CNS Tumors

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.

Introduction

- The annual incidence of CNS tumors ranges from 10 to 17 per 100,000 individuals for intracranial tumors and 1 to 2 per 100,000 individuals for intraspinal tumors.

- About one half to three-fourths are primary tumors, and the rest are metastatic.

Introduction

- Tumors of the CNS make up a larger proportion of childhood cancers, accounting for as many of 20% of all pediatric tumors.
- Childhood CNS tumors differ from those in adults in both histologic subtype and location.
- In childhood, tumors are likely to arise in the posterior fossa, whereas tumors in adults are mostly supratentorial.

Introduction

- Tumors of the nervous system have unique characteristics:
  - These tumors do not have morphologically evident premalignant or in situ stages comparable to those of carcinomas.
  - Even low-grade lesions may infiltrate large regions of the brain, leading to serious clinical deficits, inability to be resected, and poor prognosis.
  - The anatomic site of the neoplasm can influence outcome independent of histologic classification due to local effects (e.g., a benign meningioma may cause cardiorespiratory arrest from compression of the medulla).
  - Even the most highly malignant gliomas rarely spread outside of the CNS.

Introduction

- Symptoms of CNS tumors include:
  - Seizures, headaches, vague symptoms
  - Focal neurologic deficits related to the anatomic site of involvement
- The rate of growth may correlate with the history and duration of symptoms.

Introduction

- CNS tumors 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)
  - Tumor from elsewhere in the body spreading to the CNS (metastases)

Gliomas

- Astrocytomas
- Oligodendrogliomas
- Ependymomas

Astrocytomas

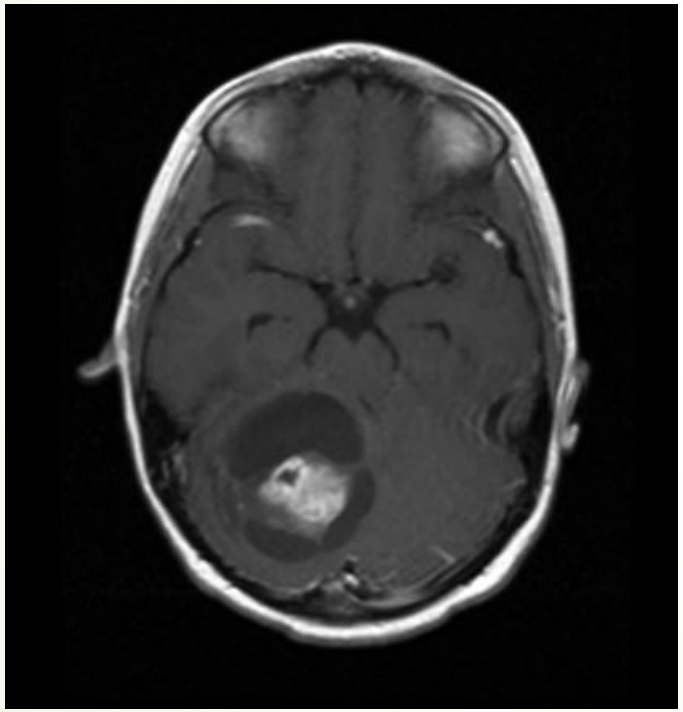
- Pilocytic (Grade I):
  - Children and young adults
  - Commonly cerebellum
  - Relatively benign
- Fibrillary:
  - 4th to 6th decade
  - Commonly cerebral hemisphere
  - Variable grades:
    - Diffuse astrocytoma (Grade II)
    - Anaplstic astrocytoma (Grade III)
    - Glioblastoma (Grade IV)

Pilocytic Astrocytoma

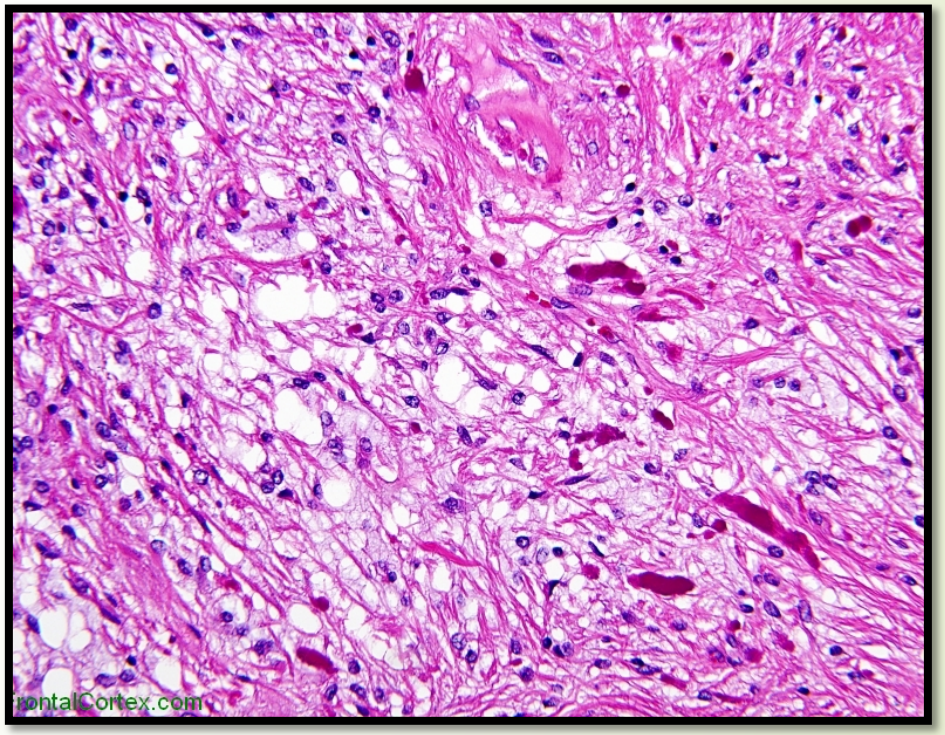
- Cystic with a mural nodule
- Well circumscribed
- "hairlike"=pilocytic processes that are GFAP positive
- Rosenthal fibers & hyaline granular bodies are often present
- Necrosis and mitoses are typically absent

Pilocytic Astrocytoma

Radiology



Microscopy



Astrocytomas

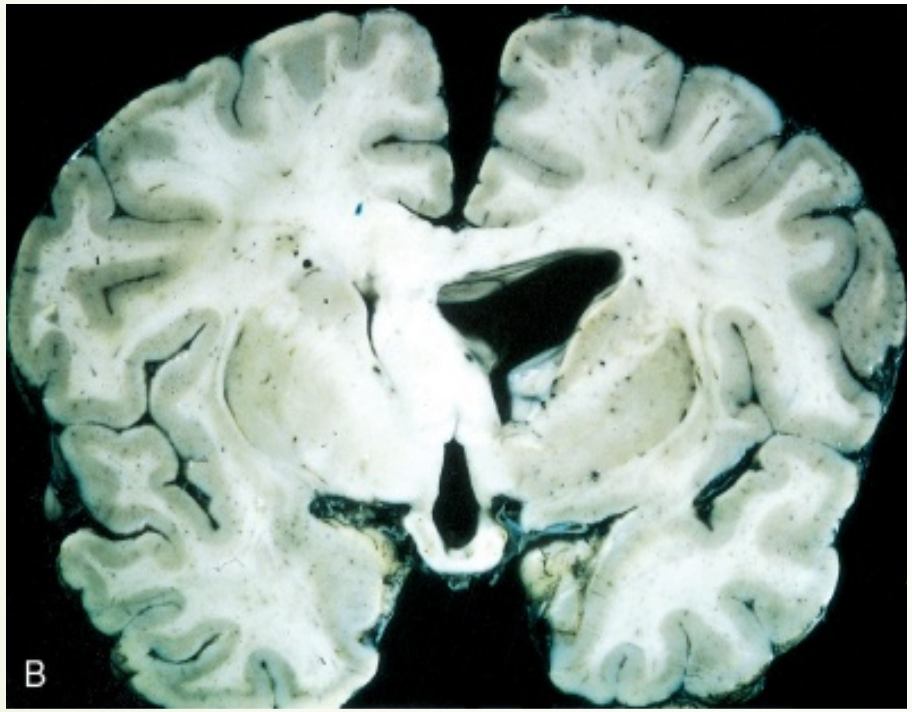
- Well differentiated "diffuse astrocytoma" (WHO grade II):
  - Static or progress slowly (mean survival of more than 5 years)
  - Moderate cellularity
  - Variable nuclear pleomorphism

- Anaplstiac astrocytoma (WHO grade III):
  - More cellular
  - Greater nuclear pelomrophism
  - Mitosis

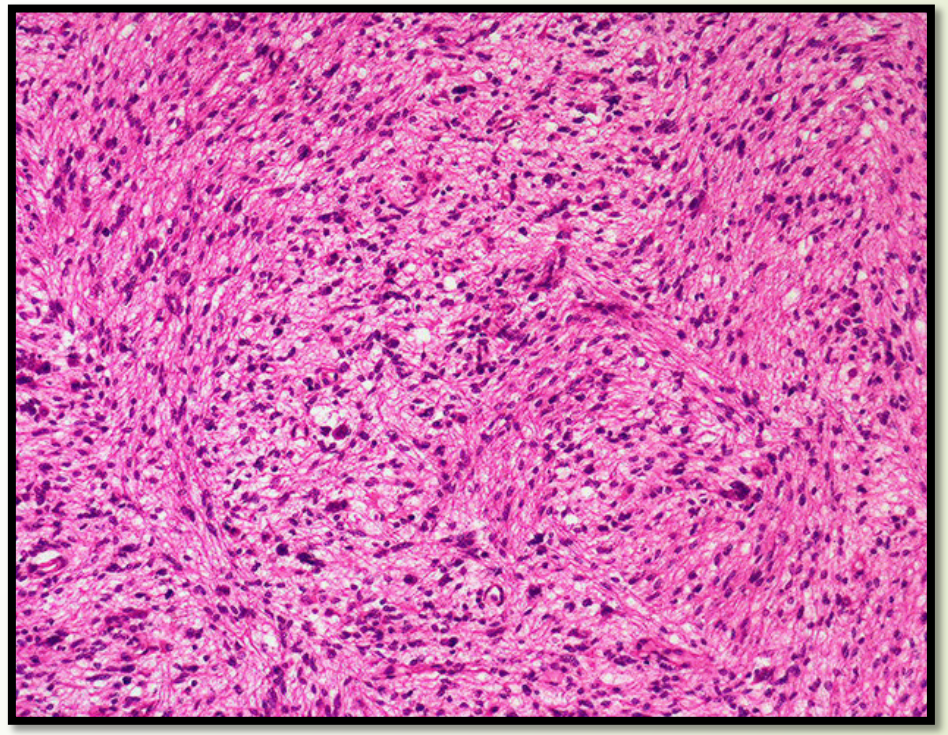
- Glioblastoma (WHO grade IV):
  - With treatment, the mean survival is of 8-10 months
  - All the features of anaplastic astrocytoma, plus necrosis and/or vascular or endothelial cell proliferation

Diffuse Astrocytomas

Macroscopy



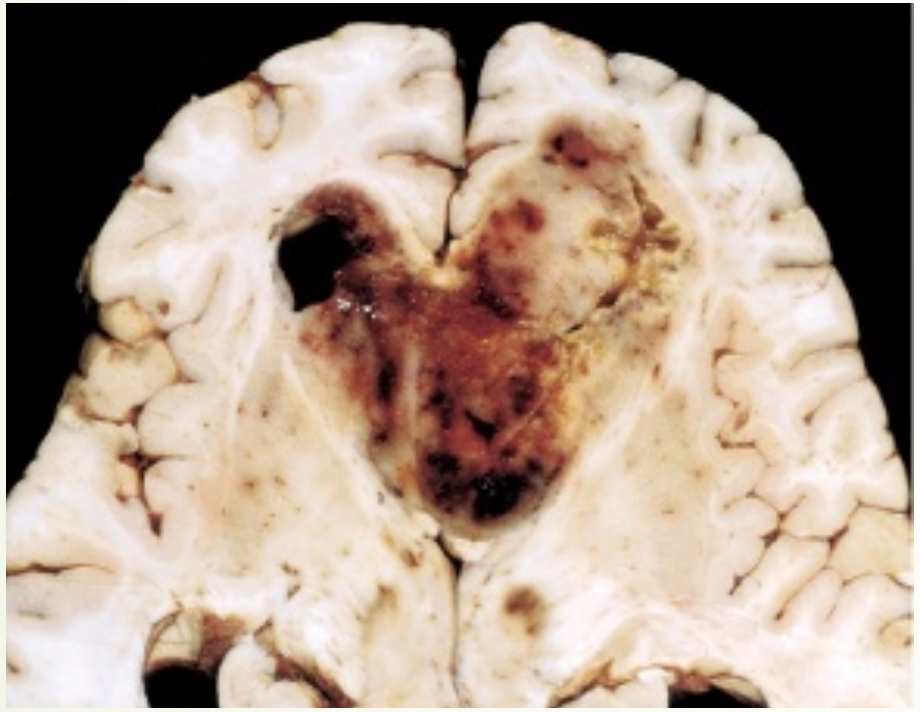
Microscopy



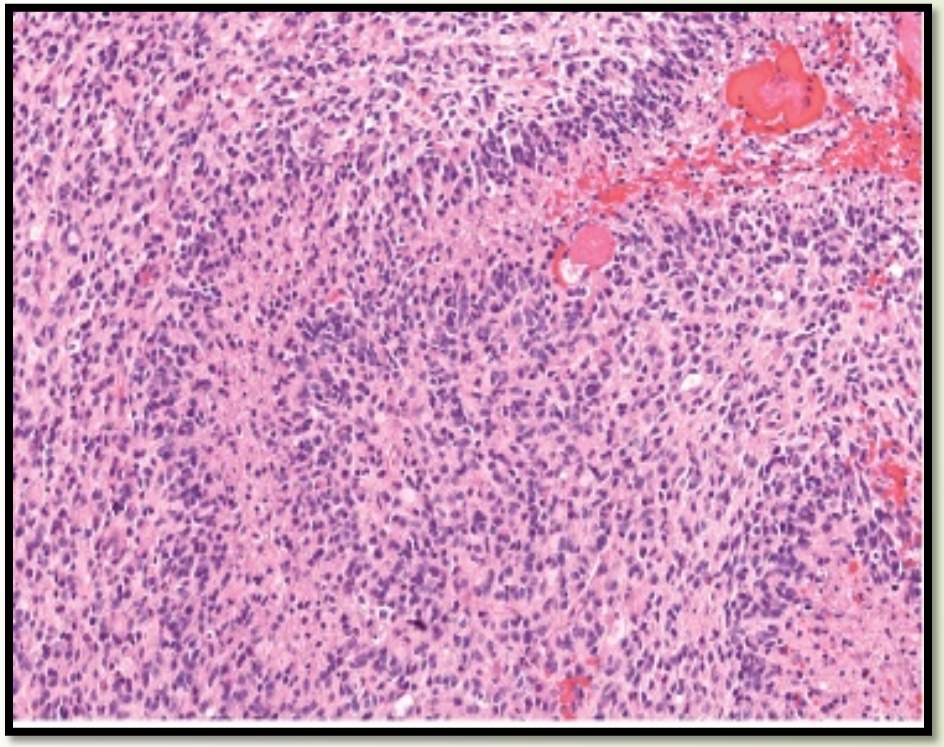
Note that diffuse astrocytoma are poorly demarcated

Glioblastoma Multiforme

Macroscopy



Microscopy



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.
- Primary glioblastomas are characterized by amplification of the epidermal growth factor receptor (EGFR) gene.
- Secondary glioblastomas share p53 mutations that characterizes low-grade gliomas.

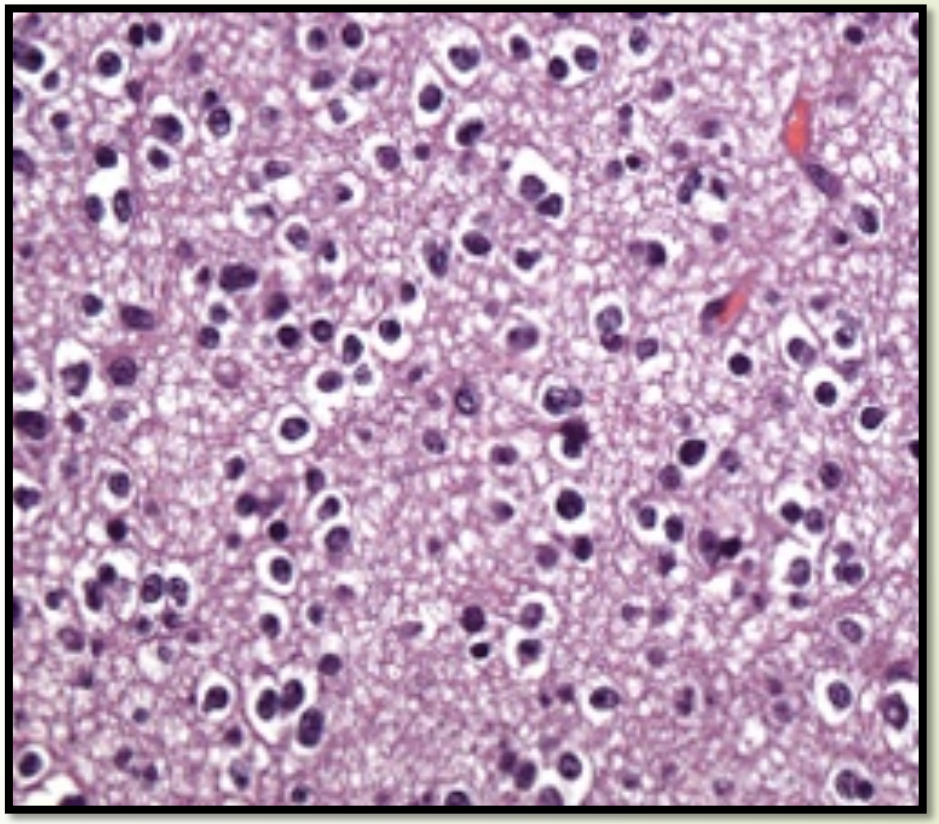
Oligodendroglioma

- The most common genetic findings are loss of heterozygosity for chromosomes 1p and 19q.
- 4^{th} and 5^{th} decades
- Cerebral hemispheres, with a predilection for the white matter
- Better prognosis than astrocytomas (5 to 10 years with treatment)
- The prognosis of the anaplastic type is worse than the conventional type.

Oligodendroglioma(grade II)

- 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

→ *What additional features are needed for anaplastic oligodendroglioma (grade III)?*



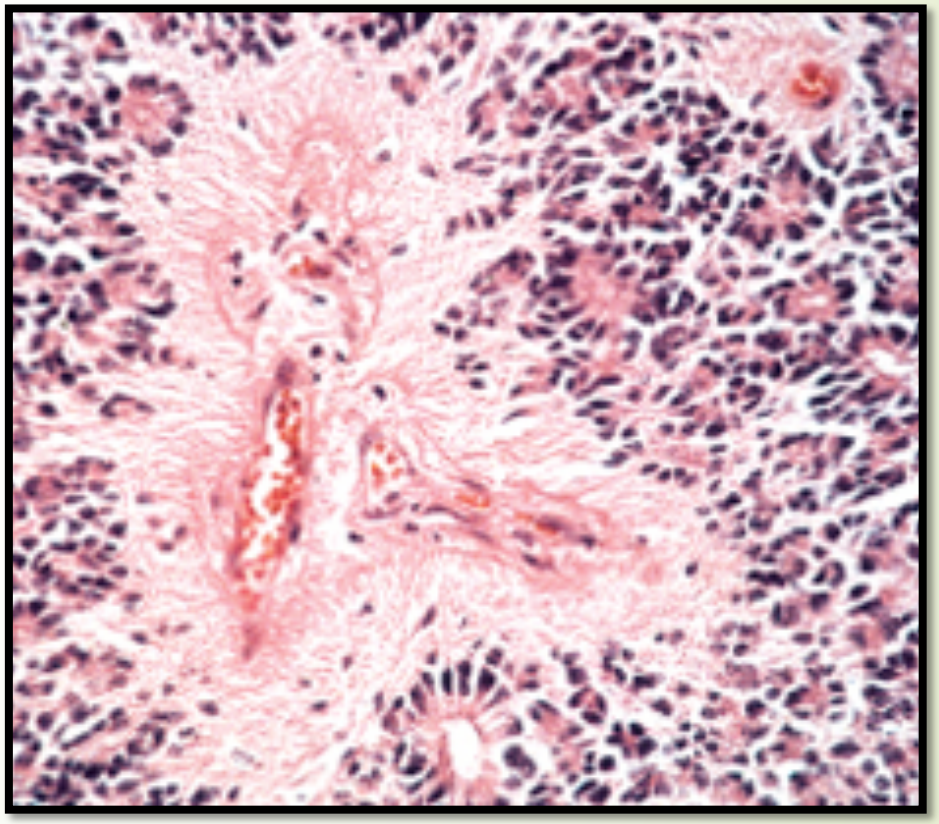
Ependymoma (grade II)

- They occur in the first two decades of life.
- They most often arise next to the ependyma-lined ventricular system, including the central canal of the spinal cord.
- They typically occur near the fourth ventricle.
- In adults, the spinal cord is their most common location.

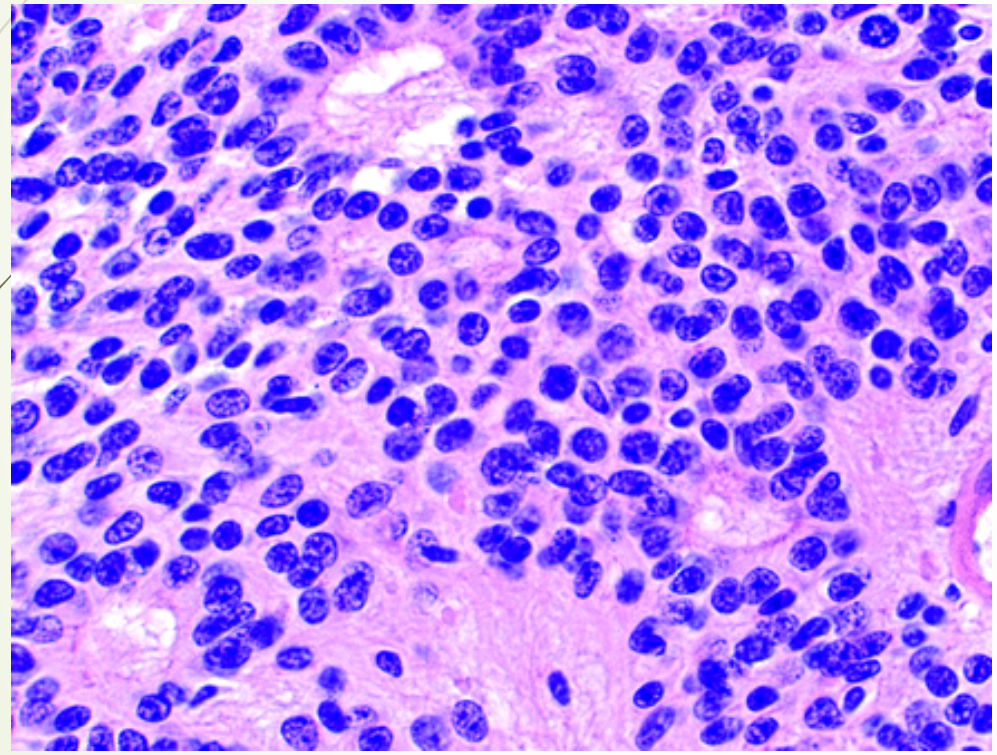
Ependymoma

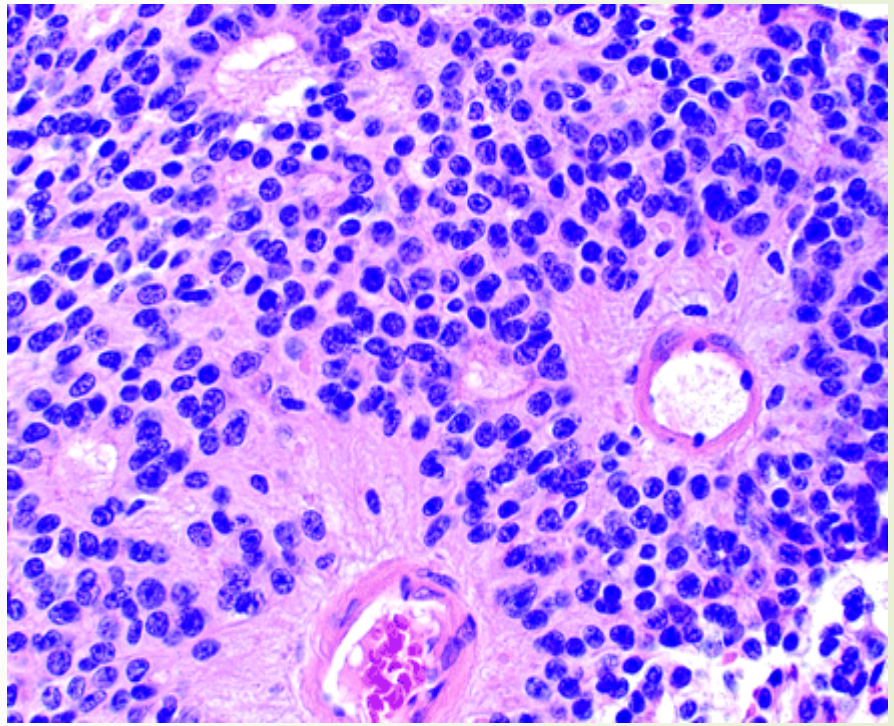
- Tumor cells may form round or elongated structures (**rosettes, canals**) more frequently present are **perivascular pseudorosettes** in which tumor cells are arranged around vessels with an intervening zone containing thin ependymal processes.

- Anaplastic ependymomas (grade III) show increased cell density, high mitotic rates, necrosis and less evident ependymal differentiation



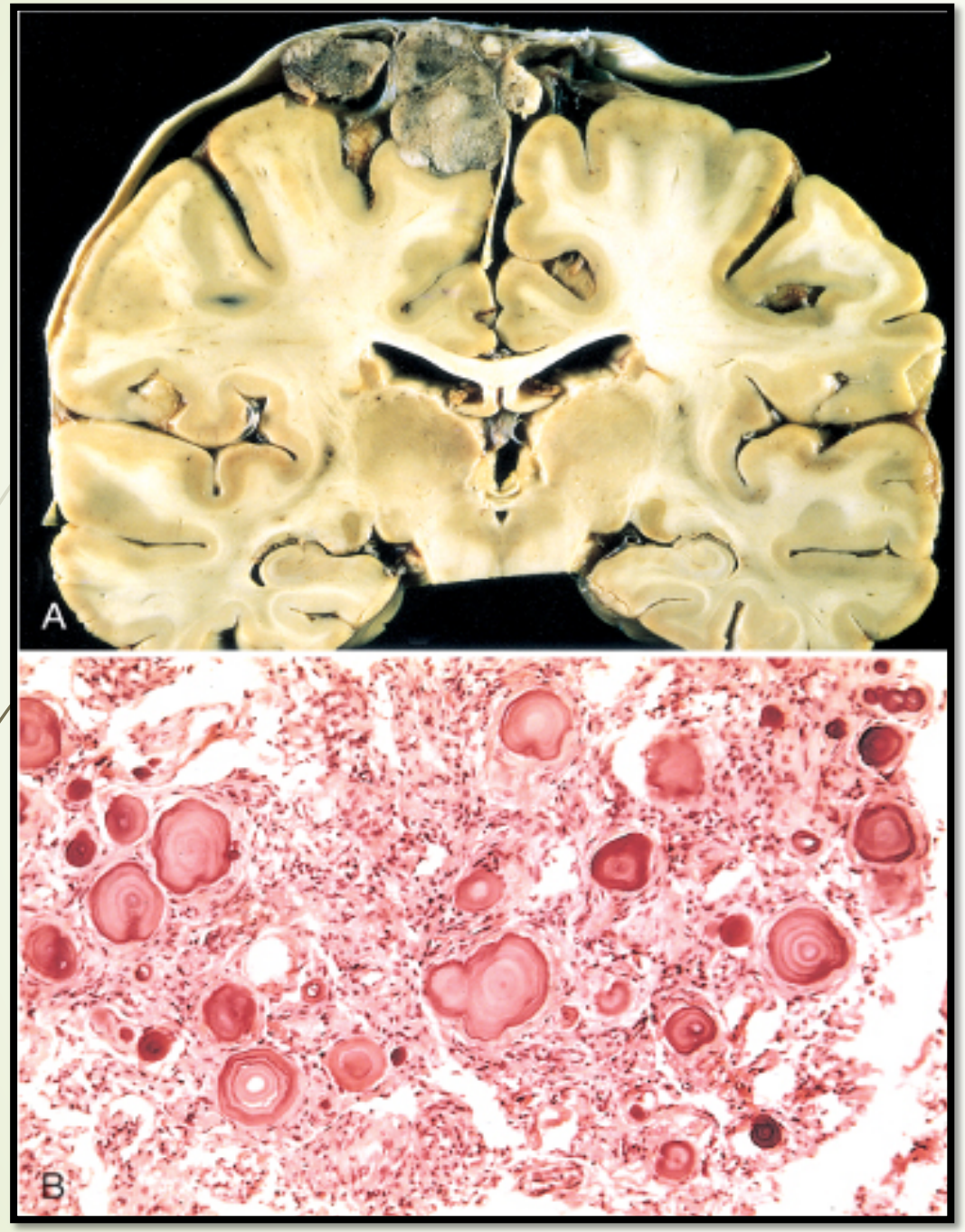
Ependymoma





Meningioma

- They are often low grade tumors of adults.
- They originate from the meningothelial cell of the arachnoid
- Although most meningiomas are easily separable from underlying brain, some tumors infiltrate the brain.
- The presence of brain invasion is associated with increased risk of recurrence.



Meningioma

- A, A parasagittal multilobular meningioma attached to the dura with compression of the underlying brain.
- B, Meningioma with a whorled pattern of cell growth and psammoma bodies.

Meningioma

- Main subtypes (grade I):
  - Meningothelial
  - Fibroblastic
  - Transitional
  - Psammomatous
  - Secretory

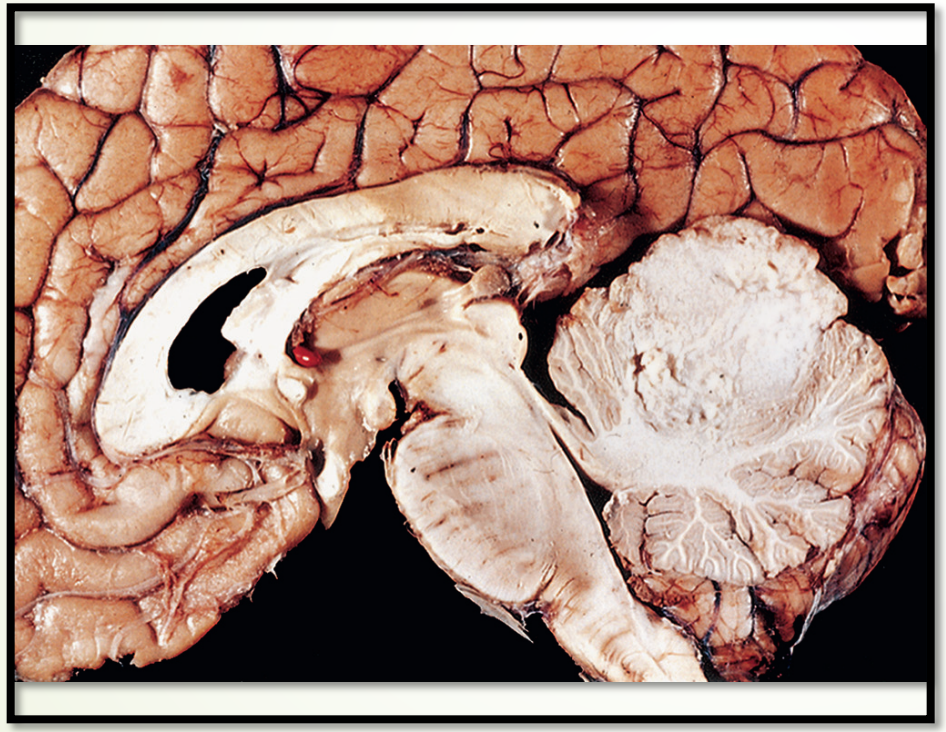
  - Atypical meningiomas (grade II): (prominent nucleoli, increased cellularity, pattern-less growth), and often have a higher mitotic rate. These tumors demonstrate more aggressive local growth and a higher rate of recurrence.
  - Anaplastic (malignant) meningiomas (grade III): are highly aggressive tumors that may resemble a highgrade sarcoma or carcinoma.

Medulloblastoma

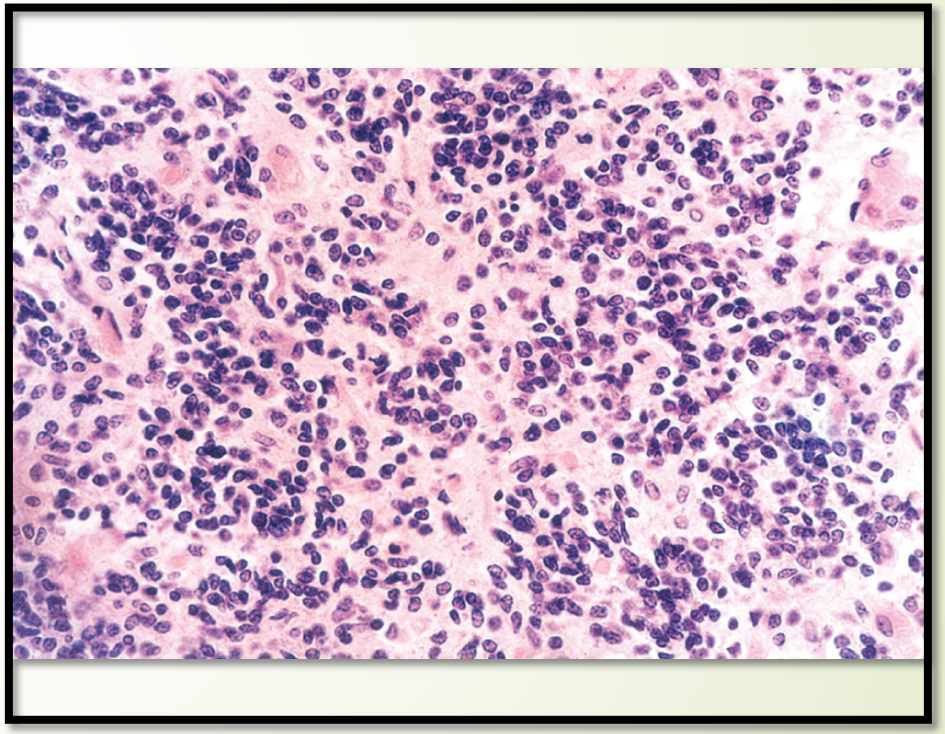
- They occur in children and exclusively in the cerebellum.
- Neuronal and glial markers may be expressed, but the tumor is often largely undifferentiated.
- The tumor is highly malignant, and the prognosis for untreated patients is dismal; however, it is exquisitely radiosensitive.
- With total excision and radiation, the 5-year survival rate may be as high as 75%.

Medulloblastoma

Macroscopy



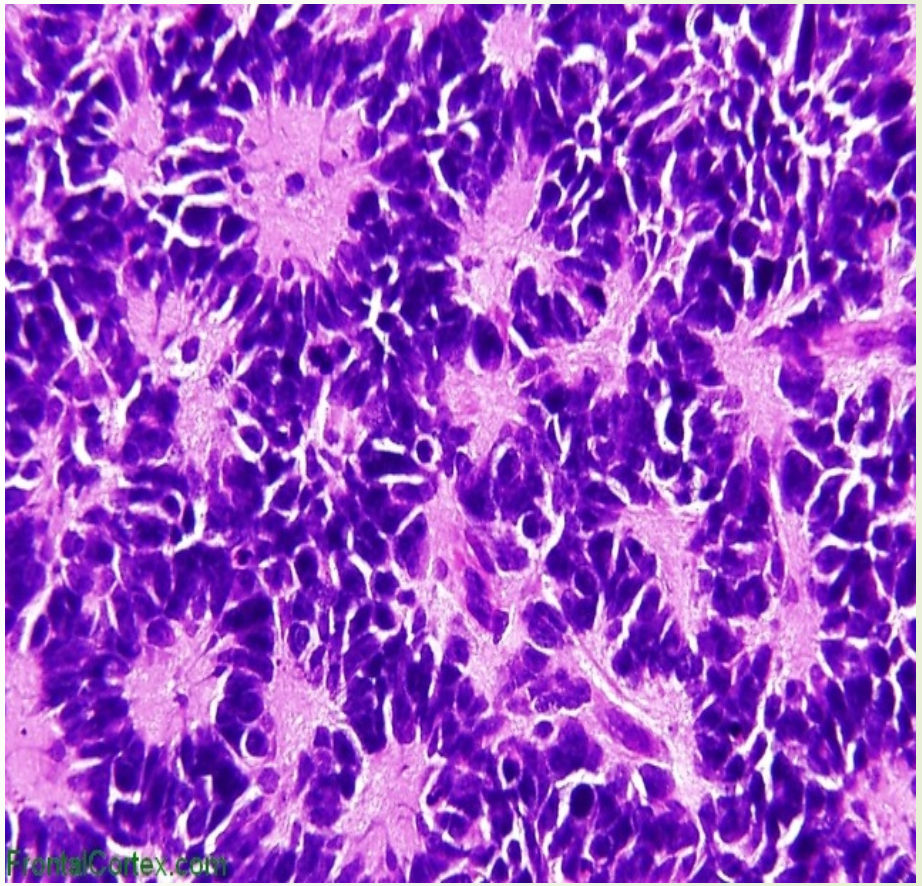
Microscopy



The tumor is extremely cellular, with sheets of anaplastic ("small blue") cells with little cytoplasm and hyperchromatic nuclei; mitoses are abundant

Medulloblastoma

- Often, focal neuronal differentiation is seen in the form of the Homer Wright or neuroblastic rosette
- they are characterized by primitive tumor cells surrounding central neuropil (delicate pink material formed by neuronal processes).



Schwannoma

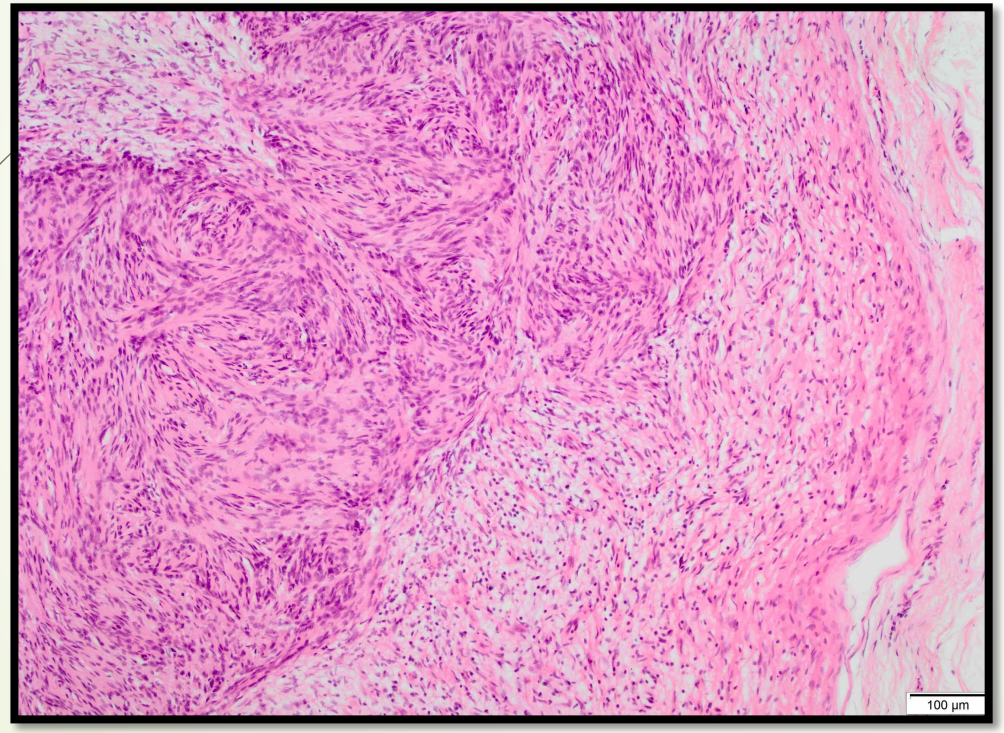
- Benign

- May occur in soft tissues, internal organs, or spinal nerve roots.
- The most commonly affected cranial nerve is the vestibular portion of the eighth nerve. Tumors arising in a nerve root or the vestibular nerve may be associated with symptoms related to nerve root compression, which includes hearing loss in the case of vestibular schwannomas.
- They are attached to the nerve but can be separated from it

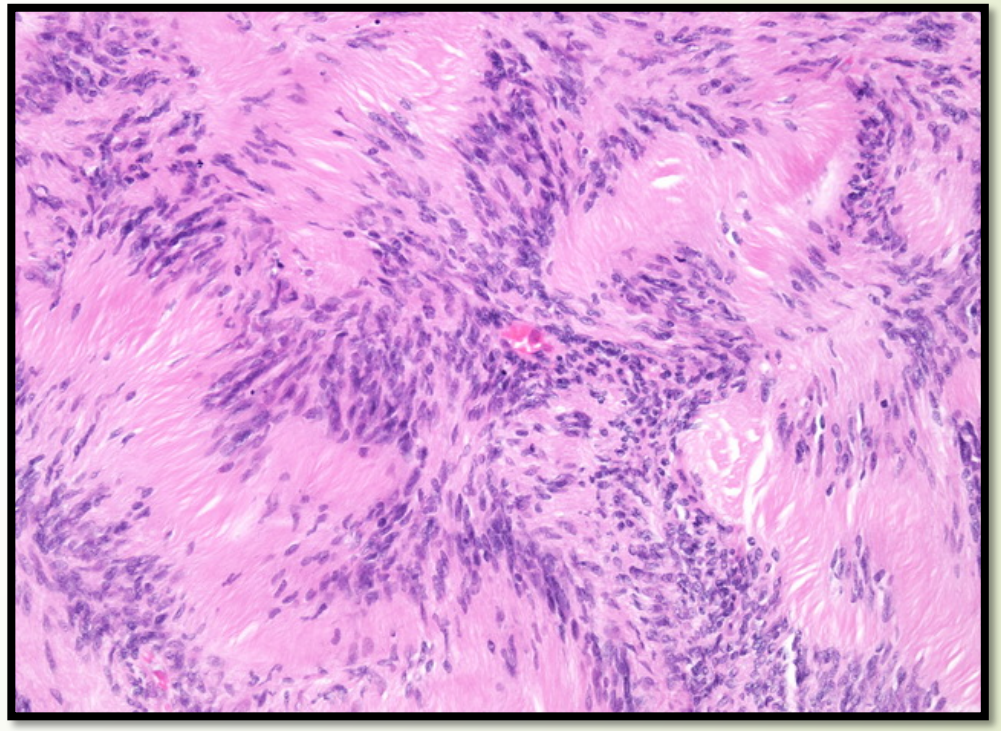
- Sporadic schwannomas are associated with mutations in the NF2 gene, however bilateral acoustic schwannoma is associated with NF2 syndrome.

Schwannoma

Biphasic pattern



Verocay Bodies



Schwannoma

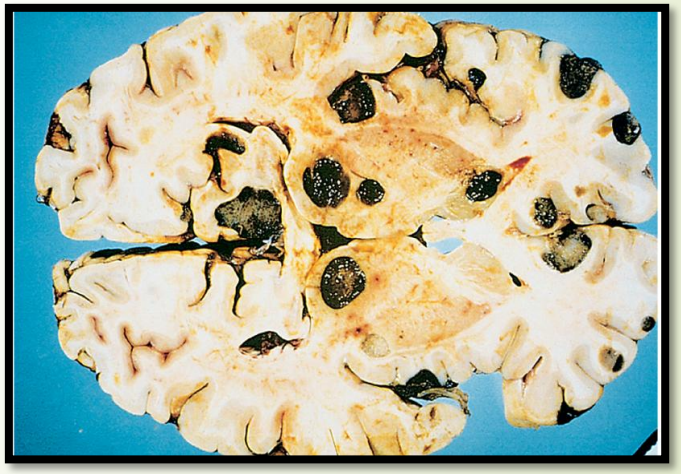
- Microscopically:
  - Biphasic pattern: cellular Antoni A pattern and a less cellular Antoni B pattern.
  - Nuclear-free zones of processes that lie between the regions of nuclear palisading and termed ***Verocay bodies***

Neurofibroma

- Neurofibromas are benign tumors of peripheral nerves and they cannot be separated from the nerve trunk (in comparison to shcwannomas)
- Examples include: cutaneous neurofibroms or in peripheral nerve solitary neurofibroma.
- These arise sporadically or in association with type 1 neurofibromatosis.
- Plexiform neurofibromas, mostly arise in individuals with NF1 syndrome with a potential malignant transformation.

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 most common primary sites for metastases.
- The metastatic deposits are usually sharply demarcated with a surrounding edema.



Homework !

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

- 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?

Reference

Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10th ed. Elsevier; 2017. Philadelphia, PA.

End of Lecture

Thank You