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?

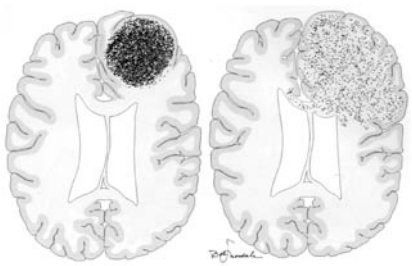
Epidemiology of Brain Tumors

- 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

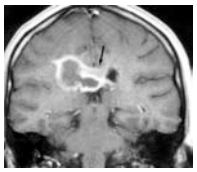
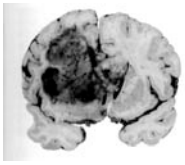
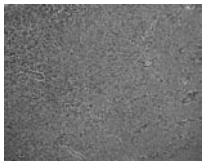
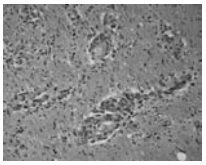


Well Circumscribe Diffusely Infiltrating

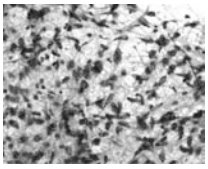
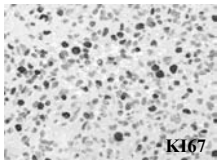
Glioblastoma Multiforme

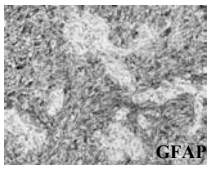
- Most common adult primary brain tumor
- Peak incidence is between 45 and 70
- Often present with seizures or subtle deficits
- MRI shows ring-enhancing lesion
- Glioma cells diffusely infiltrate the brain,
- But almost never metastasize to other organs
- Atypia, Mitosis, Endothelial proliferation,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

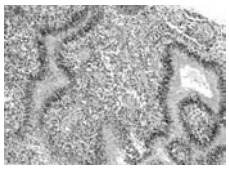
Glioblastoma Multiforme

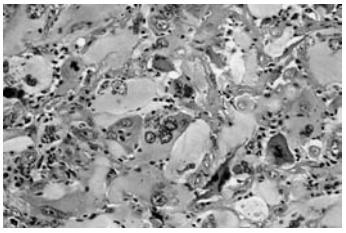





Glioblastoma Multiforme

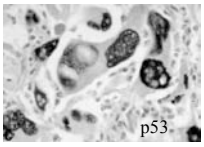



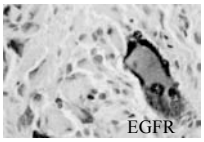






Giant cell GBM

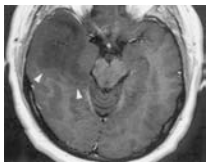
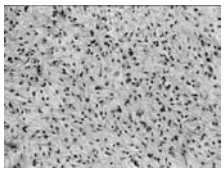
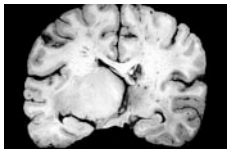
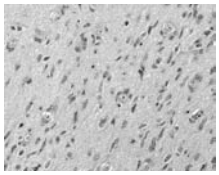




Low Grade Diffuse Astrocytoma

- 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**itoses	**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%)

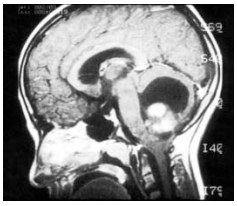
Secondary glioblastoma
-LOH 10q
-DCC overexpression (50%)

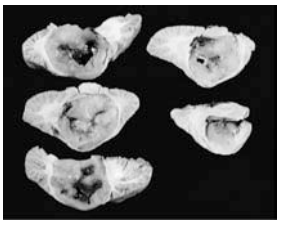
Primary glioblastoma
-EGFR overexpression (60%)
-LOH 10p and 10q
-PTEN mutations/loss (30%)
-P16 deletions (30%-40%)
-MDM2 overexpression (50%)

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

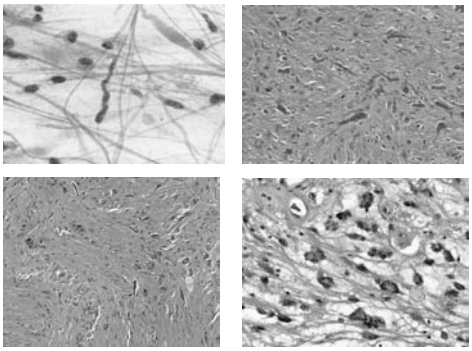
Pilocytic Astrocytoma

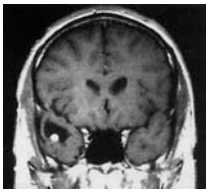




cystic with an enhancing mural nodule in the cerebellum

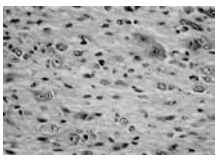
Pilocytic Astrocytoma





Ganglioglioma

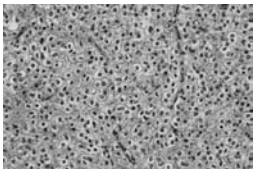
- Associated with seizures
- Children or young adults
- Cytic with enhancing mural nodule
- Often involves temporal lobe



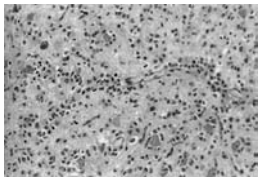
- Neoplastic neurons and glia
- Malignant progression involves the glial component

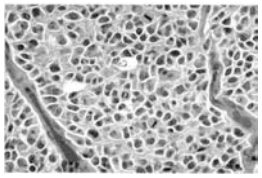
Oligodendroglioma

- 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



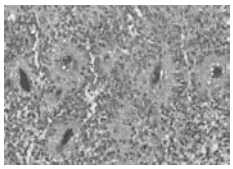


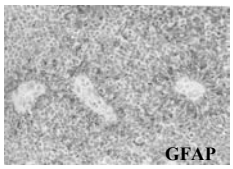
Anaplastic Oligodendroglioma

Ependymoma

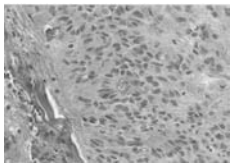
- Most common in children and young adults
- Arise adjacent to the ventricular system, most commonly in the posterior fossa and spinal cord
- Often present with signs of increased intracranial pressure, ataxia, motor or sensory deficits
- Distinctive histologic features include perivascular pseudorosettes 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

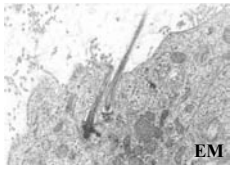
Ependymona





GFAP



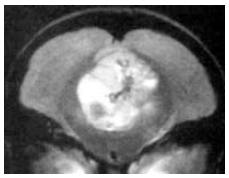


EM

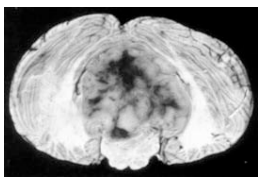
Medulloblastoma

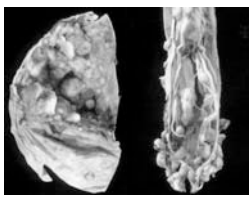
- Malignant, poorly differentiated tumor of the cerebellum
- Predominantly seen in children
- Present with ataxia and intracranial hypertension
- Composed of densely packed cells with hyperchromatic nuclei and scant cytoplasm
- Homer-Wright (neuroblastic) rosettes
- High mitotic activity
- Tumor cells 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%

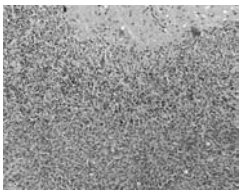
Medulloblastoma



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

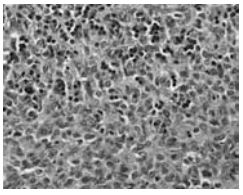


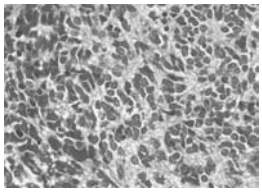




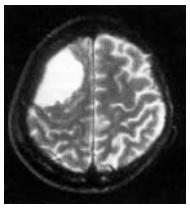
Medulloblastoma invading the cerebellar cortex.

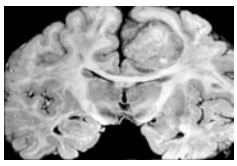
Note the difference between the tumor cells and granule cell neurons.





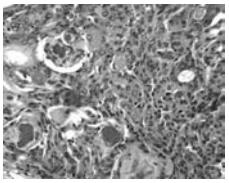
Meningioma

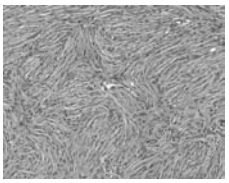


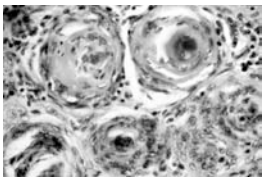


- Slow growing, benign tumors (WHO grade I)
- Most occur in adults
- female bias
- Imaging shows dural based enhancing mass
- Grow as well demarcated, firm-rubbery mass
- Attached to dura and compress adjacent brain
- Frequently invades dura and bone
- Invasion into brain indicates malignant behavior

Meningioma

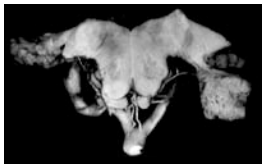


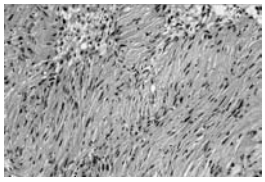




- Meningothelial memingiomas have whorls and psamomma bodies
- Fibroblastic meningiomas

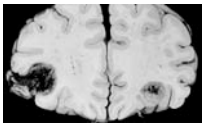
Schwannoma





- 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

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