CNS Tumors

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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

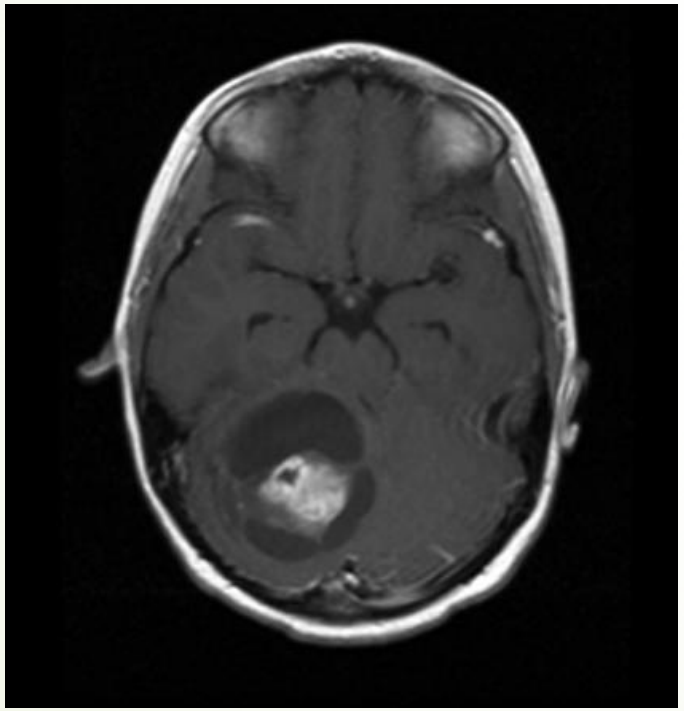
- Pilocytic (Grade I):
  - Children and young adults
  - Commonly cerebellum
  - Relatively benign
- Fibrillary:
  - 4th to 6th decade
  - Commonly cerebral hemisphere
  - Variable grades:
    - Diffuse astrocytoma (Grade II)
    - Anaplstic astrocytoma (Grade III)
    - Glioblastoma (Grade IV)

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



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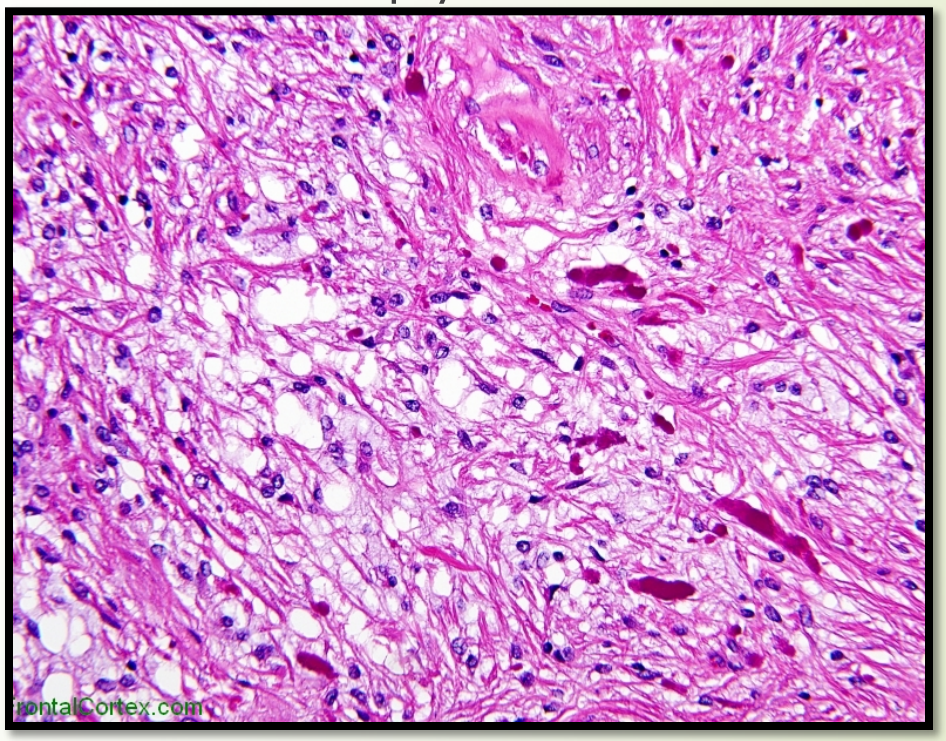


Astrocytomas

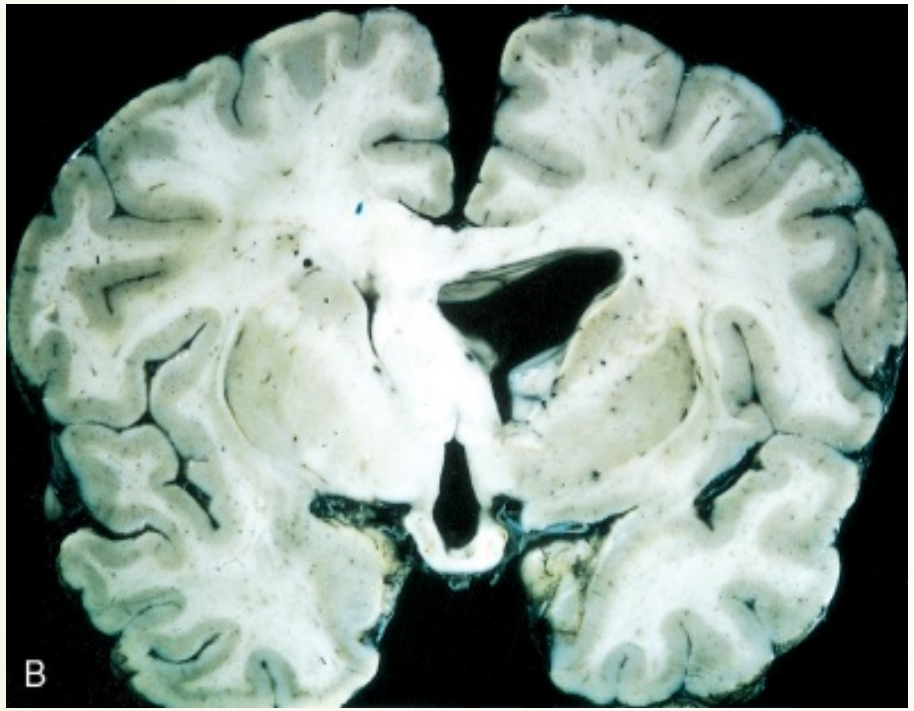
- Well differentiated "diffuse astrocytoma" (WHO grade II):
  - Static or progress slowly (mean survival of more than 5 years)
  - Moderate cellularity
  - Variable nuclear pleomorphism

- 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



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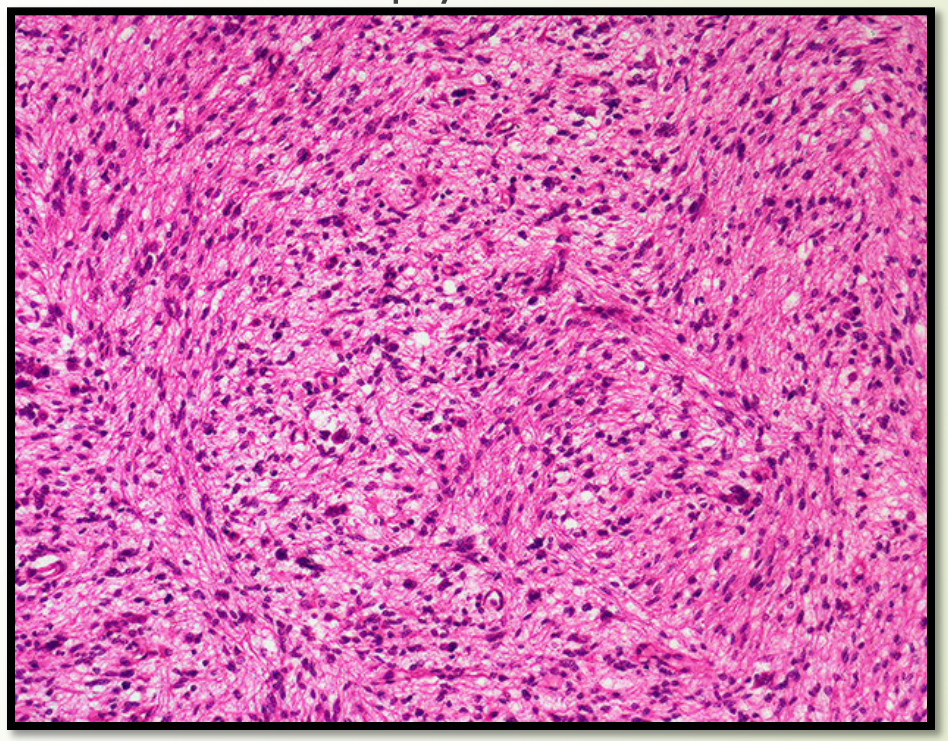
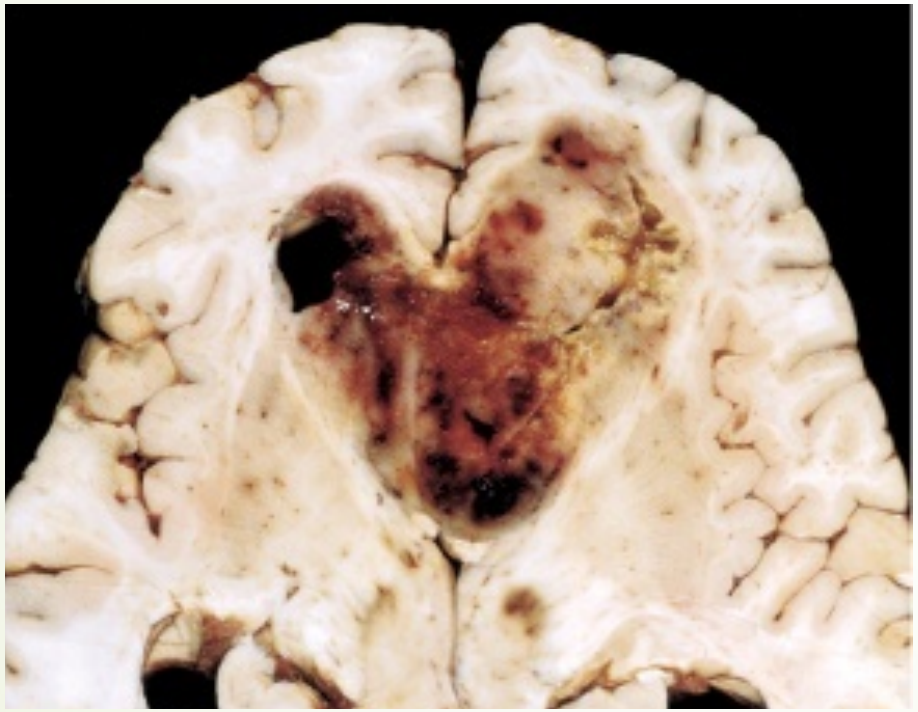


Note that diffuse astrocytoma are poorly demarcated

Glioblastoma Multiforme

Macroscopy



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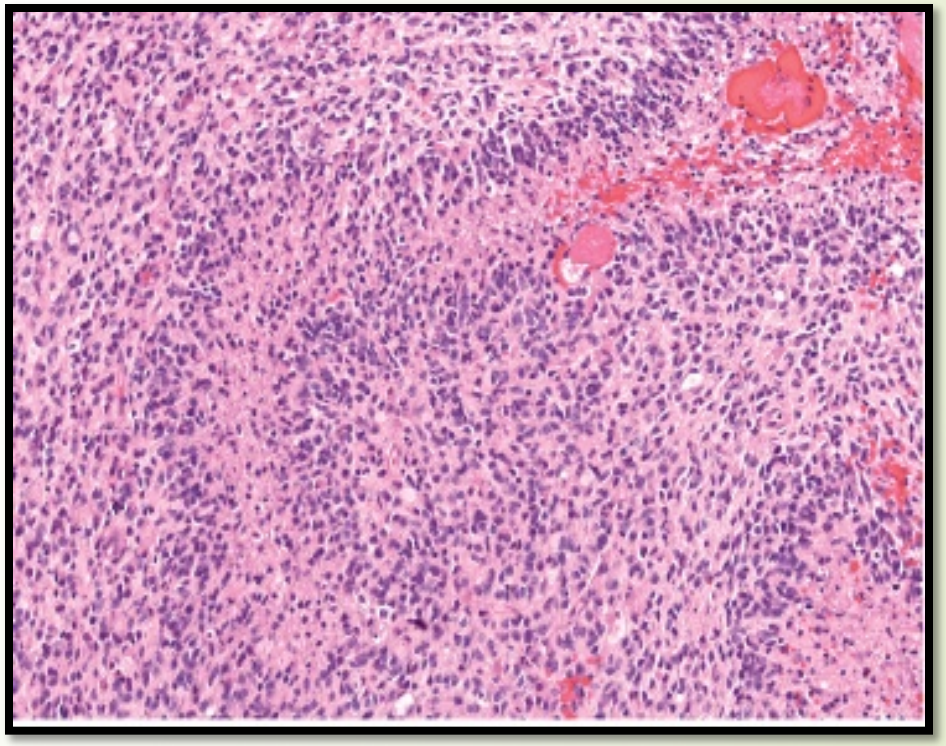


Astrocytomas

- 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.

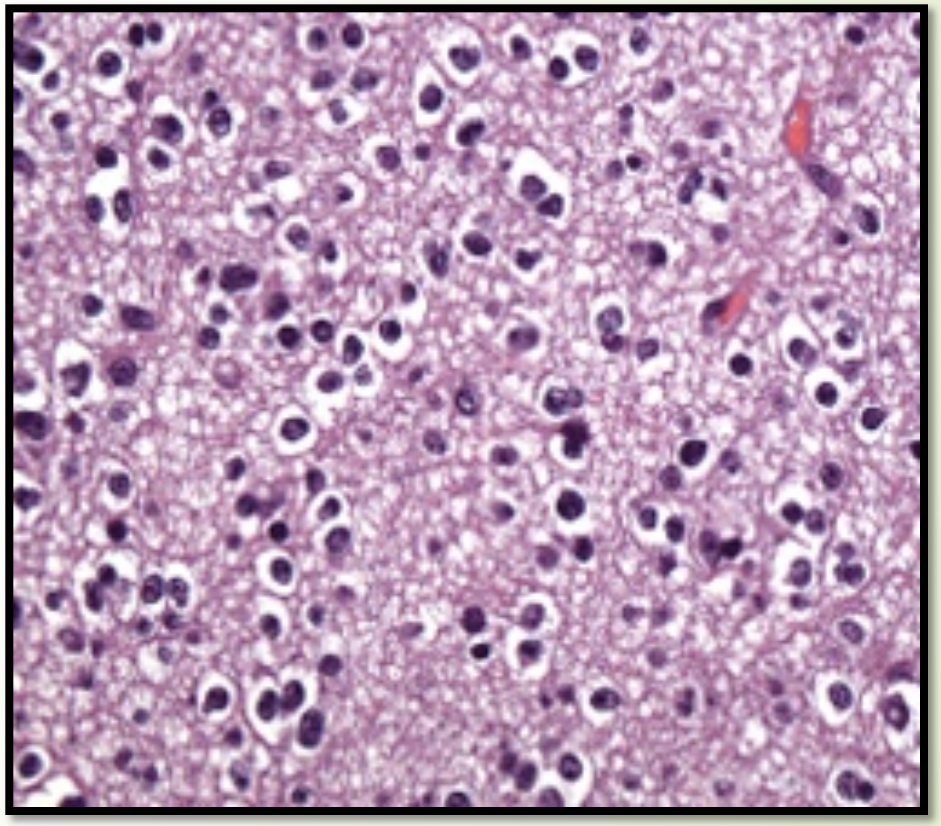
Oligodendroglioma

- 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

- 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?*



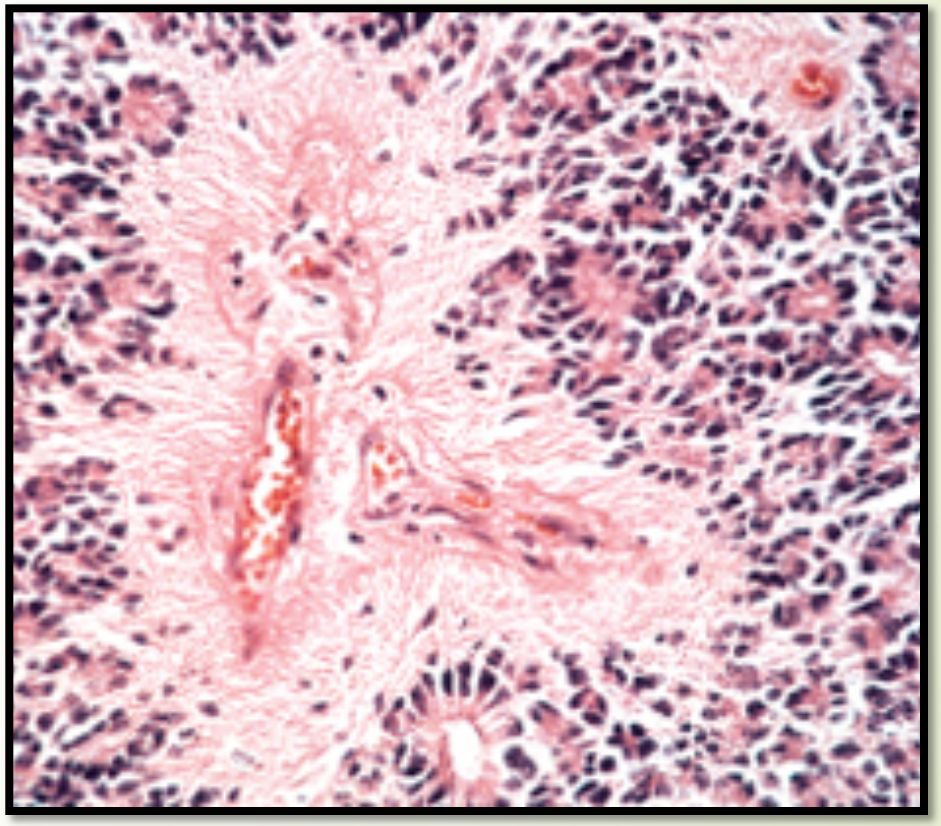
Ependymoma

- 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

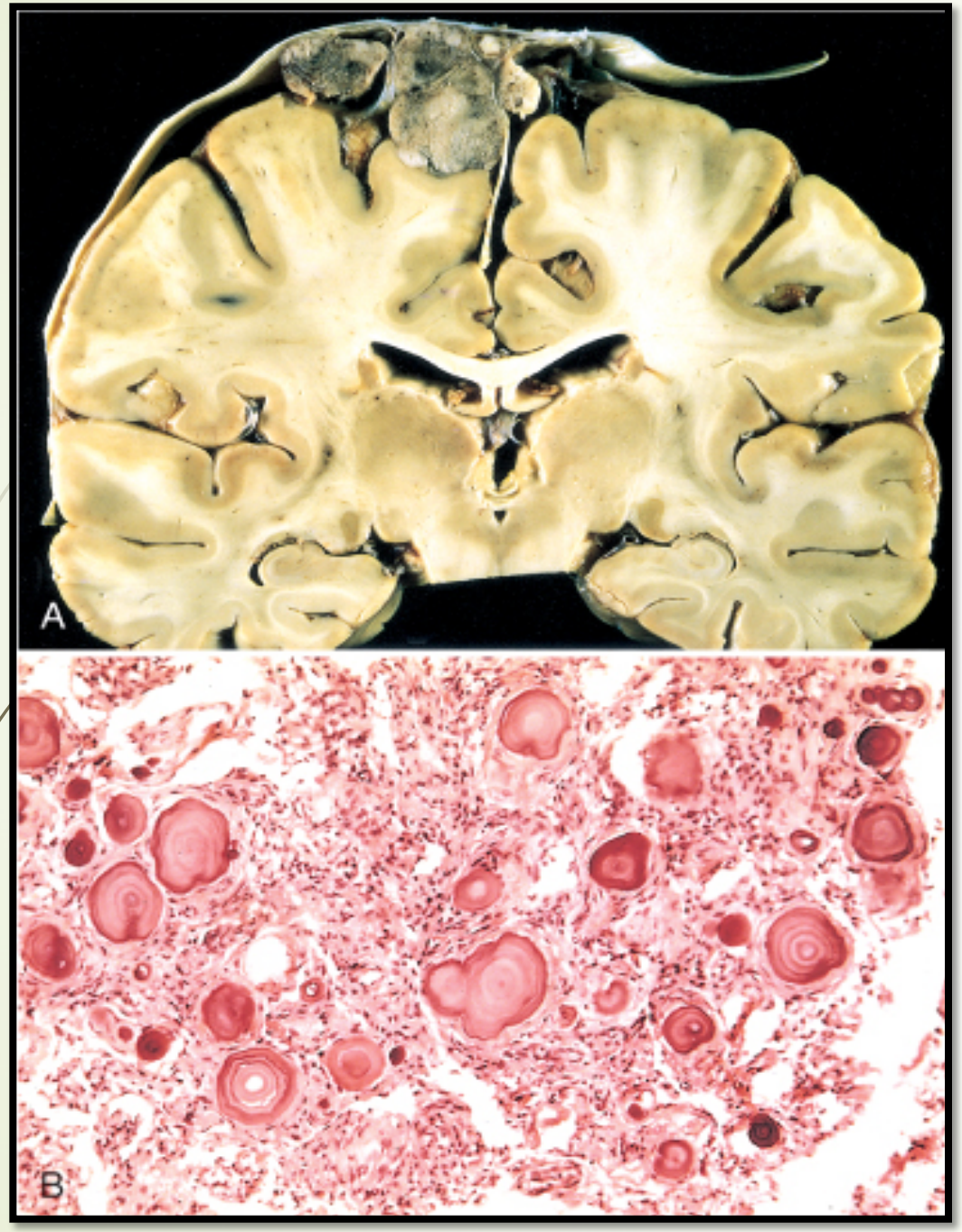
- Tumor cells may form round or elongated structures (**rosettes, canals**) more frequently present are **perivascular pseudorosettes** in which tumor cells are arranged around vessels with an intervening zone containing thin ependymal processes.

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



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

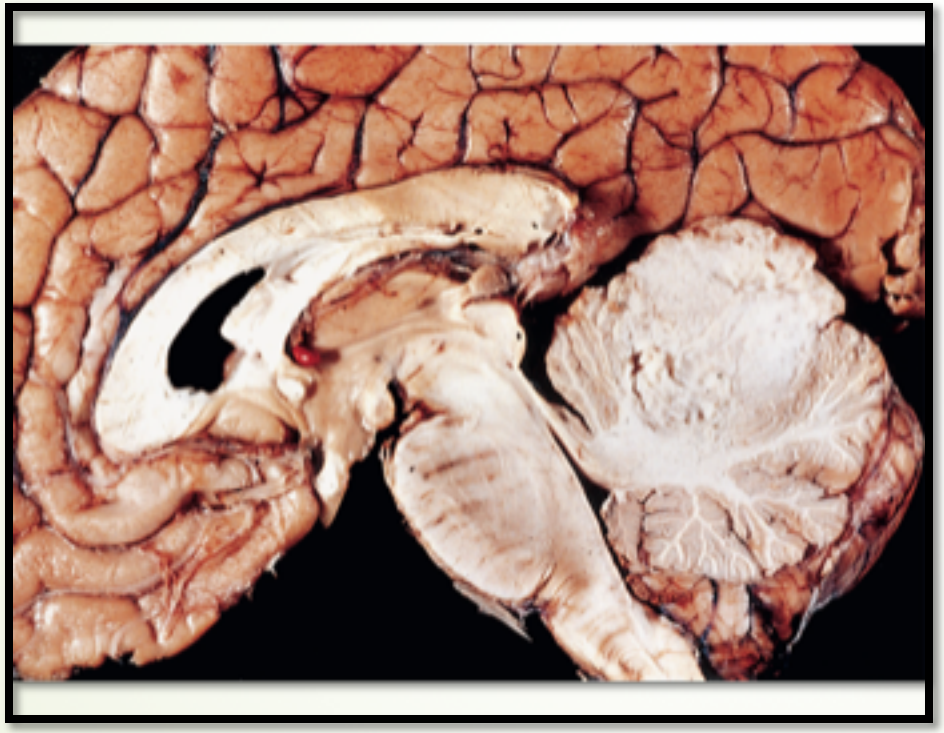
- Main subtypes (grade I):
  - Meningothelial
  - Fibroblastic
  - Transitional
  - Psammomatous
  - Secretory
- Also note:
  - Atypical meningiomas (grade II)
  - Anaplastic (malignant) meningiomas (grade III)

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



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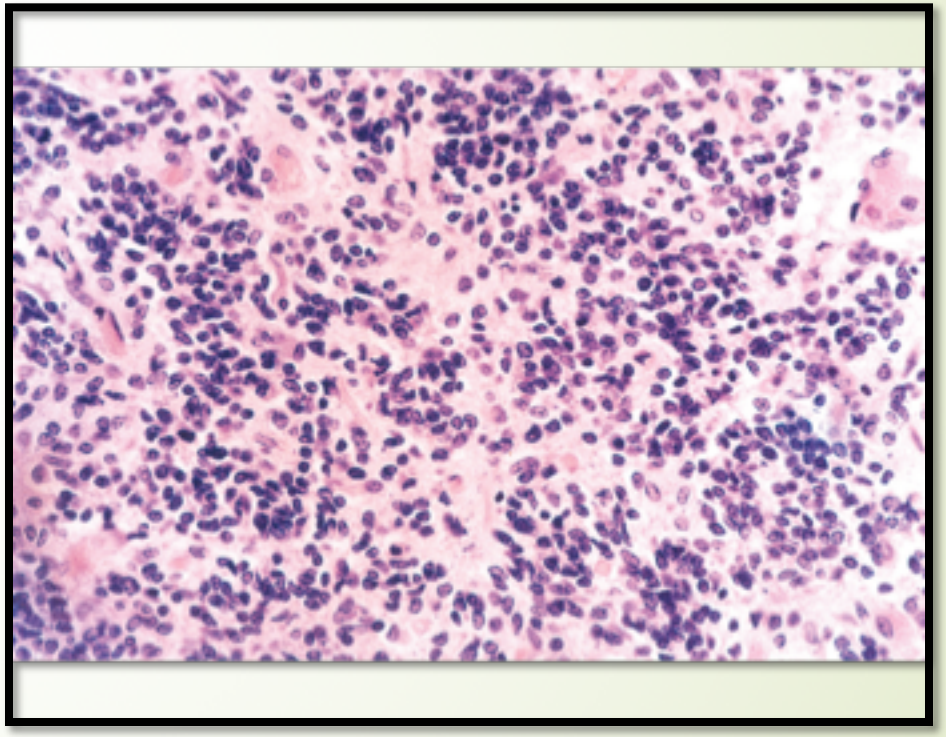


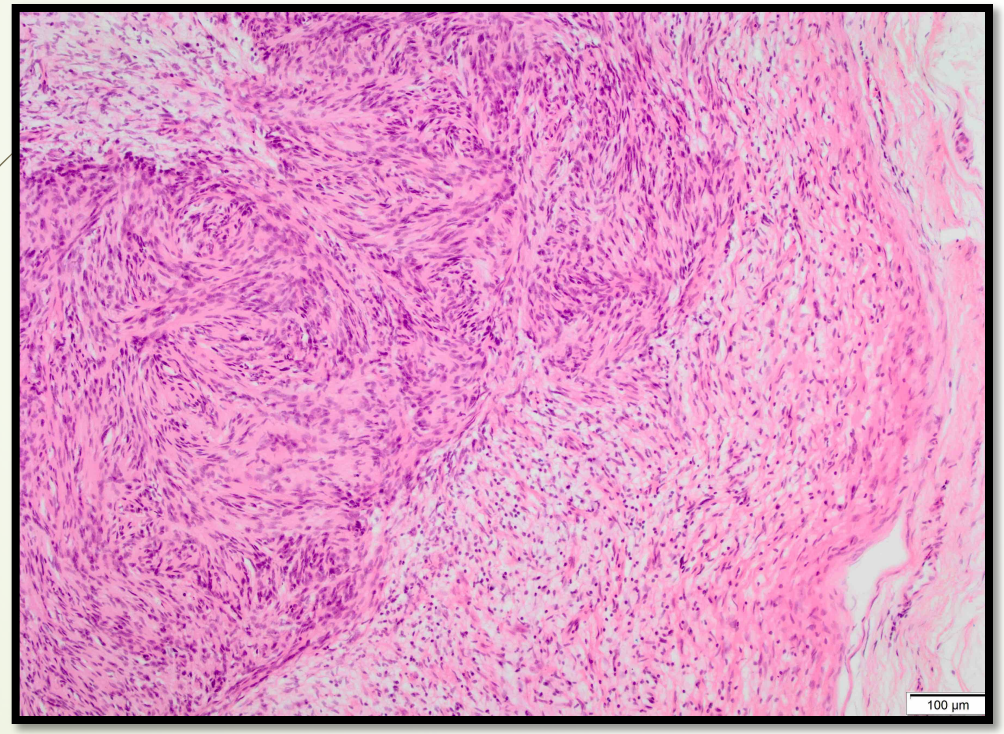
The tumor is extremely cellular, with sheets of anaplastic ("small blue") cells with little cytoplasm and hyperchromatic nuclei; mitoses are abundant

Schwannoma

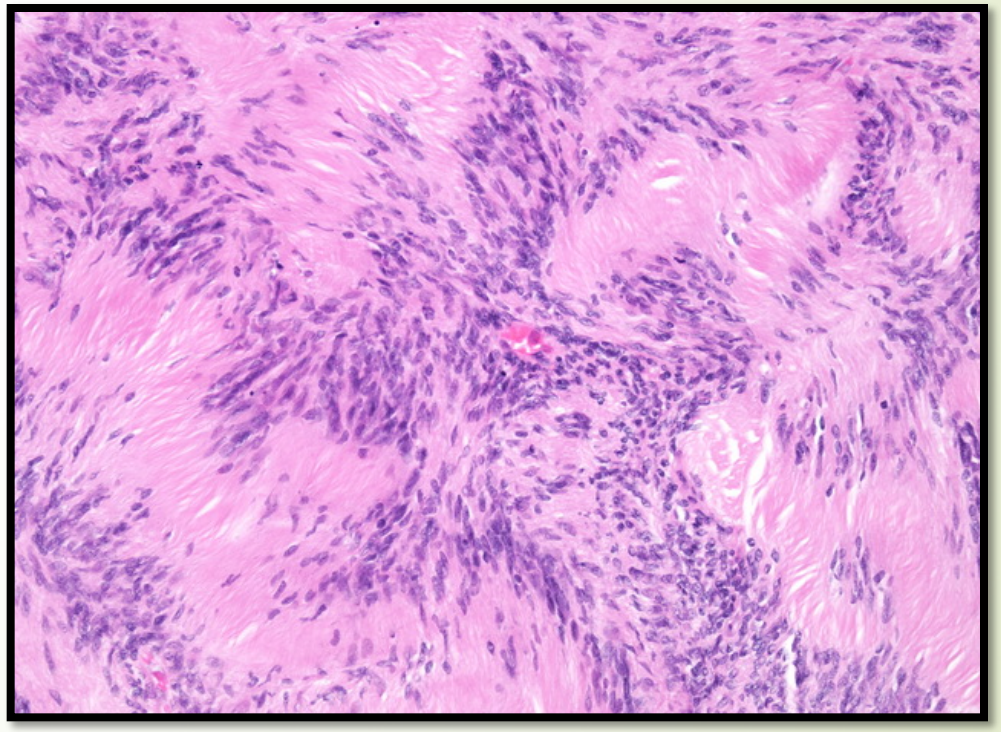
- Benign
- In the CNS, they are often encountered within the cranial vault in the cerebellopontine angle, where they are attached to the vestibular branch of the eighth nerve, causing tinnitus and hearing loss.
- They are attached to the nerve but can be separated from it
- Sporadic schwannomas are associated with mutations in the NF2 gene, however bilateral acoustic schwannoma is associated with NF2 syndrome.

Schwannoma

Biphasic pattern



Verocay Bodies



Schwannoma

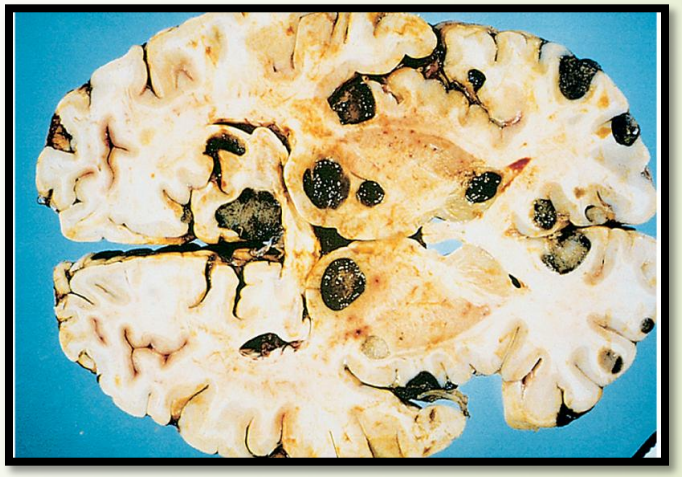
- Microscopically:
  - Biphasic pattern: cellular Antoni A pattern and a less cellular Antoni B pattern.
  - Nuclear-free zones of processes that lie between the regions of nuclear palisading and termed ***Verocay bodies***

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.



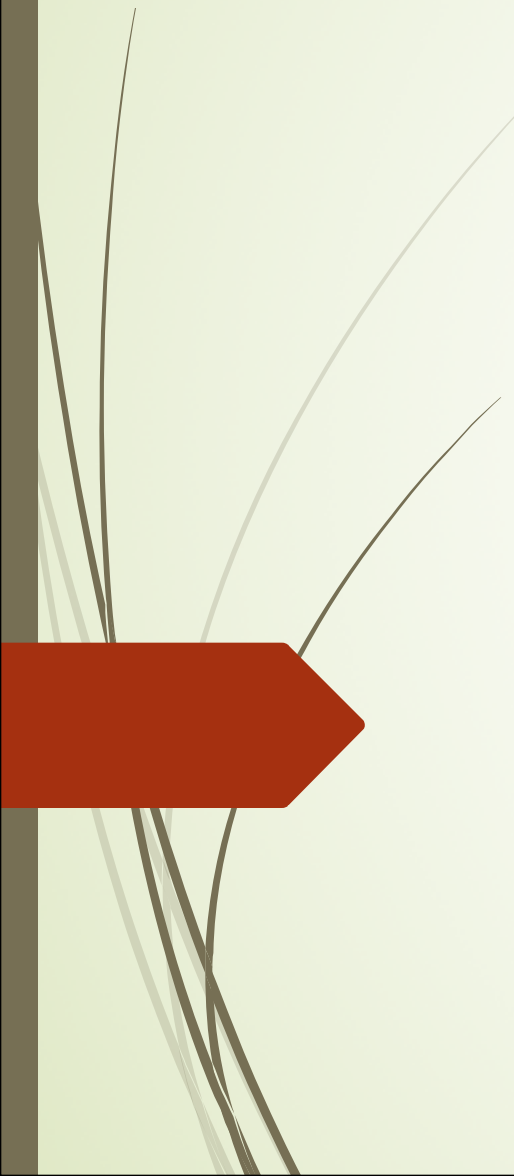
Homework !

- 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