TUMORS OF THE CNS

Tumors of the CNS may originate in the brain or spinal cord (primary tumors), or metastatic tumors. Both benign and malignant CNS tumors are capable of producing neurologic impairment depending upon their site. Primary CNS tumors or intracranial tumors include: tumors arising from *constituent cells of the brain* (with the sole exception of microglial cells) and from *the supporting tissues.* Childhood brain tumors arise from more primitive cells (e.g. neuroblastoma, medulloblastoma).

The term glioma is used for all tumors arising from neuroglia, or more precisely, from neuroectodermal epithelial tissue. Gliomas are the most common of the primary CNS tumors and collectively account for 40% of all intracranial tumors. They include tumors arising:

- *from astrocytes* (astrocytomas and glioblastoma multiforme);
- *from oligodendrocytes* (oligodendroglioma);
- *from ependyma* (ependymoma); *from choroid plexus* (choroid plexus papilloma).

Gliomas are disseminated to other parts of the CNS by CSF but they rarely ever metastasize beyond the CNS.

Tumors of the nervous system have unique characteristics

• They do not have detectable 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 and poor prognosis.

• The anatomic site of the neoplasm can influence outcome independent of histologic classification due to local effects.

• Even the most highly malignant gliomas rarely spread outside of the CNS.

Glioma

1- Astrocytomas

They are the most common type of gliomas. In general, they are found in the late middle life with a peak in 6th decade of life. They occur predominantly in the cerebral hemispheres, and occasionally in the spinal cord. The most common presenting signs and symptoms are seizures, headaches, and focal neurologic deficits related to the anatomic site of involvement.

Morphologic Features

WHO classification of astrocytomas is widely used which divides them into 3 grades from grade II (low grade) to grade IV (glioblastoma multiforme).

GRADE II DIFFUSE ASTROCYTOMA (fibrillary, infiltrating) it is a low-grade tumor having good prognosis which mainly occur in children. the tumor with ill-defined boundaries – For this reason, it may be difficult to completely remove these tumors during surgery.

GRADE III (ANAPLASTIC) ASTROCYTOMA. It generally evolves from lower grade of astrocytoma.

GRADE IV ASTROCYTOMA (GLIOBLASTOMA MULTIFORME).

It is known that this tumor arises by neoplastic transformation of mature astrocytes. It is the most aggressive of astrocytomas.

GROSS Grade II and III astrocytomas are poorly defined, gray, infiltrative tumors that expand and distort the invaded brain without forming a discrete mass. cut sections of the tumor is firm or soft and gelatinous; cystic degeneration may be seen.

In glioblastoma, there is variation in the gross appearance There are yellow necrotic tissue with cystic degeneration and hemorrhage.

MICROSCOPY: in low-grade (WHO grade II) astrocytomas there are a mild to moderate increase in the number of glial cell nuclei, variable nuclear pleomorphism, and an intervening astrocytic cell processes that give the background a fibrillary appearance. The transition between neoplastic and normal tissue is indistinct, and tumor cells can be seen infiltrating normal tissue many centimeters from the main lesion.

Anaplastic astrocytomas are more densely cellular and have greater nuclear pleomorphism; mitotic figures are present.

Glioblastoma has a histologic appearance similar to that of anaplastic astrocytoma, as well as either necrosis (commonly present as serpiginous bands of necrosis with palisaded tumor cells along the border) or microvascular endothelial proliferation.

N.B pilocytic Astrocytoma (WHO grade I) : relatively benign , often cystic, typically occur in children and young adult and involve the cerebellum necrosis and mitosis are absent and contain microcysts microscopically.

2- Oligodendroglioma

It is an uncommon glioma of oligodendroglial origin and may develop in isolation or may be mixed with other glial cells. The tumor commonly presents in 3rd to 4th decades of life. It occurs in the cerebral hemispheres, most commonly in the frontal lobes or within the ventricles.

X-ray examination and CT scan reveal a well-defined mass with small foci of calcification.

According to the WHO classification oligodendroglioma grade into 2 different categories grade II and III (anaplastic) which charecterised by necrosis and microvascular/ endothelial proliferation.

GROSS is well-circumscribed, grey-white and gelatinous mass having cystic areas, foci of hemorrhages and calcification.

MICROSCOPY The tumor is characterised by uniform cells with round to oval nuclei surrounded by a clear halo of cytoplasm and well-defined cell membranes. Tumor cells tend to cluster around the native neurons forming *satellitosis.*

3- Ependymoma

Ependymoma is derived from the layer of epithelium that lines the ventricles and the central canal of the spinal cord. It occurs chiefly in children and young adults (below 20 years of age). Typically, it is encountered in the fourth ventricle (posterior fossa tumor).

GROSS Ependymoma is a well-demarcated tumor but complete surgical removal may not be possible due to close proximity to vital structures in the medulla and pons.

MICROSCOPY The tumor is composed of uniform epithelial (ependymal) cells forming rosettes, canals and perivascular pseudorosettes.

POORLY-DIFFERENTIATED AND EMBRYONAL TUMORS

Medulloblastoma

Medulloblastoma is the most common variety of primitive neuroectodermal tumor. The most common location is the cerebellum in the region of roof of fourth ventricle, in the midline of cerebellum, in the vermis, and in the cerebellar hemispheres. Medulloblastoma is a highly malignant radiosensitive tumor and can spreads to local as well as to distant sites.

GROSS The tumor protrudes into the fourth ventricle as a soft, grey-white mass or invades the surface of the cerebellum.

MICROSCOPY Medulloblastoma is cellular composed of small, poorly-differentiated cells with ill-defined cytoplasmic processes grow in sheets and a tendency to be arranged around blood vessels and occasionally forms (Homer-Wright rosettes) in which the nuclei of the malignant cells disposed in circular fashion about tangled cytoplasmic process.

PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

Primary CNS lymphoma, occurring mostly as diffuse large B cell lymphomas, accounts for 2% of extranodal lymphomas and 1% of intracranial tumors. It is the most common CNS neoplasm in immunosuppressed persons, in whom the tumors are nearly always positive for the oncogenic Epstein-Barr virus. In non-immunosuppressed populations, the age spectrum is relatively wide, with the incidence increasing after 60 years of age. Regardless of the clinical context, primary brain lymphoma is an aggressive disease with relatively poor response to chemotherapy as compared with peripheral lymphomas.

Patients with primary brain lymphoma often are found to have multiple tumor nodules within the brain parenchyma, yet involvement outside of the CNS is an uncommon late complication. Lymphoma originating outside the CNS rarely spreads to the brain parenchyma; when it happens, tumor usually is also within the CSF or involvement of the meninges.

TUMORS OF MENINGES

The most common tumor arising from the pia-arachnoid is meningioma accounting for 20% of intracranial tumors.

Meningioma

Meningiomas arise from the cap cell layer of the arachnoid. Their most common sites are in the front half of the head and include: lateral cerebral convexities, midline along the falx cerebri adjacent to the major venous sinuses parasagittally, and olfactory groove. They are usually found in 2nd to 6th decades of life. Most meningiomas are benign and can be removed successfully.

GROSS Meningioma is well-circumscribed, solid, spherical mass of varying size (1-10 cm in diameter). The tumor is generally firmly attached to the dura and indents the surface of the brain but rarely invades it**.** The overlying bone usually shows hyperostosis. Cut surface of the tumor is firm and fibrous, sometimes with foci of calcification.

MICROSCOPY Meningiomas are divided into 5 subtypes:

- 1. Meningotheliomatous (syncytial) meningioma. named for whorled clusters of cells without visible cell membranes that sit in tight groups
- 2. Fibrous (fibroblastic) meningioma with elongated cells and abundant collagen deposition between them.
- 3. Transitional (mixed) meningioma. which shares features of the syncytial and fibroblastic types.
- 4. Psammomatous, with numerous psammoma bodies.
- 5. Anaplastic (malignant) meningioma. Rarely, a meningioma may display features of anaplasia and invade the underlying brain or spinal cord. This pattern of meningioma is associated with extraneural metastases, mainly to the lungs.

Metastatic Tumors

Metastatic lesions, mostly carcinomas, account for approximately one fourth to one half of intracranial tumors. The most common primary sites are lung, breast, skin (melanoma), kidney, and gastrointestinal tract—together these account for about 80% of cases. Metastases form sharply demarcated masses, often at the gray-white junction, and elicit edema.

The boundary between tumor and brain parenchyma is sharp at the microscopic level with surrounding reactive gliosis.

In addition to the direct and localized effects produced by metastases, paraneoplastic syndromes may involve the peripheral and central nervous systems, sometimes even preceding the clinical recognition of the malignant neoplasm patients with paraneoplastic syndromes have antibodies against tumor antigens which may give rise to :

- **Subacute cerebellar degeneration** with destruction of Purkinje cells resulting in ataxia,
- **Limbic encephalitis** causing a subacute dementia
- **Subacute sensory neuropathy** leading to altered pain sensation, with loss of sensory neurons from dorsal root ganglia.