CNS tumors

They are ether: 1- primary tumors 2- secondary (METASTATIC TUMORS)

1-primary tumors:

1- 2% of all CA, but 20% of CA in children.

Incidence: Intracranial 10-17/100,000.

Intraspinal 1-2/100,000

2- 50-75% are primary.

3-In children, majority are infratentorial.

4-In adults, majority are supratentorial.

5-Do not have premalignant or in situ stage.

6-Even low grade lesions can infiltrate widely.

7-Anatomic site can influence outcome, regardless of type & grade due to local effect or non-resectability.

Presentation: Localizing signs ± ↑ ICP

Assessment: History, Physical examination, Neurologic exam, LP (including cytology), CT, MRI, Brain angiography, Biopsy

Primary Tumors – Etiology:

1-Radiation: Often 5-25 years after treatment of pituitary adenoma or craniopharyngioma

2- Cell phones: Mobile phones use electromagnetic radiation

3-Inherited familial tumor syndromes: most AD linked to tumor suppressor gene inactivation

4-Neurofibromatosis Type I & Type II – Variety of CNS & peripheral nerve tumors ± other systemic manifestations

5-Tuberous sclerosis – CNS hamartomas, astrocytoma, subependymoma (TUBERS),

6- extracerebral lesions including benign skin lesions, renal tumors

7-Von Hippel-Lindau – hemangioblastoma, renal carcinoma, renal cysts

8-Li-Fraumeni – inherited p53 mutation glioma, many types of tumors

9-Immunosuppression

Classification of NS Tumors:

Classified according to cell of origin & degree of differentiation. However, slowly growing entities may undergo transformation into more aggressive tumors.

WHO grading system: Important for treatment.

1- Gliomas: Astrocytoma & variants, Oligodendroglia, Ependymoma

2- Neuronal Tumors: Central neurocytoma, Ganglioglioma, Dysembryoplastic neuroepithelial tumor

3- Embryonal (Primitive) Neoplasms: Medulloblastoma

4- Other Parenchymal Tumors: primary CNS Lymphoma, Germ Cell Tumors

5- Meningiomas

6- Nerve Sheath Tumors: Schwannoma, Neurofibroma

7- Metastatic Tumors

1-Glioma:

a- Astrocytoma:

Commonest glioma (glial tumor), Different types, Different age groups.

Many mutations especially in **p53, RB, PI3K, IDH-1 & IDH-2**

Positive immunostaining for IDH1 is important in identifying low grade **Ki-67** usually done for all cases.

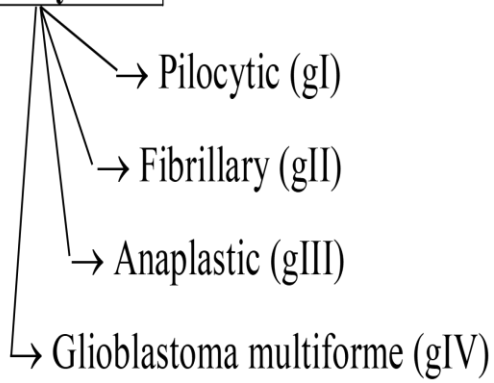
Gross Appearance: Solid or cystic, ± calcification, ± necrosis.

No clearly defined margin in low grade tumors

ASTROCYTOMA/ GRADE: **WHO Grading**: Mitotic activity , Vascular proliferation , NECROSIS

Some high grade tumors (Glioblastoma) occur de novo & not from transformation of low grad

(I) **Astrocytomas:**



Astrocytoma types:

	WHO Grade (1)Pilocytic Astrocytoma	WHO Grade (II) Diffuse Astrocytoma	WHO Grade (III) Anaplastic Astrocytoma	WHO Grade (IV) Glioblastoma
Age group	**Most in children**	**Any age, more in adults**	**Adult tumor**	**More in adults**
Site affected	, Cerebellum, optic pathways, 3rd ventricle	more in cerebrum	supratentorial but can occur anywhere in the brain.	Supratentorial enhancing tumor with edema
Most common cause	Molecular: KIAA1549-BRAF fusion is the most common genetic event in pilocytic astrocytoma. It is Negative for IDH mutations; May be positive for BRAF mutation	80% of WHO grade II gliomas have IDH mutations All astrocytomas are GFAP+, variable Ki-67	80% of WHO grade III gliomas have IDH mutations All astrocytomas are GFAP+, variable Ki-67	All astrocytomas are GFAP+, variable Ki-67
Morphology	Bipolar astrocytes, Microcysts & Rosenthal Fibers, eosinophilic granular bodies. Radiology: Often cystic with mural enhancing nodule.	Fine fibrillary network with minimal pleomorphism Proliferation of astrocytes-Pleomorphic,	More cellular and pleomorphic May show numerous Gemistocytes No microvascular proliferation or palisading necrosis	Cellular pleomorphic tumor with prominent mitoses Microvascular proliferation present PALISADING NECROSIS present

		hyperchromatic no mitotic figures Admixed in a fibrillary stroma		
GRADES	Low grade (relatively benign), no mitoses	Well differentiated/low grade	Aggressive Adult tumor	**---PROMINENT MITOSES**
NOTES	------	Commonest (up to 80% adult gliomas)	Aggressive Adult tumor,	The WHO grading system is important in prognosis & in outlining type of therapy

- Prognosis depend on grade, site & Age (child versus > 65)
- Low grade:
- Surgery
- Radiotherapy in selected cases

- High grade:
- Dexamethasone
- Surgery: Extent of tumour resection correlates with survival
- Radiotherapy
- Chemotherapy

b-OLIGODENDROGLIOMA:

Age group	• More in adults
Affected site	• in cerebrum
Cause	• 1p/19q co-deletion as well as IDH mutation is mandatory for diagnosis
Morphology	• Histology: • Small uniform cells with clear cytoplasm • Debate on !!Some mixed with astrocytoma!! • Absent or minimal mitoses • Typical FRIED EGG APPEARANCE
Grades	• WHO Grade: • Grade II • Anaplastic oligodendroglioma - Grade III
Notes	• Calcification is common • Better prognosis than astrocytoma similar grade

c- EPENDYMOMA: Slow growing tumor

Age group	Children, young adults
Affected site	Cell of origin: ependymal cells lining the ventricles in ventricle or spinal cord Can metastasize via CSF mostly 4th. Ventricle in 0-20years of age, in ≥ 20 years Lumbosacral region OR lat. or 3rd.ventricle
Morphology	Gross: gray, fleshy mass Radiology: Uniformly enhancing mass, well demarcated usually in ventricle or spinal cord
Grades	Grade II or Anaplastic Grade III
Notes	May cause obstructive hydrocephalus Rx: Surgery, Radiotherapy
Histology	Classical or Myxopapillary (usually located in lumbosacral region). Ependymal true rosettes and canals Perivascular pseudorosettes Myxopapillary is more loose & mucoid (papillae with myxomatous changes)

2- Embryonal (Primitive) Neoplasms:

Medulloblastoma Rapidly growing tumor

Age group	20% of pediatric brain tumors
Site affected	Roof of the 4th ventricle, obstructing pathway of C.S.F Any midline cerebellar or roof of 4th. ventricle tumor in a child is a medulloblastoma till proven otherwise! Can be lateral cerebellar, more in young adults
Morphology	
Histology	Sheets of small undifferentiated blue hyperchromatic cells with numerous mitoses Homer-Wright Rosettes Neurofibrillary background
Grades	WHO Grade IV
Cause	MYC amplification– poor. WNT - favorable
Notes	Primitive small cell (blue cell) tumor Hydrocephalus & ↑ICP occur early Rx.: Resection + Radiation entire neuraxis since spreads along CSF

3- MENINGIOMA

Age group	Most in adult females
Affected site	Arises from meninges on surface of brain or spinal cord Parasagittal, Falx, sphenoid, ventricles
Cause	Tumor cells contain PR receptors NF2 gene inactivating mutation, even in 50% of non-NF2 meningiomas
Morphology	Well-defined solid Dural-based mass Compressing brain but easily removed Can invade the Skull & Venous sinuses, but this does not affect grade Can invade the underlying brain: IMPORTANT in prognosis: increased recurrence rate
Grades	Majority are benign but may recur Some types more likely to be aggressive
Many subtypes	Syncytial , Fibroblastic , Transitional, Psammomatous (PSAMMOMA BODIES) ,Secretory, Many Others
Notes	Prognosis depends on SIZE, LOCATION, GRADE & Surgical ACCESSIBILITY

4- Neuronal tumors

Central neurocytoma	▪ Low grade intraventricular (3rd or Lat) ▪ Neuropil
Ganglioglioma	▪ Age ≤ 30yrs, presents with seizures ▪ Mixture of low grade Astro. + mature neurons ▪ Anywhere but most temporal
Dysembryoplastic neuroepithelial tumor	▪ Low grade childhood tumor ▪ Nodular tumor in superficial temporal lobe ▪ Seizure

5- LYMPHOMA

Primary usually multiple peri-ventricular nodular tumor (1% of IC-tumors)

High grade B cell Lymphoma

Most common CNS tumor in immunosuppressed

Most frequent in AIDS patients with EBV infection.

Poor response to chemoRx

May be secondary lymphoma due to spread from peripheral lymphoma to CNS is usually to meninges rather than into brain.

6- GERM CELL TUMORS: Primary – midline (pineal & suprasellar) 90% - First 2 decades of life

Most common type: Germinoma

2-sacondry tumors:

METASTATIC TUMORS:

	Brain metastases	Leptomeningeal Metastases
Origin tumor site	Origin of solid primary tumors: Lung (most common) , Breast ,Gastrointestinal, Kidney, Melanoma Less common but with special propensity to metastasize to brain: Germ cell tumors, Thyroid	Clinically evident in 8% of patients with metastases, Breast, lung, gastrointestinal adenocarcinoma, Melanoma, Lymphoma & Leukemia
Way of metastation	disseminate by blood & parallel anatomic distribution of regional blood flow: Grey-white matter junction Border zone between MCA and PCA distributions	Haematogenous Shedding of cells into subarachnoid space from superficial brain metastasis Growth along peripheral nerves (squamous cell carcinoma, non-Hodgkin lymphoma)
Notes	More common than primary Often multiple Marked edema is seen around metastasis	Meningeal carcinomatosis

Spinal Cord tumors

- Extraspinal: Metastatic, Lymphoma
- Extradural intraspinal: Metastatic, Lymphoma
- Intradural:

  Extramedullary: Schwannoma

  Meningioma

  Intramedullary: Ependymoma

  Astrocytoma