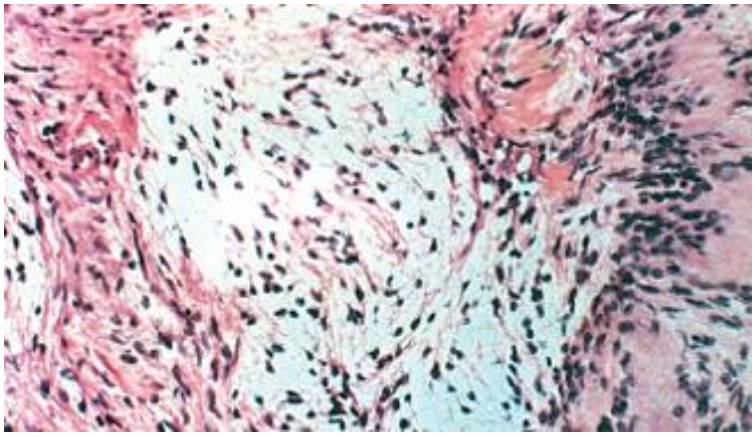
  - If the schwannoma is in the CN 8 (vestibulocochlear) of both sides, then it is diagnostic for type 2 neurofibromatosis syndrome
  - If single-sided, it is not a must to be neurofibromatosis type 2 but it can be.

- On gross inspection, most schwannomas appear as circumscribed masses abutting an adjacent nerve.
- On microscopic examination, Cellular Antoni A pattern and less cellular Antoni B. They are comprised of a uniform proliferation of neoplastic Schwann cells.

  In the dense Antoni A areas (in the right side of the picture), bland spindle cells with buckled nuclei arranged into intersecting fascicles. These cells often align to produce nuclear palisading.

- Axons are largely excluded from the tumor. Thick-walled hyalinized vessels often are present.
- Nuclear-free zones of processes that lie between the regions of nuclear palisading are termed Verocay bodies

Pseudo-palisading



Neurofibroma:

- A tumor of nerve components including Schwann cells.
- Proliferation of components of nerve structure.
- Schwannoma can be part of it but not vice versa.

- Benign peripheral nerve sheath tumor. Not encapsulated. Examples: (*cutaneous neurofibroma*) or in peripheral nerve (*solitary neurofibroma*).
- Many different kinds of cells are involved (Schwann cells, mast cells, fibroblast-like cells and perineurial-like cells).
- More haphazard cell growth than schwannoma.
- These arise sporadically or in association with type 1 neurofibromatosis, rarely malignant.
- Neurofibromas cannot be separated from nerve trunk (in comparison to schwannoma).

Schwannomas can be surgically excised because it is a small circumscribed mass, while neurofibroma crosses tissue boundaries.

- Three important subtypes are recognized:

Subtypes	Grow	Characteristic
Localized cutaneous neurofibromas	Superficial nodular or polypoid tumors.	Either as solitary sporadic lesions or as often multiple lesions in the context of (NF1).
Plexiform neurofibromas	Diffusely within the confines of a nerve or nerve plexus.	Surgical enucleation of such lesions is therefore difficult and is often associated with lasting neurologic deficits. These tumors are associated with a small but real risk of malignant transformation.
Diffuse neurofibromas	As infiltrative proliferations	Can take the form of large, disfiguring subcutaneous masses.

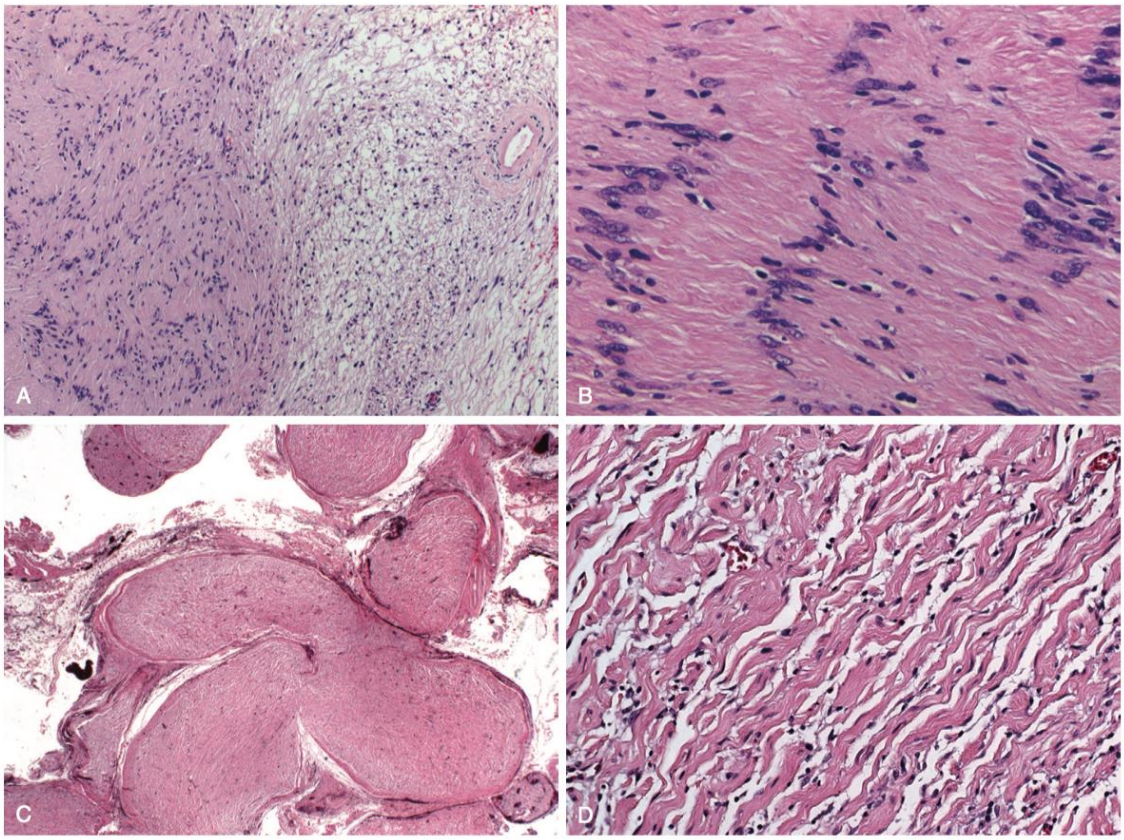


Figure 21–7 Schwannoma and plexiform neurofibroma. **A** and **B,** Schwannoma. As seen in **A,** schwannomas often contain dense pink Antoni A areas (*left*) and loose, pale Antoni B areas (*right*), as well as hyalinized blood vessels (*right*). **B,** Antoni A area with the nuclei of tumor cells aligned in palisading rows. **C** and **D,** Plexiform neurofibroma. Multiple nerve fascicles are expanded by infiltrating tumor cells **(C),** which at higher power **(D)** are seen to consist of bland spindle cells admixed with wavy collagen bundles likened to carrot shavings.

Metastatic Tumors:

They are tumors from sources outside the CNS. Carcinomas are the most common.

- 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.
- Form sharply demarcated masses with edema.

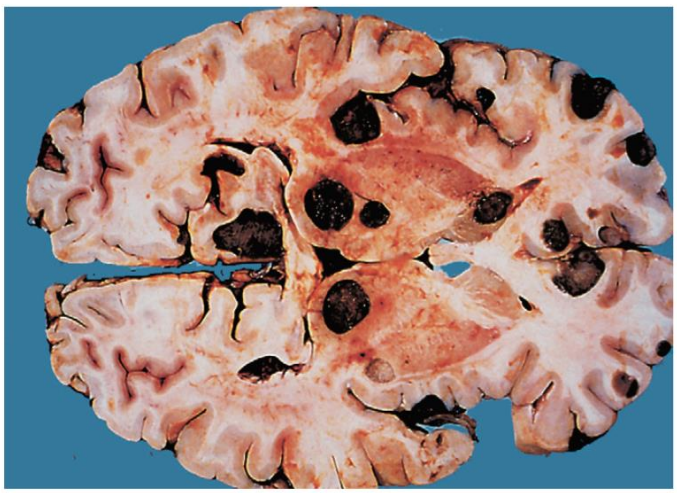


Figure 22–32 Metastatic melanoma. Metastatic lesions are distinguished grossly from most primary central nervous system tumors by their multicentricity and well-demarcated margins. The dark color of the tumor nodules in this specimen is due to the presence of melanin.

Metastatic tumors:

- Very common in brain
- How can you tell that it is a metastatic and not a primary brain tumor:
  1- There are multiple masses. (In general, multiple masses do not indicate primary tumor rather metastasis even in liver and lung)
  2- They are well demarcated. (But malignant)

Homework

Familial Tumor Syndromes:

Describe the inheritance pattern and the main features of:

- **Type 1 Neurofibromatosis:**
  - An autosomal dominant disorder caused by mutations in the tumor suppressor neurofibromin, encoded on the long arm of chromosome 17 (17q).
  - Disruption of neurofibromin function and Ras hyperactivity.
  - The neurofibromin allele is mutated in tumors arising in the setting of NF1, which include neurofibromas of all three main types, malignant peripheral nerve sheath tumors, optic gliomas, and other glial tumors.
  - Patients with NF1 exhibit learning disabilities, seizures, skeletal abnormalities, vascular abnormalities with arterial stenoses, pigmented nodules of the iris (*Lisch nodules*), and pigmented skin lesions (axillary freckling and café au lait spots) in various degrees.
- **Type 2 Neurofibromatosis:**
  - Affected patients carry a dominant loss of function mutation of the merlin gene on chromosome 22.
  - Merlin is a cytoskeletal protein that functions as a tumor suppressor by facilitating E-cadherin– mediated contact inhibition
  - Despite the name of the syndrome, neurofibromas are not a feature of NF2.
  - Patients are at risk of developing multiple schwannomas, meningiomas, and ependymomas.
  - The presence of bilateral vestibular schwannomas is a hallmark of NF2.

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? NF1

Tumors of the Central Nervous System Summary:

- 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.

Check Your Understanding

MCQs:

1- Commonest primary CNS tumor in adults?

A. Glioblastoma multiform
B. Low-grade astrocytoma
C. Meningioma
D. Ependymoma
E. Medulloblastoma

2- A common benign tumor in children is:

A. Ependymoma
B. Medulloblastoma
C. Pilocystic Astrocytoma
D. Glioblastoma

3- A 29-year-old woman presents with tinnitus and a sensori-neural hearing loss on the left. The excised mass was seen near the cerebellopontine angle, arising from the left VIIIth nerve. Histology showed a tumor comprising of benign spindle shaped cells with Antoni A and Antoni B type of patterns. What is your diagnosis?

A. Ependymoma
B. Astrocytoma
C. Schwannoma
D. Medullaoblastoma
E. Glioblastoma multiforme

4- An MRI reveals a large tumor occupying much of the left parietal lobe of a middle aged female patient. An attending resident looks at the image and states that it's the most common kind of intracranial tumor with, unfortunately, typically a poor prognosis. Such tumors are called…

A. Schwannomas
B. Oligodendrogliomas
C. Meningiomas
D. Astrocytomas
E. Ependymomas

1. A 2. C 3. C 4. D

5- A 73 year-old-woman attends the clinic complaining of unilateral tinnitus and unilateral hearing loss. On physical examination there is discrete facial weakness and loss of corneal reflex on the same side as the symptoms. Where would the anatomic location be most likely, in order to produce the signs and symptoms in this patient?

A. Frontal cortex
B. Anterior pituitary
C. Anterior horn of upper spinal cord
D. Cerebellopontine angle
E. Lateral ventricle

6- The following list of primary malignancies accounts for the majority of metastatic brain tumors:

A. Lung, breast, melanoma
B. Testis, ovary, melanoma
C. Lung, prostate, uterus
D. Pancreas, melanoma, ovary
E. Salivary gland, ovary, testis

7- Which of the following criteria are used for the diagnosis of oligodendroglioma?

A. Pleomorphic glial cells, high mitotic activity, pseudopalisading, and vascular endothelial proliferation
B. Cyst with mural nodule, pilocytic astrocytes with Rosenthal fibers
C. Well circumscribed nodule, whorls of spindle-shaped cells, and psammoma bodies
D. Well circumscribed nodule, "fried-egg" cells, and chicken-wire capillary pattern

8- Pathomorphologic criteria for diagnosis of meningioma are:

A. Well circumscribed nodule, whorls of spindle-shaped cells, and psammoma bodies.
B. Cyst with mural nodule, pilocytic astrocytes with Rosenthal fibers.
C. Well circumscribed nodule, "fried-egg" cells, and chicken-wire capillary pattern.
D. Pleomorphic glial cells, high mitotic activity, pseudopalisading, and vascular endothelial proliferation.

5.D 6.A 7. D 8. A

9- Mutations in IDH1 and IDH2 are common in which tumor?

A. Low-grade diffuse astrocytoma.
B. Glioblastoma
C. Anaplastic astrocytoma.
D. Pilocytic astrocytoma.

10-The most common genetic findings in oligodendroglioma:

A. Loss of heterozygosity for chromosomes 11p and 19q
B. Loss of heterozygosity for chromosomes 1p and 1.9q
C. Loss of heterozygosity for chromosomes 1p and 19q
D. Loss of heterozygosity for chromosomes 1p and 9q

9.A 10. C

SAQs:

1. **What is the important thing that dedicates the dangerousness of a CNS tumor?**

   The location of the tumor, as a benign tumor could be fatal depending on its location.

2. **What are the clinical features that will be present in a patient with a CNS tumor?**

   A- The symptoms could be general as a headache or seizers.
   B- Or it could be localized symptoms related to the defected area.

3. **What are the histological features that will determine if the tumor is of grade 4?**

   1- Cell necrosis. 2- Vascular proliferation.

Contact us: Pathology435@gmail.com

Team Members:

فهد العبداللطيف	نوف التويجري
محمد الدغيثر	الجوهرة المزروع
معاذ باعشن	بدور جليدان
عبدالناصر الوابل	دانيا الهنداوي
عبدالرحمن الزامل	ديما الفارس
محمد الزاحم	كيان كعكي
عبدالعزيز الزيدان	كوثر الموسى
عبدالله الفريح	لميس آل تميم
ابراهيم الشايع	لينا إسماعيل
تركي الناصر	لولو الصغيّر
محمد الفضل	مريم سعيدان
	منيرة السلولي
	منيرة العمري
	نجود الحيدري
	نورة الخراز
	هديل الغرير

قال ﷺ: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق