Tumors of the Nervous System

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What I want to cover

- What are the most common types of brain tumors?
- Who gets them?
- How do they present?
- What do they look like?
- How do they behave?

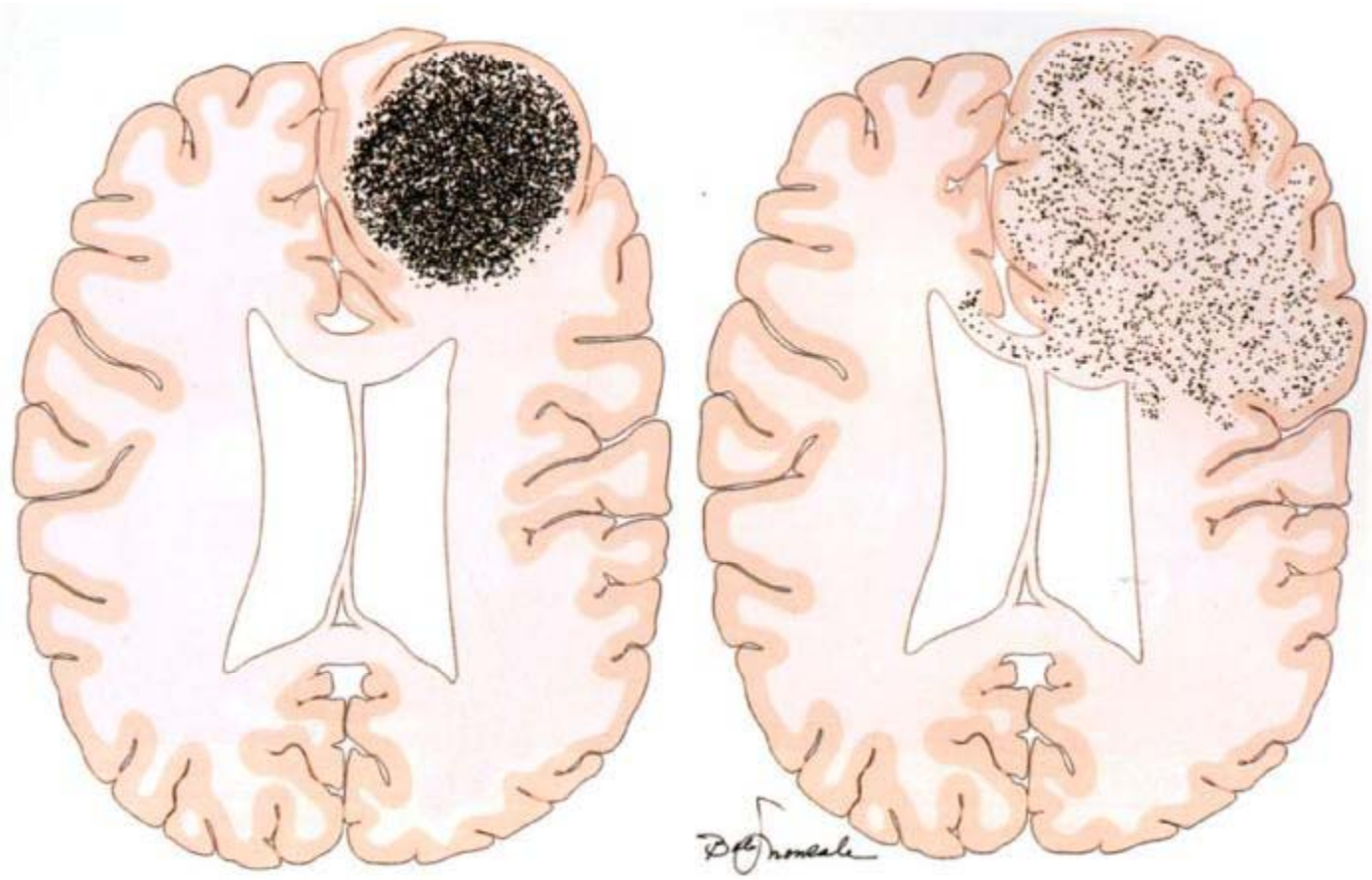
Epidemiology of Brain Tumors

- Annual incidence of 10-20 per 100,000
- 2.5% of all cancer deaths
- 20% of childhood tumors

Common Nervous System Tumors

- Gliomas
  - Diffuse Astrocytoma-Glioblastoma Multiforme
  - Pilocytic Astrocytoma
  - Oligodendroglioma
  - Ependymoma
- Medulloblastoma
- Meningioma
- Schwannoma
- Metastatic

Different types of growth patterns



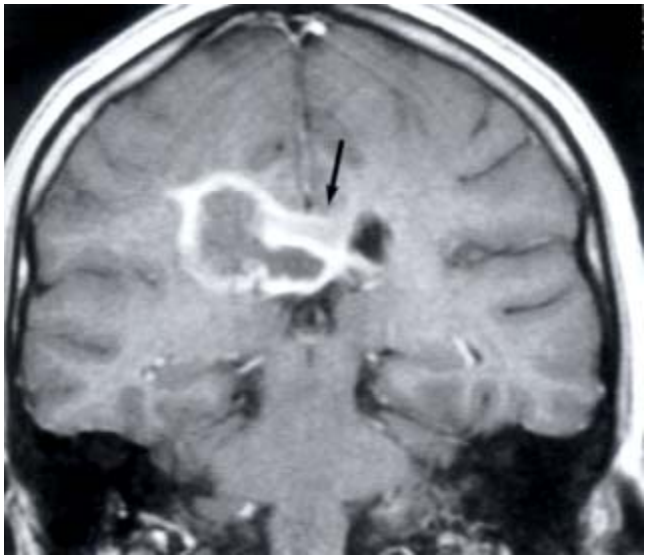
Well Circumscribed

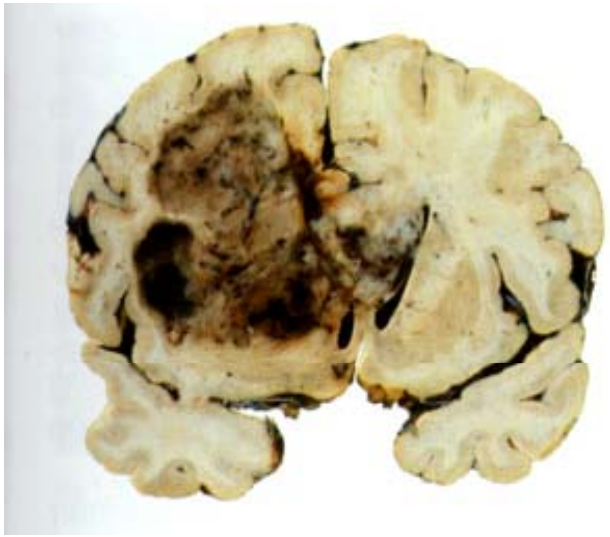
Diffusely Infiltrating

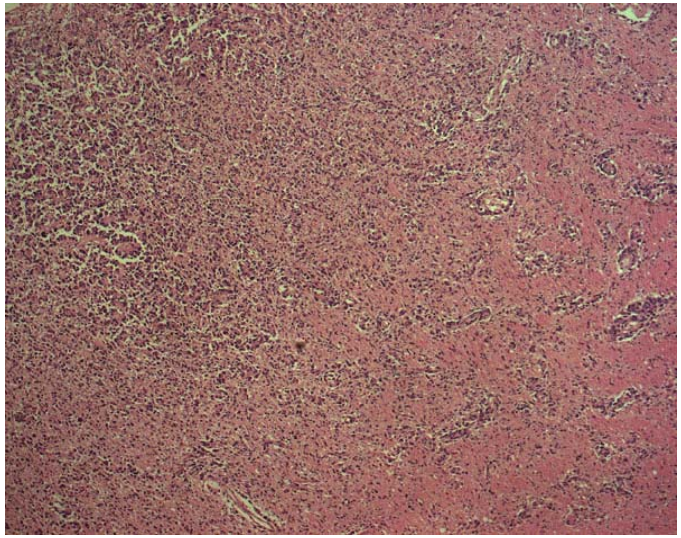
Glioblastoma Multiforme

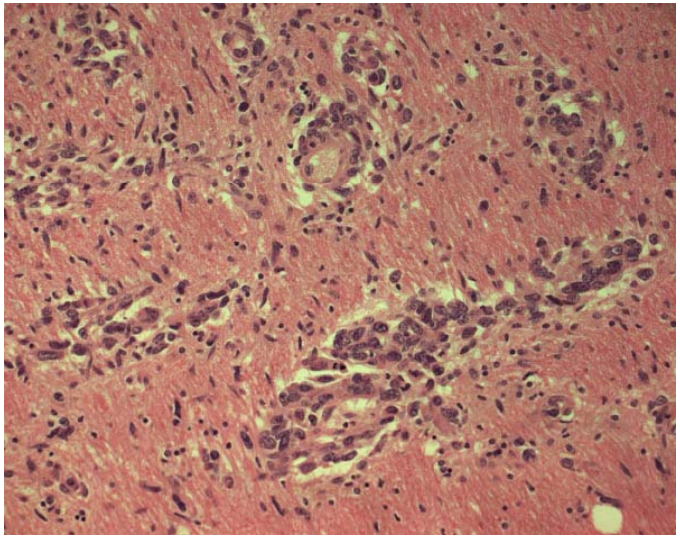
- Most common adult primary brain tumor
- Peak incidence is between 45 and 70
- Often present with seizures or subtle deficits
- MRI shows ring-enhancing lesion
- Glioma cells diffusely infiltrate the brain,
- But almost never metastasize to other organs
- Atypia, Mitosis, Endothelial proliferation, Necrosis
- Heterogeneous both phenotypically and genetically
- Average survival of less than 1 year

Glioblastoma Multiforme

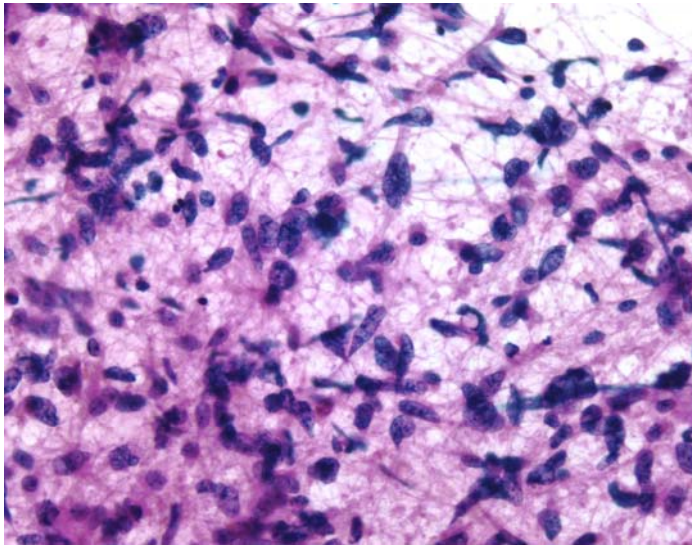


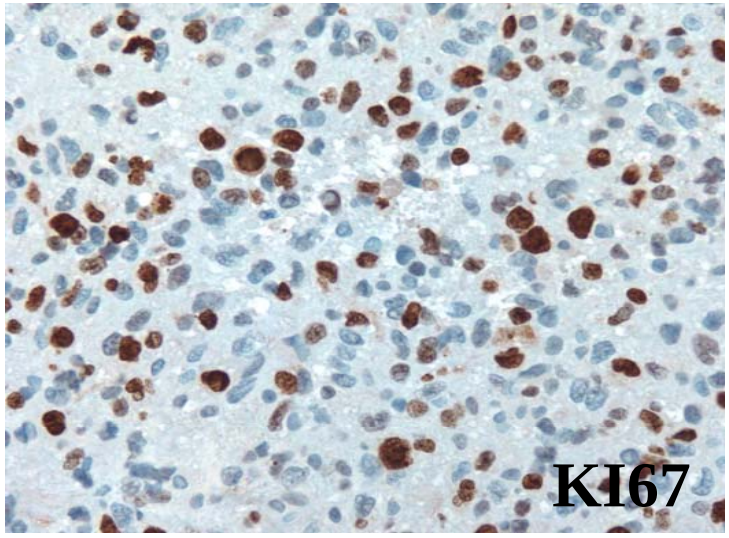


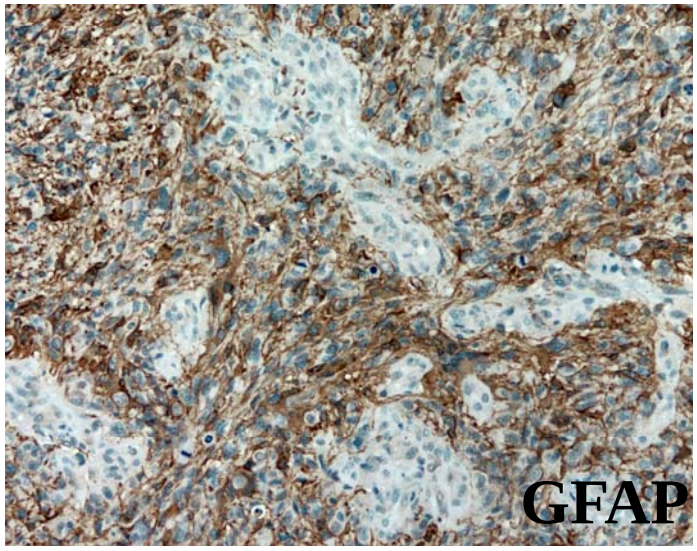


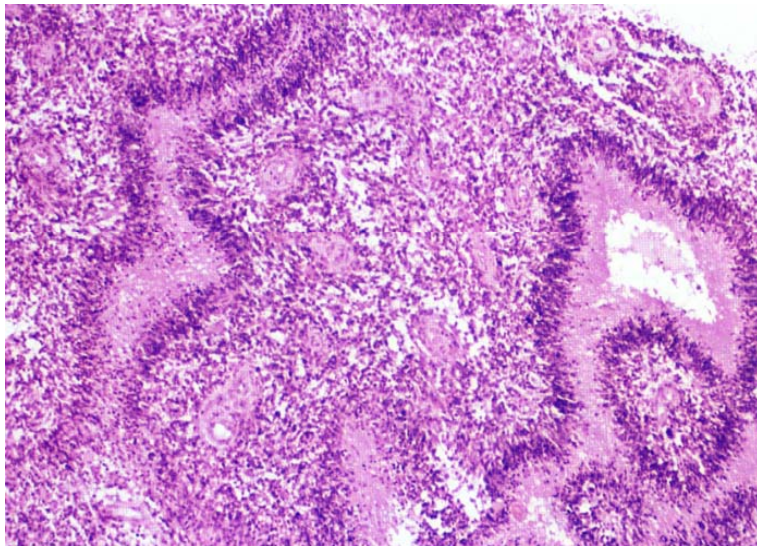


Glioblastoma Multiforme

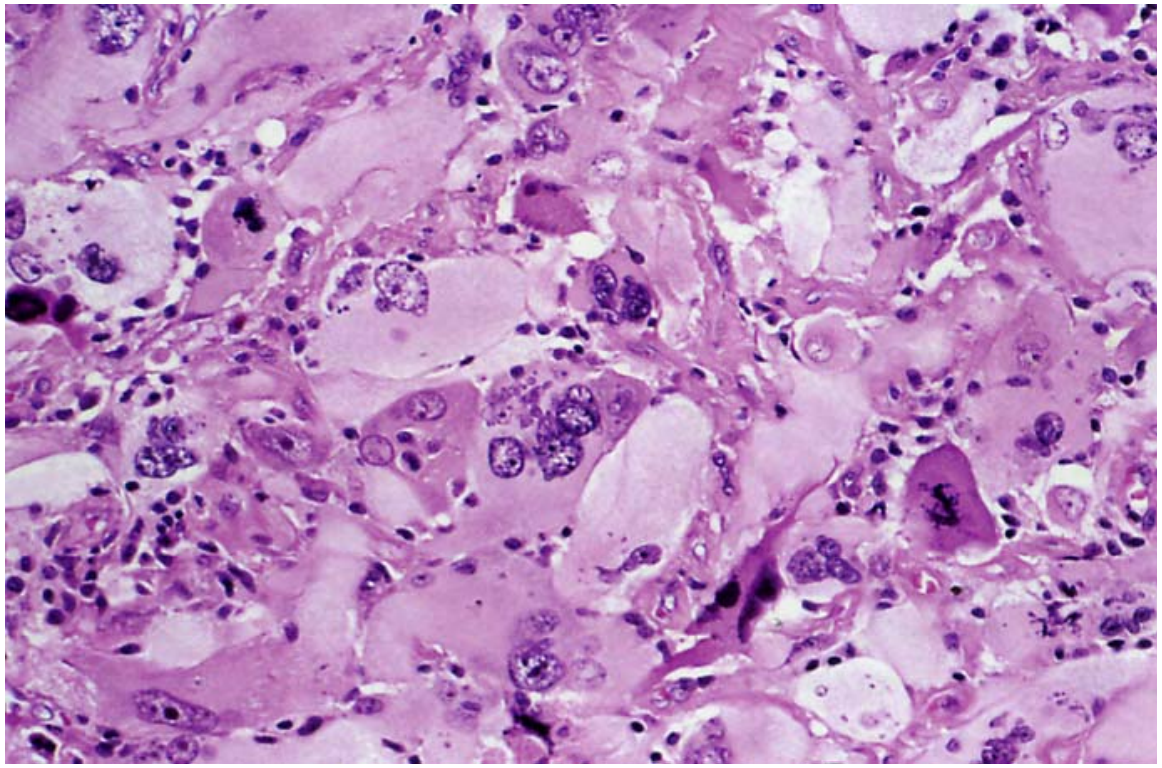


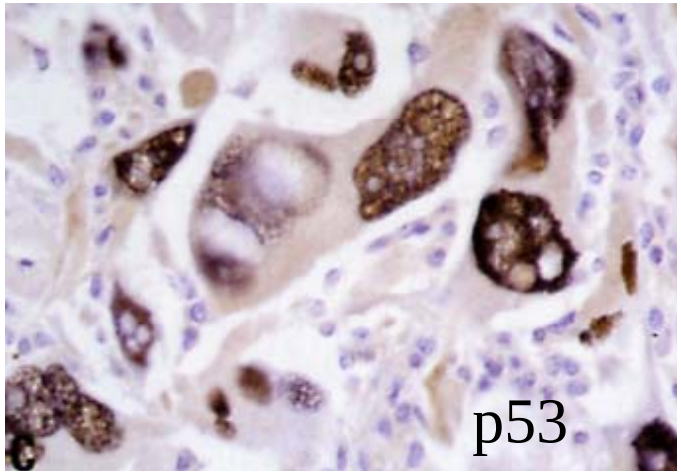


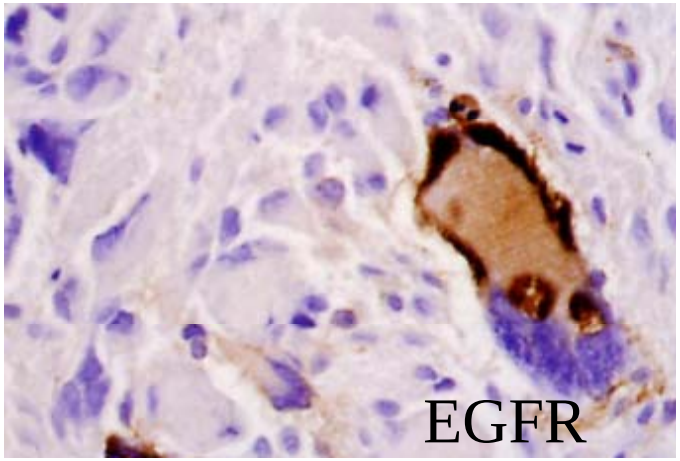




Giant cell GBM



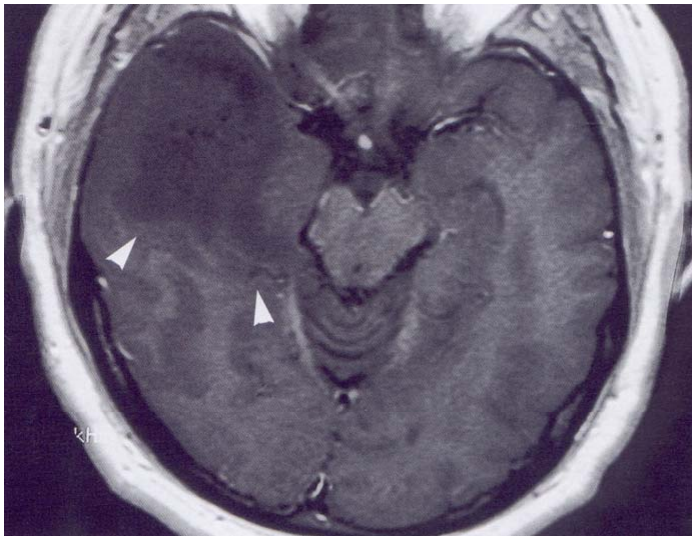


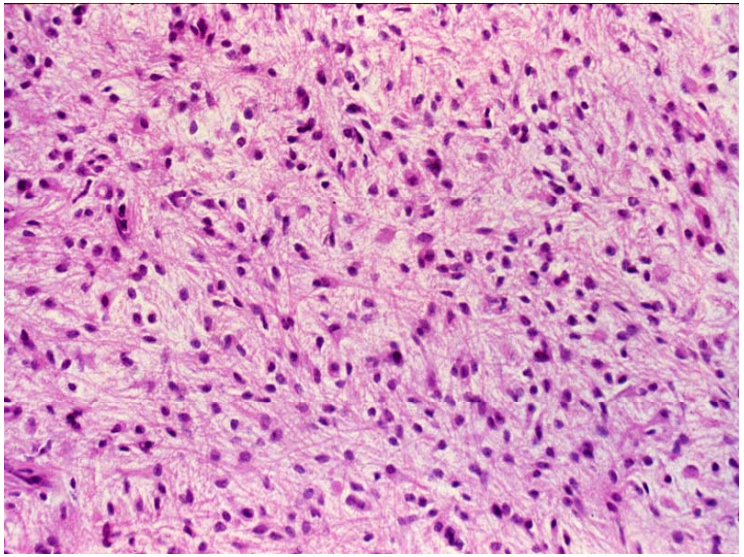


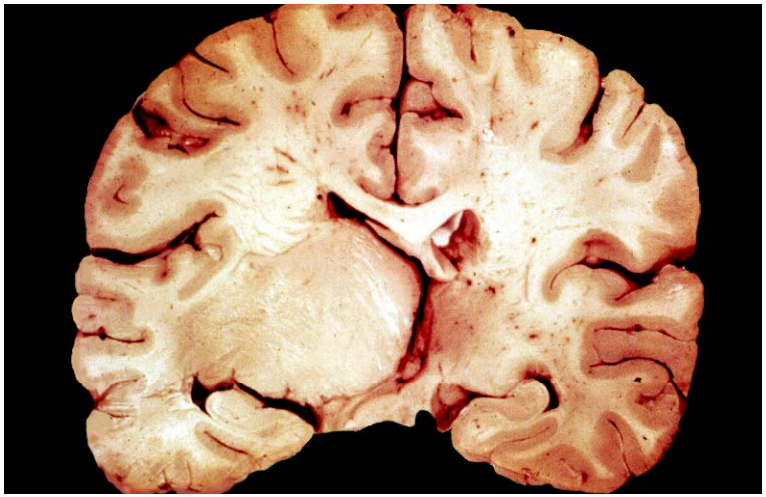
Low Grade Diffuse Astrocytoma

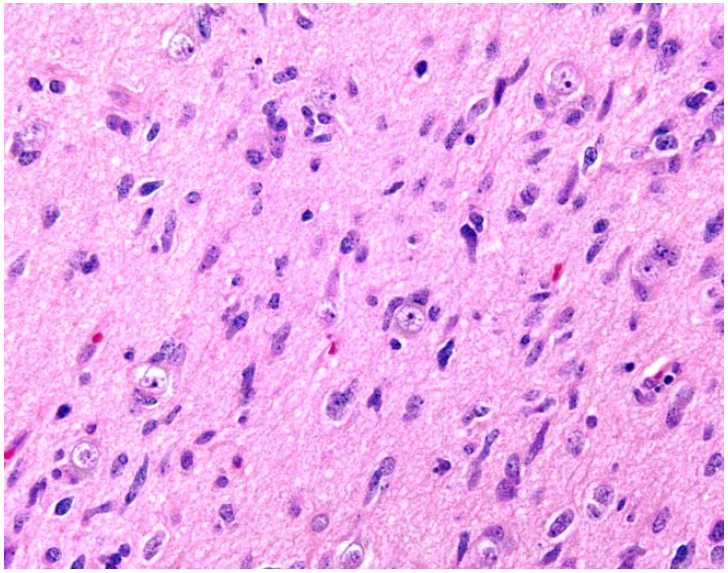
- Peak age of incidence is 3rd and 4th decade
- Frequently present with seizures or subtle cognitive abnormalities
- MRI shows an ill-defined non-enhancing lesion, most commonly in the cerebrum
- Moderate nuclear atypia, very few mitotic figures
- Glioma cells diffusely infiltrate the brain, but almost never metastasize to other organs
- Recur and progress to Anaplastic Astrocytoma and Glioblastoma Multiforme

Low Grade Astrocytoma (WHO grade II)









WHO Grading of Diffuse Fibrillary Astrocytomas

	WHO grade	**A**typia	**M**itose s	**E**ndothelial Proliferation	**N**ecrosis	Average Survival
Astrocytoma	II	+	+/-	-	-	6-8 years
Anaplastic Astrocytoma	III	+	+	+/-	-	2-3 Years
Glioblastoma Multiforme	IV	+	+	+	+	< 1 year

Genetic Alterations in the Evolution of Primary and Secondary Glioblastoma

Low Grade Astrocytoma

-p53 mutations (65%)

-PDGF/ PDGFR overexpression (60%)

AnaplasticAstrocytoma

-LOH 19q (50%)

-RB alterations (25%)

Secondary glioblastoma

-LOH 10q

-DCC overexpression (50%)

Primary glioblastoma

-EGFR overexpression (60%)

-LOH 10p and 10q

-PTEN mutations/loss (30%)

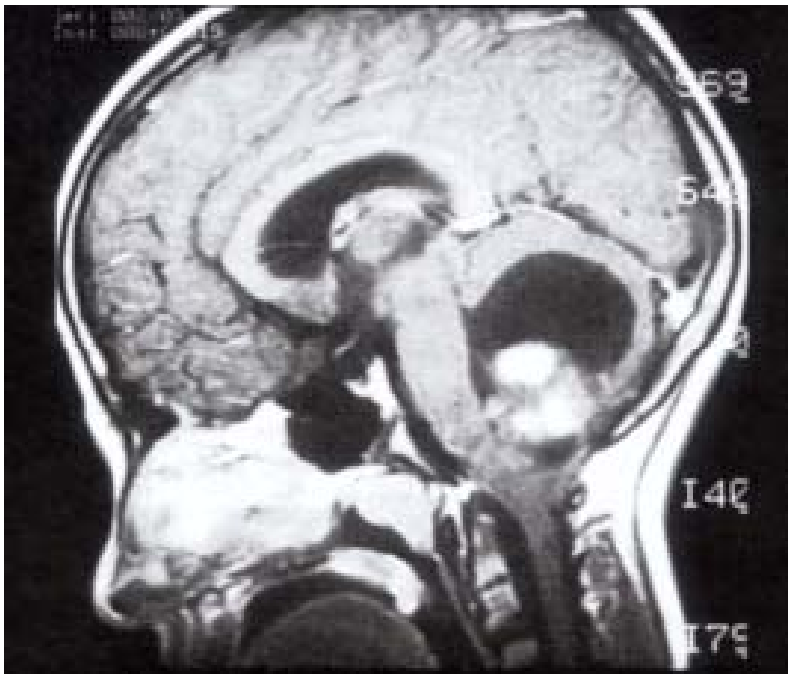
-P16 deletions (30%-40%)

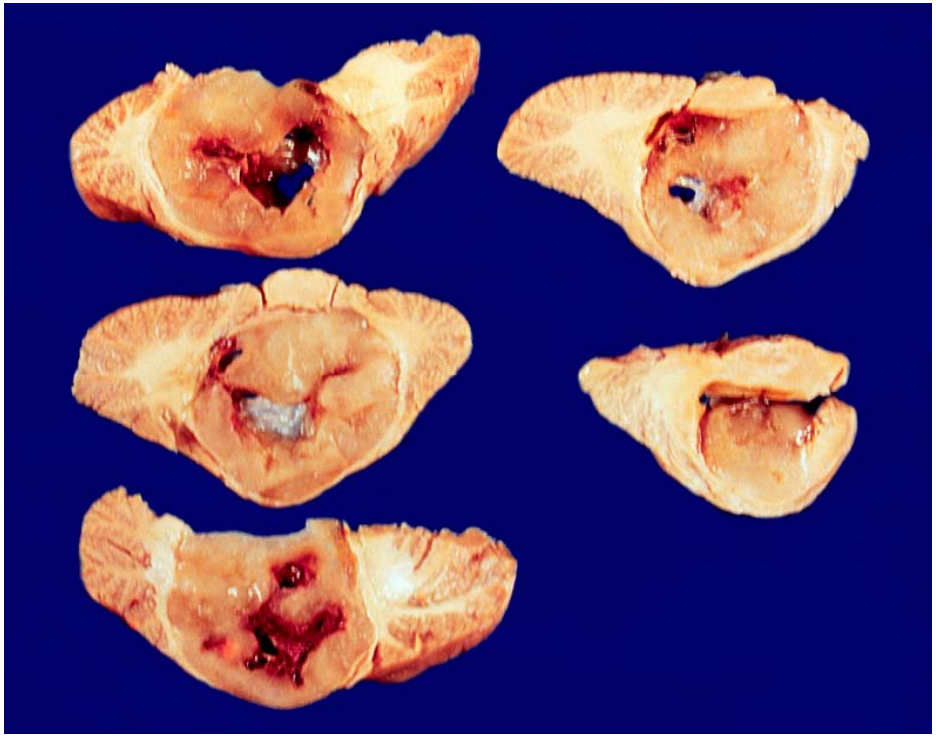
-MDM2 overexpression (50%)

Pilocytic Astrocytoma

- Relatively benign (WHO grade I)
- Typically occurs in children and young adults
- Often presents with focal neurological signs or increased intracranial pressure
- Common locations are cerebellum, optic nerve, cerebrum, brainstem
- Often cystic with an enhancing mural nodule
- Composed of bipolar cells with “hairlike” process
- Rosenthal fibers are often present
- Molecular genetics are distinct from diffuse fibrillary astrocytomas
- Good prognosis after complete resection

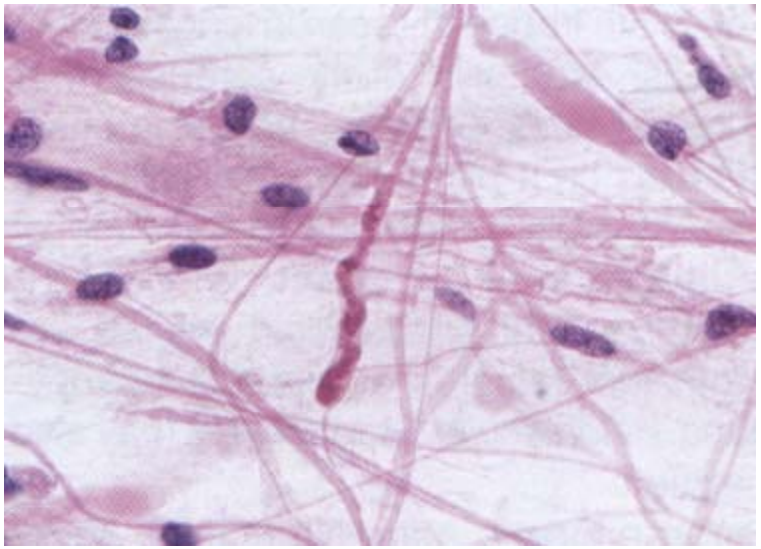
Pilocytic Astrocytoma

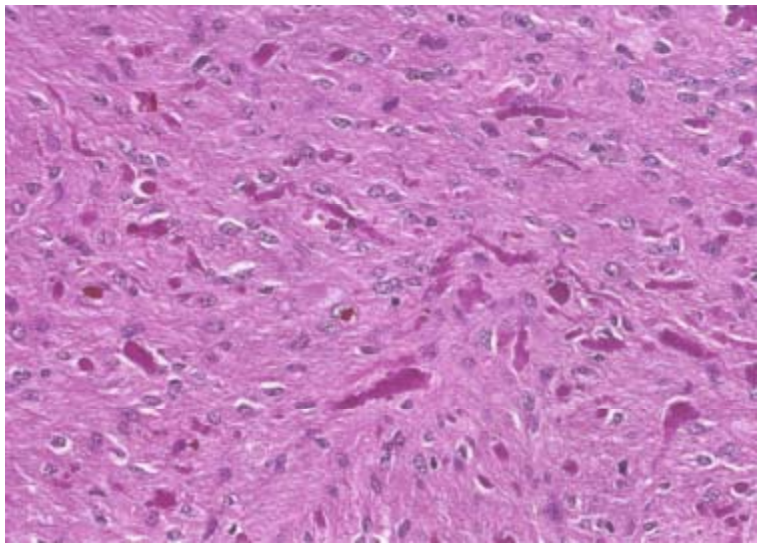


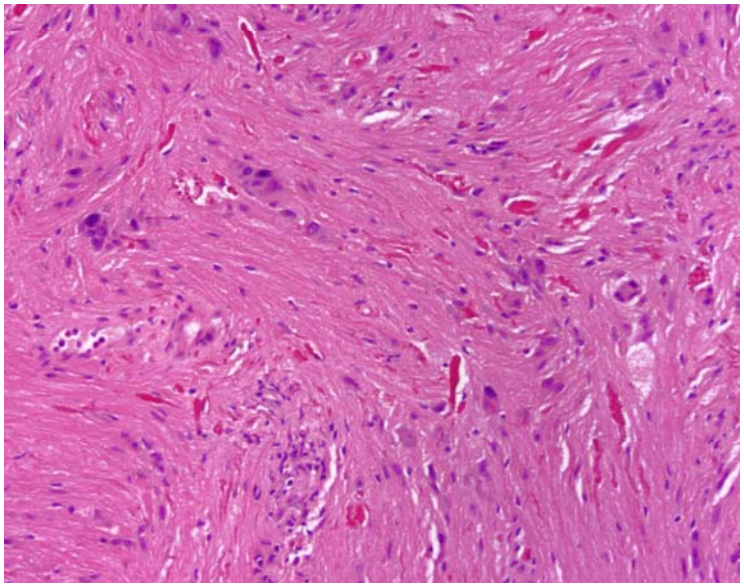


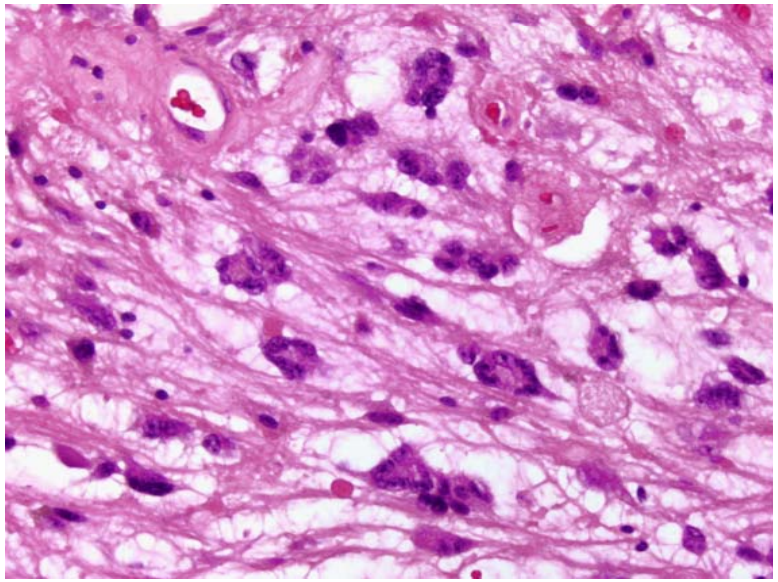
cystic with an enhancing mural nodule in the cerebellum

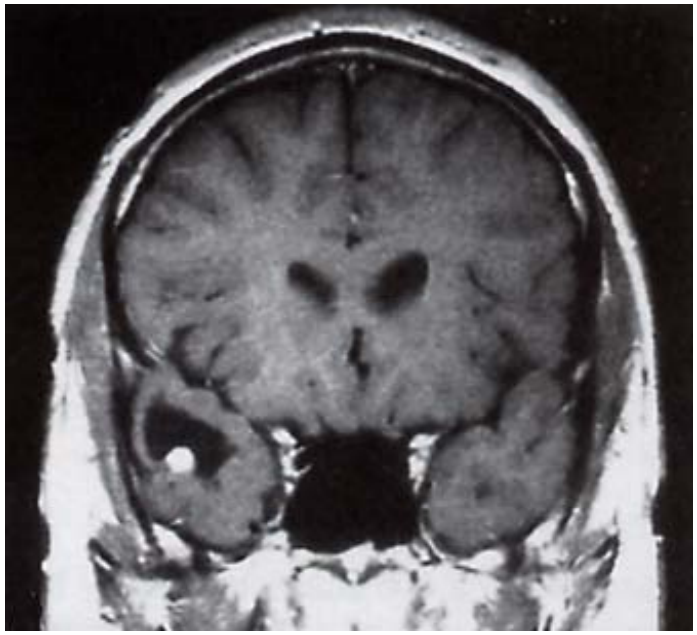
Pilocytic Astrocytoma





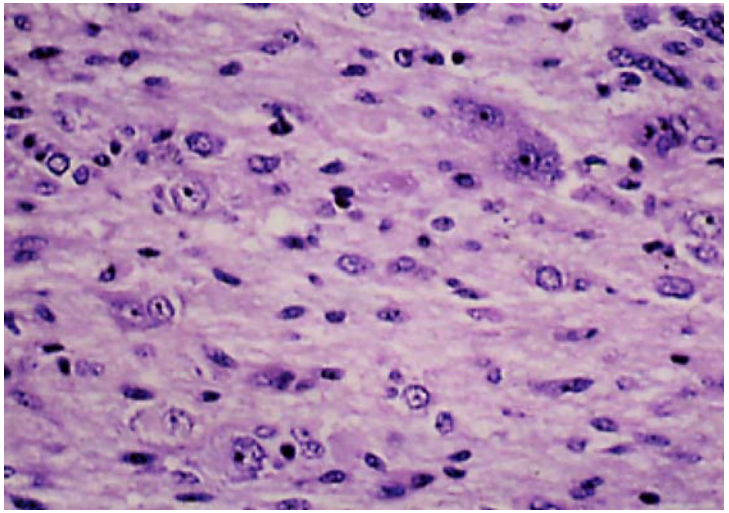






Ganglioglioma

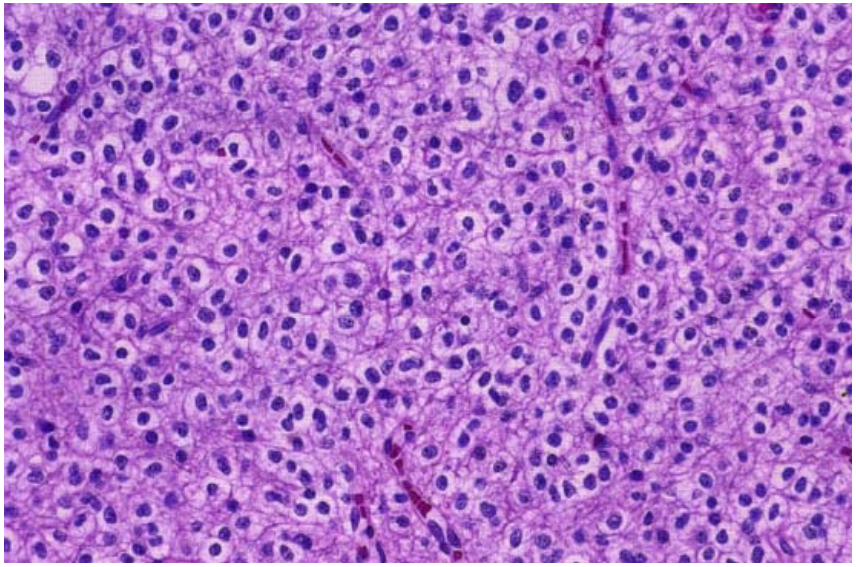
- Associated with seizures
- Children or young adults
- Cytic with enhancing mural nodule
- Often involves temporal lobe



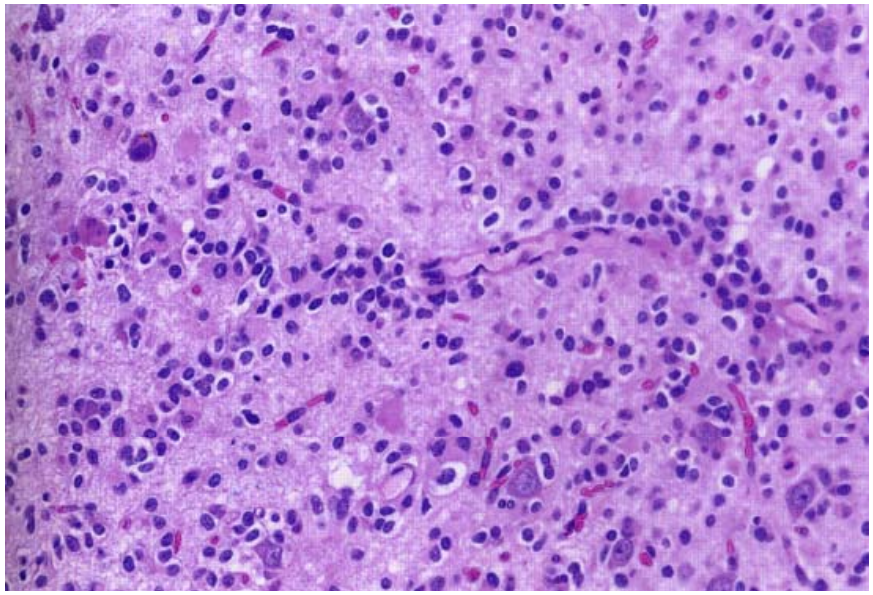
- Neoplastic neurons and glia
- Malignant progression involves the glial component

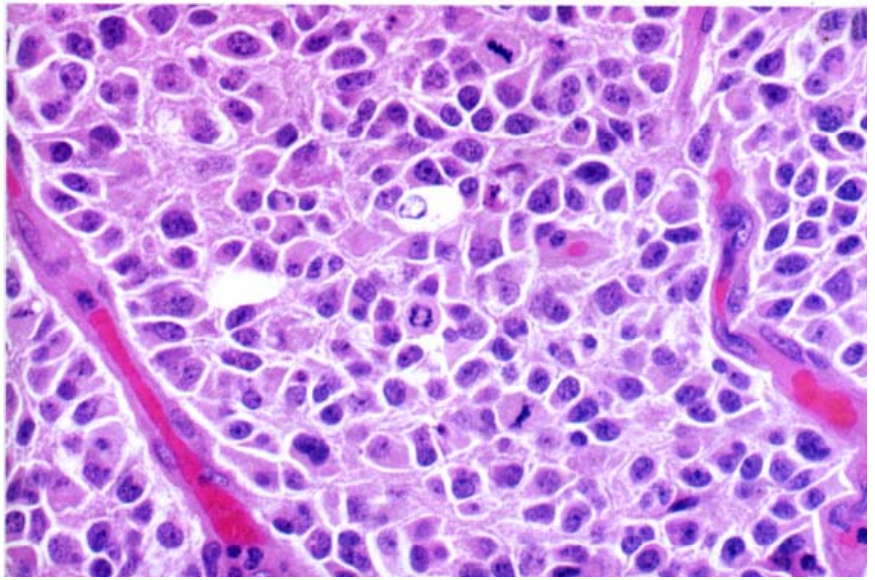
Oligodendroglioma

- Most common in forth and fifth decade
- Usually involve cerebral hemispheres
- Usually present with seizures and/or headache
- Composed of sheets of cells with round regular nuclei and clear cytoplasm (fried egg appearance)
- Dense network of branching capillaries
- Diffusely infiltrate the cortex and white matter
- Anaplastic oligodendroglioma shows atypia, mitoses, endothelial proliferation and necrosis
- Tumors with LOH of 1p and 19q are responsive to chemotherapy



Oligodendroglioma



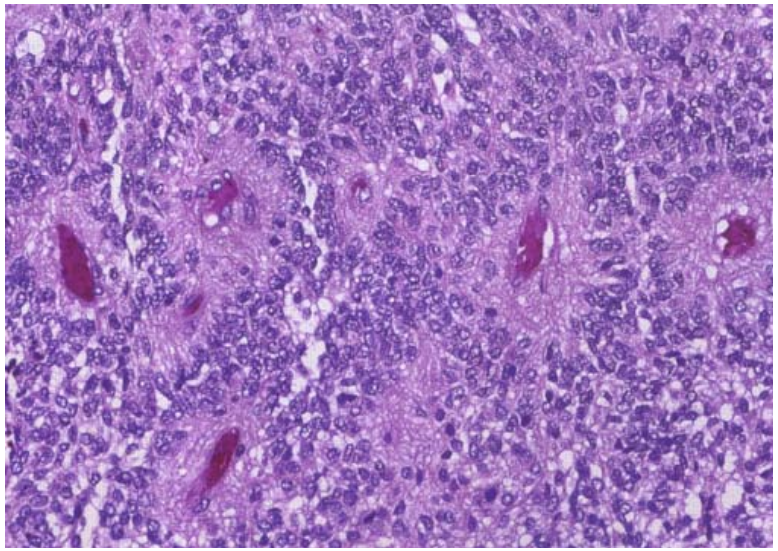


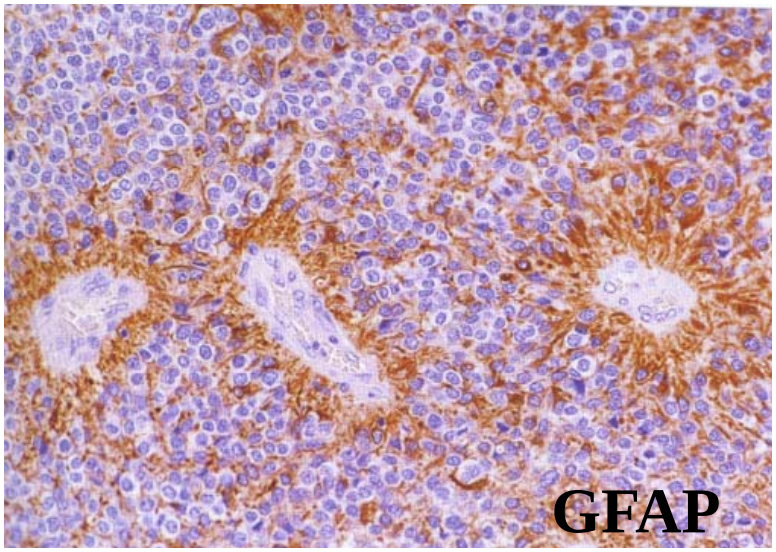
Anaplastic Oligodendroglioma

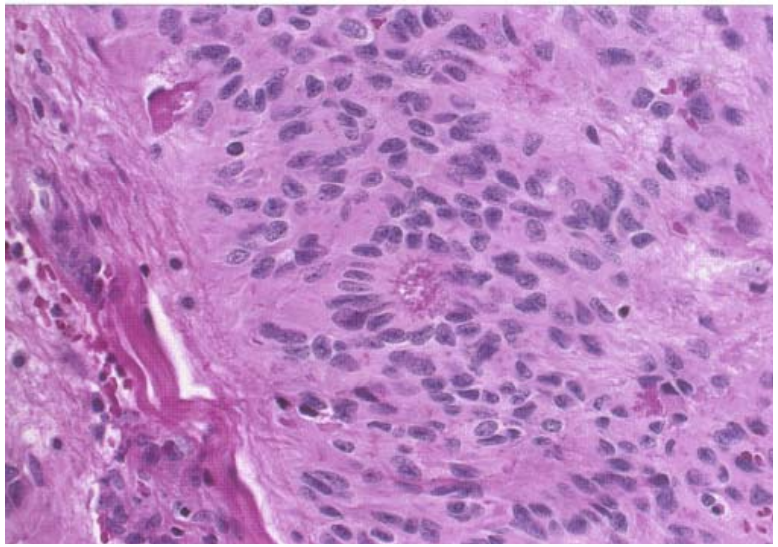
Ependymoma

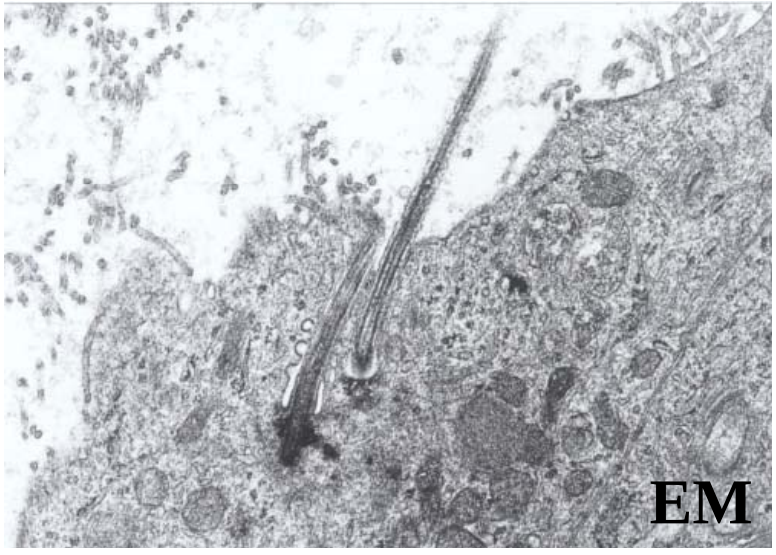
- Most common in children and young adults
- Arise adjacent to the ventricular system, most commonly in the posterior fossa and spinal cord
- Often present with signs of increased intracranial pressure, ataxia, motor or sensory deficits
- Distinctive histologic features include perivascular pseudorosettes and ependymal rosettes
- Tumor cells are usually GFAP+
- Ultrastructural features include cilia, microvilli and junctional complexes
- 5 year survival of about 50% after surgical resection

Ependymona





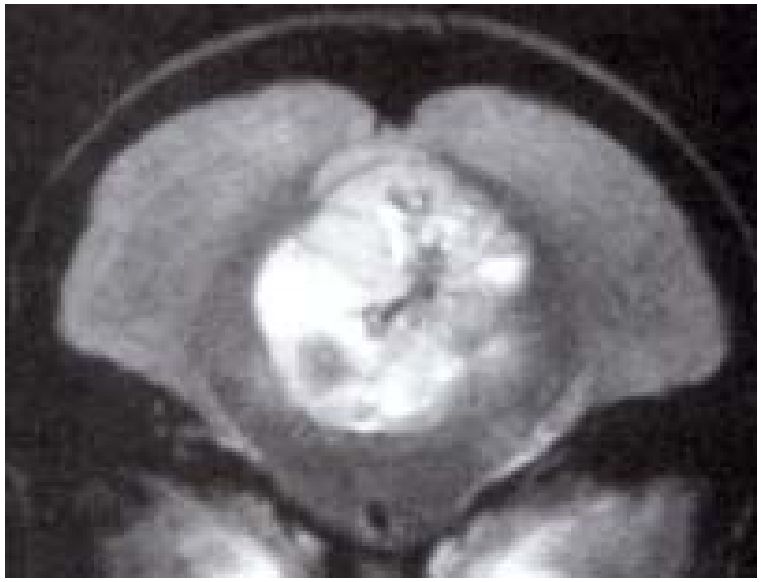




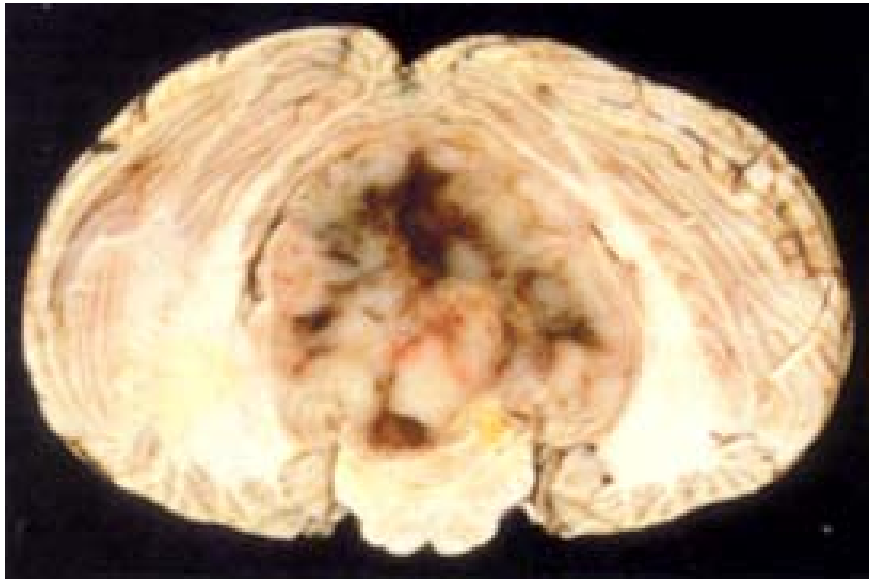
Medulloblastoma

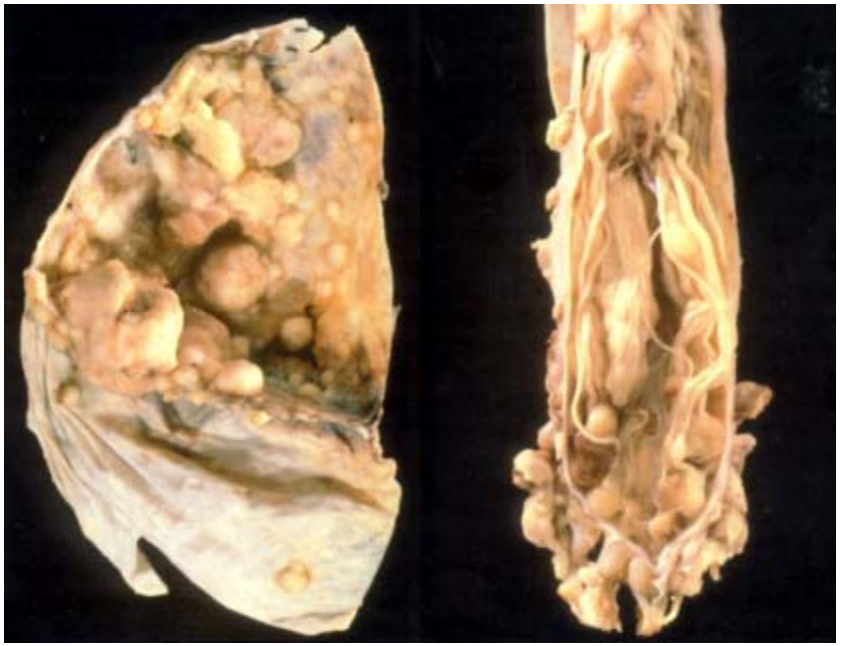
- Malignant, poorly differentiated tumor of the cerebellum
- Predominantly seen in children
- Present with ataxia and intracranial hypertension
- Composed of densely packed cells with hyperchromatic nuclei and scant cytoplasm
- Homer-Wright (neuroblastic) rosettes
- High mitotic activity
- Tumor cells may express neuronal or glial markers
- Often disseminates through the CSF (drop mets)
- Responsive to radiation and chemotherapy
- 5 year survival rate as high as 75%

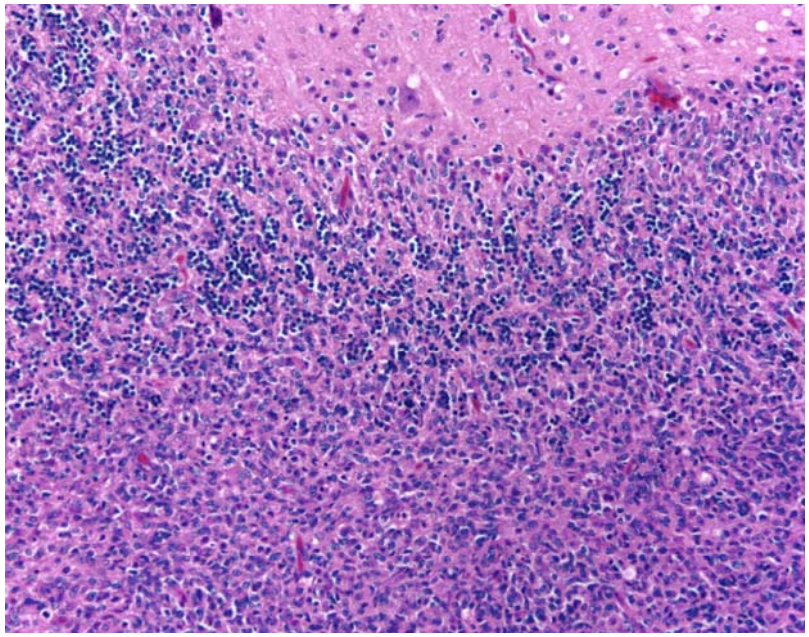
Medulloblastoma



MRI and gross images of a tumor in the vermis with CSF metastasis to the dura and cauda equina

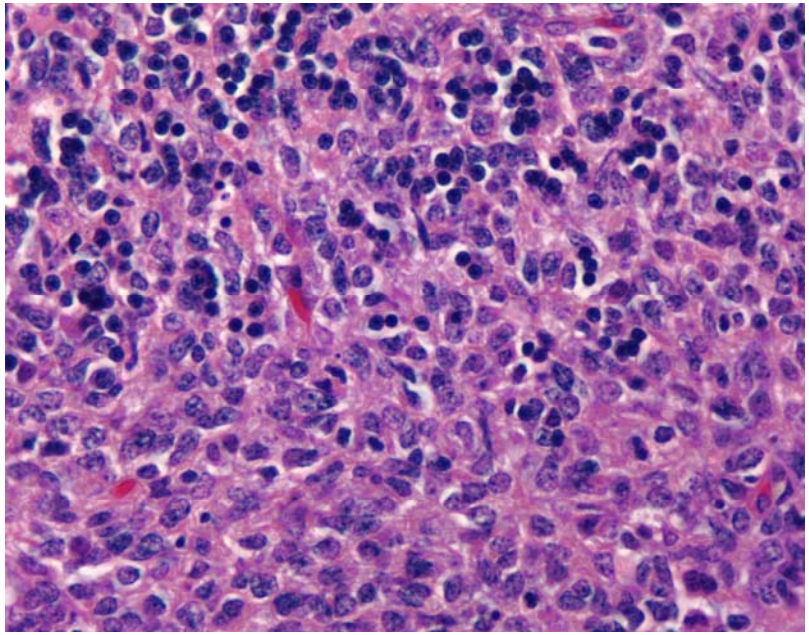


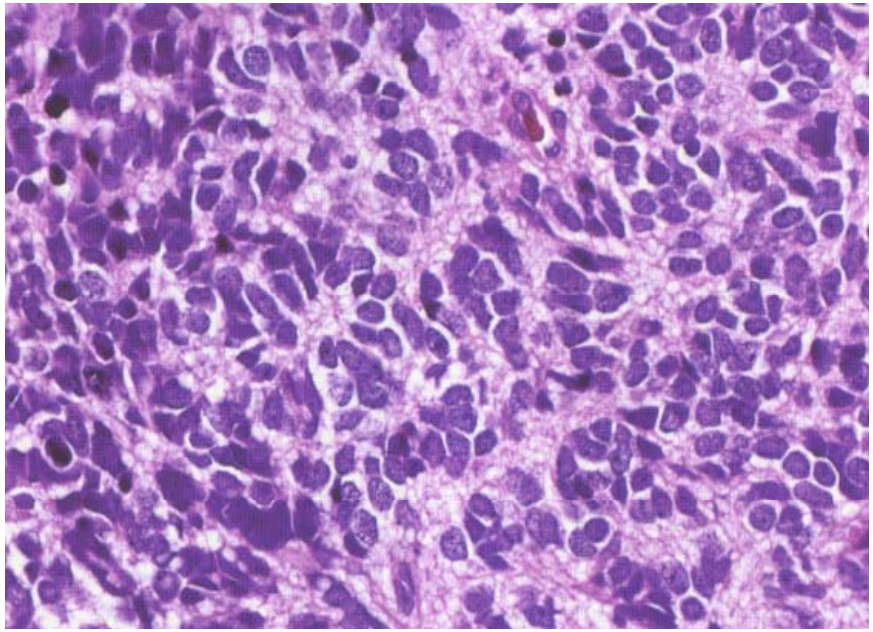




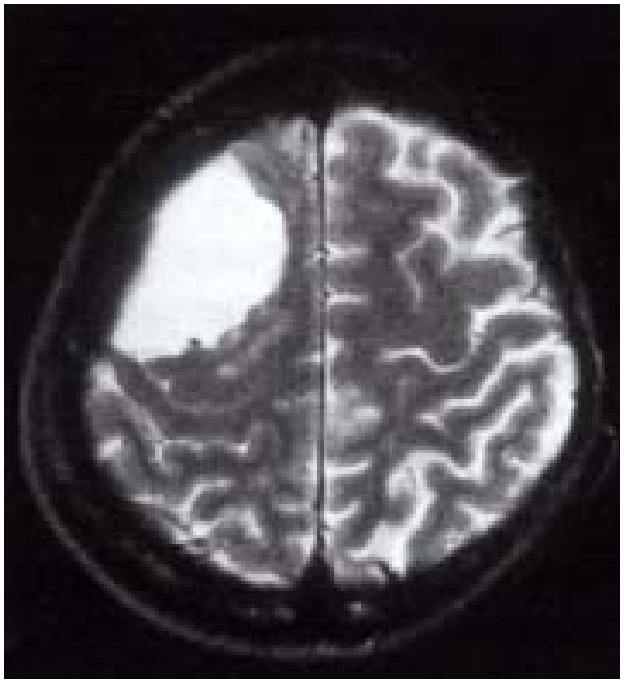
Medulloblastoma invading the cerebellar cortex.

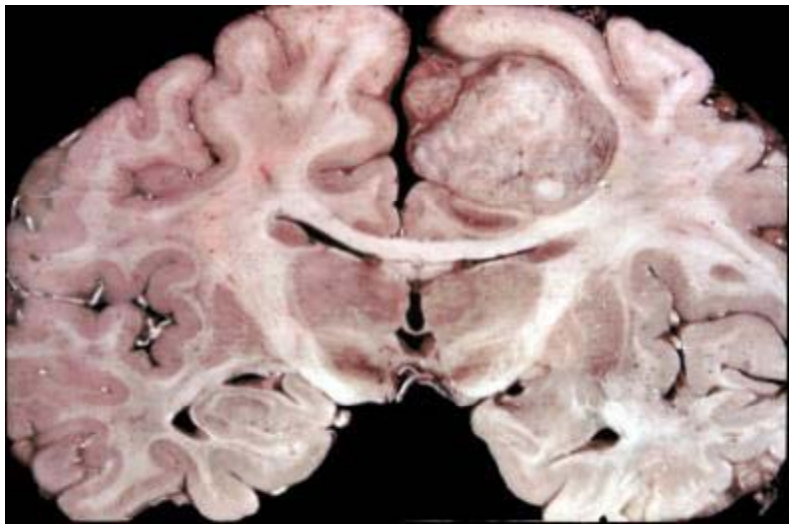
Note the difference between the tumor cells and granule cell neurons.





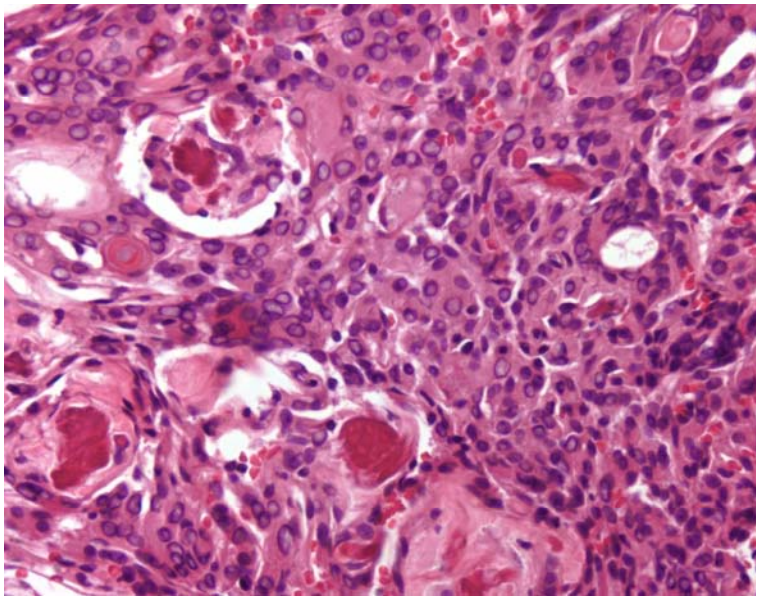
Meningioma



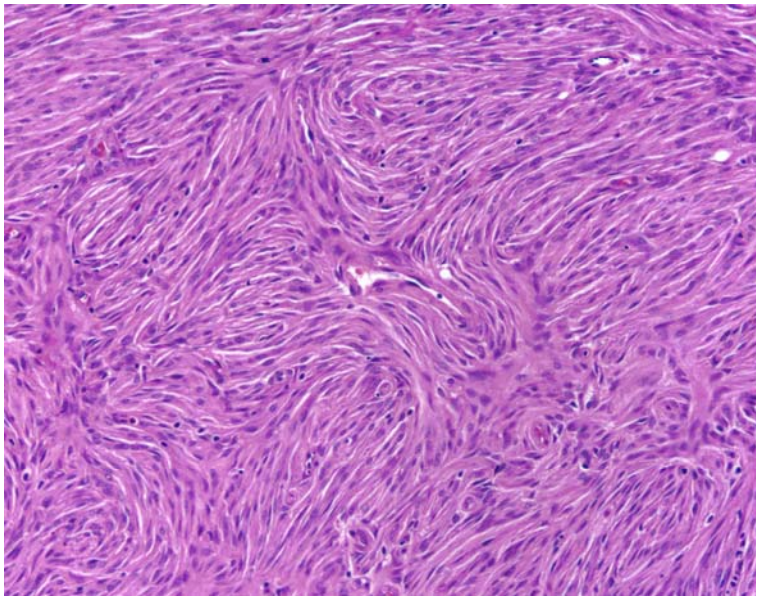


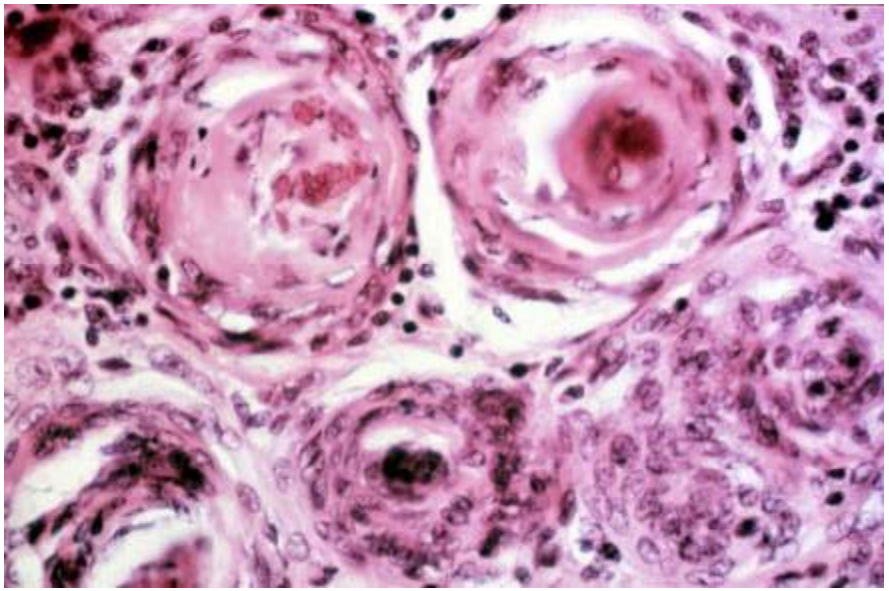
- Slow growing, benign tumors (WHO grade I)
- Most occur in adults
- female bias
- Imaging shows dural based enhancing mass
- Grow as well demarcated, firm-rubbery mass
- Attached to dura and compress adjacent brain
- Frequently invades dura and bone
- Invasion into brain indicates malignant behavior

Meningioma

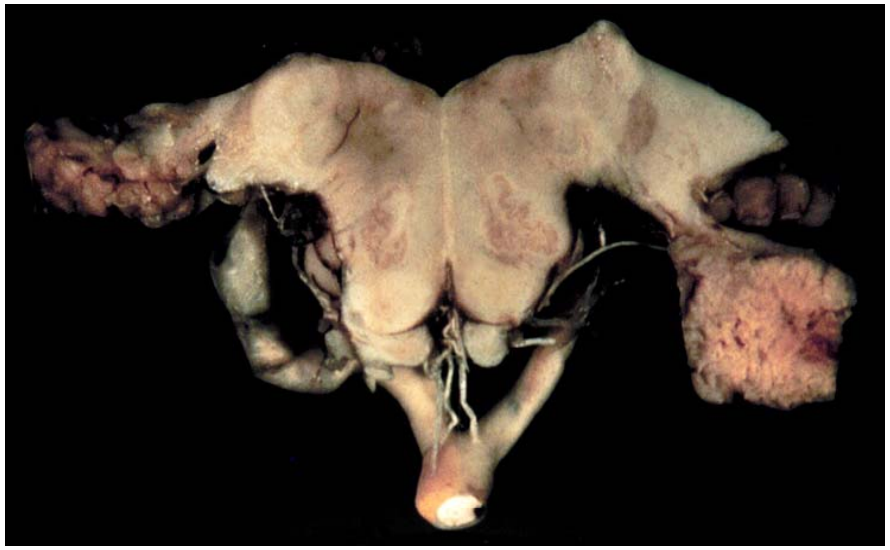


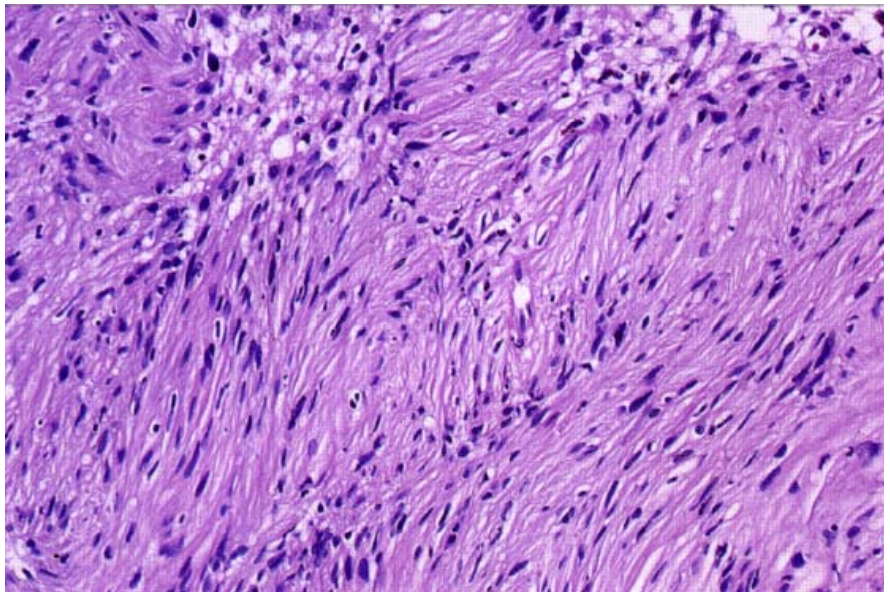
- Meningothelial memingiomas have whorls and psamomma bodies
- Fibroblastic meningiomas





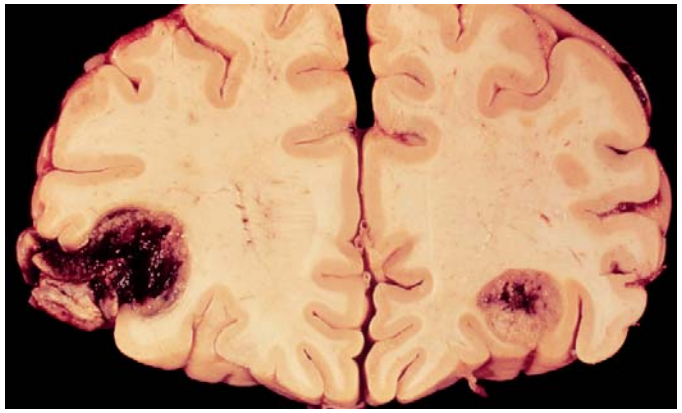
Schwannoma

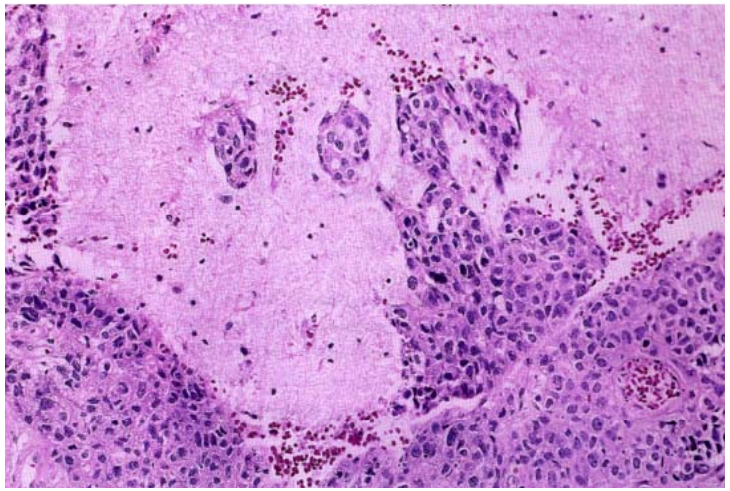




- Benign tumor of peripheral nerve (WHO grade I)
- Frequently arise from the spinal or cranial nerves
- Biphasic growth pattern hypercellular (Antoni A) and hypocellular (Antoni B)
- nuclear pallisading (Verocay bodies)
- Most are cured with surgery

Metastatic Carcinoma





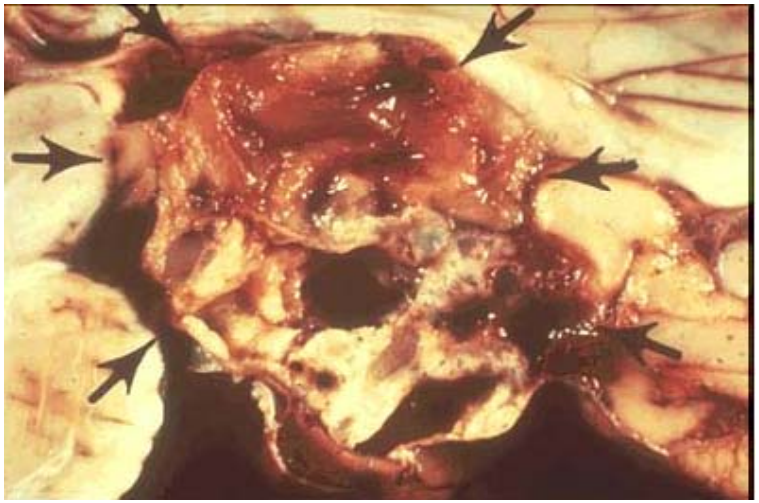
- Account for about 30% of adult brain tumors
- one or more discrete lesions, usually ring enhancing
- Frequently located in cerebrum or cerebellum
- Noninfiltrative growth pattern
- Shows histologic features of the primary tumor
- Most patients survive less than 1 year

Origin of Brain Metastases

- Lung (50%)
- Breast (15%)
- Skin/melanoma (10%)
- Kidney
- GI carcinoma

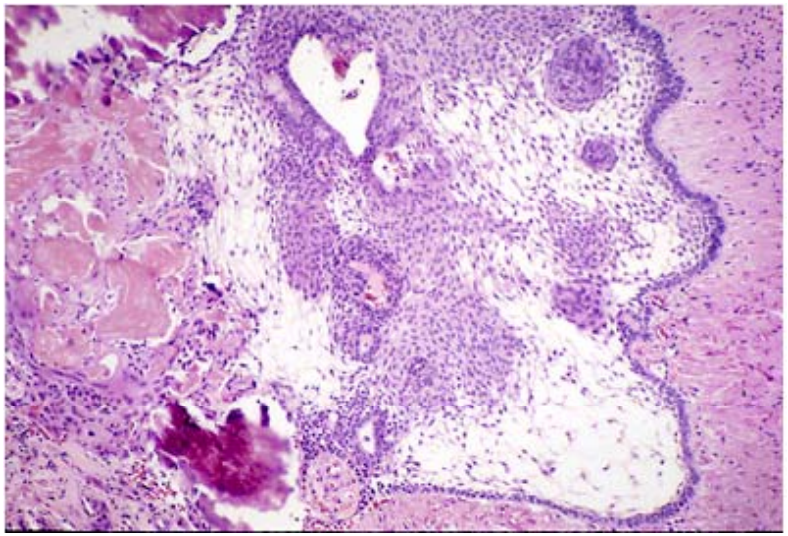
Lots of **B**ad **S**tuff **K**ills **G**lia

Craniopharyngioma



Most common non-neuroepithelial intracranial tumor in children

Suprasellar mass partially cystic, focally calcified,”Machine oil”



squamous epithelium with adamantinomatous or papillary growth pattern and nodules of “wet keratin”

Other Tumors of the Nervous System

- Pineal Parenchymal Tumor
- Germ Cell Tumor
- Primary CNS Lymphoma
- Pituitary Adenoma

Familial Cancer Syndromes

Neurofibromatosis 1	NF1	17	Neurofibromas Optic gliomas
Neurofibromatosis 2	NF2	22	Bilateral schwannomas Meningioma ependymomas
Von Hippel-Lindau	VHL	3	Hemangioblastomas
Tuberous Sclerosis	TCS1 TCS2	9 16	Subependymal Giant Cell Astrocytoma
Li-Fraumeni	p53	17	Astrocytoma, GBM PNET
Cowdens	PTEN	10	Dysplastic gangliocytoma of the cerebellum
Turcot	APC HNPCC	5 3,7	Medulloblastoma GBM
Nevoid Basal cell carcinoma syndrome	PTCH	9	Medulloblastoma