CHAPTER
23 Tumors of Central Nervous System

Malignant tumors of the central nervous system (CNS) affect the brain (85% of cases) and spinal cord (15% of cases). These tumors represent a great challenge to pathologists and clinicians. The number of possible tumors of CNS is immense, with a total of 125 histologic types and 15 variants of meningioma alone. The pathologist is faced with the problem of diagnosing a given tumor ac-curately on minute stereotactic samples or cytology smears and give a rapid decision. The neurosur-geon has to excise the tumor adequately without causing neurological morbidity. The medical onco-logist is confronted with the problem of blood-brain barriers which limits chemotherapy pene-tration into the tumor. The adoption of post-operative radiotherapy in the management of astrocytomas had signicantly improved treatment outcome of low-grade astrocytomas, but not the high grade glioblastoma. Genetic and molecular studies of these tumors may hopefully lead to the development of a more effective and individ-ualized targeted therapy in the future.

BRAIN TUMORS

GENERAL CONSIDERATIONS

Basic Histology of Numerous Cell Types

A good knowledge of the normal brain histolo -gy is necessary in order to comprehend the exten -sive profile of brain tumors (Fuller and Burger, 2007). The following is a concise outline of the main cell types.

Neuronal cells

Nerve cells are present in gray matter, basal ganglia and brain stem. Neuronal cells have abun-dant cytoplasm with surface processes (dendrites). The nucleus has prominent nucleolus. Pineal body cells are specialized neuronal cells.

Glial Cells

1. Oligodendroglial cells: so named because of the few cytoplasmic processes. They are present main -ly in gray matter, appear rounded with perinuclear halos and may be attached to nerve cells (satel-litosis).

2. Astrocytes are supporting glial cells present mainly in white matter and characterized by many fibrillary cytoplasmic processes. Astrocytes change in shape with senescence or brain injury. Corpora amylacia is a senile change, but, with injury astro-cytes becomes rounded with eosinophilic cyto-plasm (gemistocytes) which is an early reaction. The change of astrocytes to a spindle shape (fibrillary gliosis) is characteristic of chronic or healed lesions and may be associated with hyaline eosinophilic bodies or carrot-shaped Rosenthal fibers in brain matrix.

3. Ependymal cells: These are cuboidal or columnar cells which line the ventricular system (both brain surface, as well as, choroid) and the central canal of spinal cord.

4. Microglial cells are the intrinsic phagocytic cells of brain. They are small elongated cells with rod-shaped nuclei. They are evident in focal or diffuse pattern in response to injury. *Macrophages* are larger phagocytic cells that migrate to the brain from blood in reaction to infarcts and demyelination diseases. Both microglia and macrophages are CD68 positive.

5. Choroid cells: These cells together with ependymal cells form the choroid plexus present in ventricles and functions to produce CSF. Choroid is also present at surface of brain where it lines the dura.

Brain Coverings

The *dura mater* is a double layer of fibrous tissue. The outer layer represents the periosteum of skull bone, and the inner layer folds to form the falx cerebri and tentorium cerebelli. The *pia-arachnoid (leptomeninges)* forms a continuous layer under the dura. Melanocytes are normally present in leptomeninges, most abundant in front of brain stem.

Incidence

Malignant brain tumors contribute about 3% of adult cancers and 25% of pediatric malignancies. The incidence rate is 8 per 100,000 in males and 5 per 100,000 in females. Two age peaks are evident, the first in the first decade and

the other in adult life. The first peak is attributed to the high frequency of medulloblastoma in the pediatric age, whereas, the second peak is due to the predo-minance of glioblastoma in adults. Males predomi-nate in gliomas (2:1), but females predominate in meningiomas. About 50% of tumors of CNS are benign.

Etiology

1. Genetic predisposition: Only 4% of brain tumors are attributed to hereditary syndromes, and are the result of mutation of specific tumor suppressor genes (Table 23-1). All these syndromes are autosomal dominant, hence, are transmitted to 50% of offsprings.

2. Ionizing radiation: Cranial radiation to meningiomas, scabies and leukemia predisposes to gliomas.

3. Immunosuppression: AIDS or post-transplant patients predisposes to primary brain lymphomas due to associated EBV infection.

4. Chemicals: Industrial exposure to vinyl chloride predisposes to gliomas.

Molecular Oncogenesis

1. Glioblastoma: Two models were proposed to explain the development of primary and secondary subtypes of glioblastoma (Fig 23-1). Primary or *"de novo" glioblastoma*, account for 95% of cases, generally arise in older patients with short history (6 months) and is more prone histologically to be of the small cell variant. Conversely, *secondary glioblastoma* is less common (5%), affects younger patients with long history (5 years). Primary glioblastoma arises directly form glial stem cells and the main gene alterations involve p 16, EGFR and PTEN. By contrast, secondary glioblastoma progresses stepwise from lower grade astrocytomas, with TP53 as the common and early gene mutation.

Both oncogenesis models have common features distinctive from other gliomas, namely: deletion or loss of heterozygosity of chromosome 10 (LOH 10q), TP53 mutation, EGFR amplification, activation of two signal transduction pathways (RAS/MAPK and PI3K) resulting in tumor cell proliferation, as well as, arrest of apotosis (both are important causes of chemoresistance of glioblastoma). Glioblastomas also secrete matrix metalloproteinases (MMP) which degrade the extracellular matrix and facilitate tumor invasion.

2. Oligodendrogliomas have a distinctive deletion of two chromosomes, namely 1 p and 19q.

3. Ependymomas commonly exhibits deletion of chromosome 22, namely, d (22q), where the neurofibromatosis gene NF-2 is located.

4. Medulloblastoma shows genetic alterations in two signal pathways which regulate the cell cycle, namely: the sonic hedgehog Shh pathway (Gorlin syndrome) and Wnt signal pathway (Turcot syndrome).

5. Meningioma: the main chromosomal loss in

Table 23-1 Brain Tumors of Hereditary origin

Syndrome	Gene	Tumor
Neurofibromatosis (type 1)	NF-1	Astrocytoma, Optic nerve glioma
Neurofibromatosis (type 2)	NF-2	Acoustic neuroma, meningioma, ependymoma
Cowden	PTEN	Dysplastic gangliocytoma
Retinoblastoma	Rb	Pineoblastoma, glioma, meningioma
Li-Fraumeni	TP53	Neuroblastoma, Medulloblastoma
Gorlin	PTCH	Medulloblastoma, meningioma
Tuberous sclerosis	TSCI, TSC2	Subendymal giant cell astrocytoma
Turcot	APC MLH1	Medulloblastoma Astrocytoma, ependymoma
Von Hipple-Lindau	VHL	Hemangioblastoma

(Louis et al, 2007)

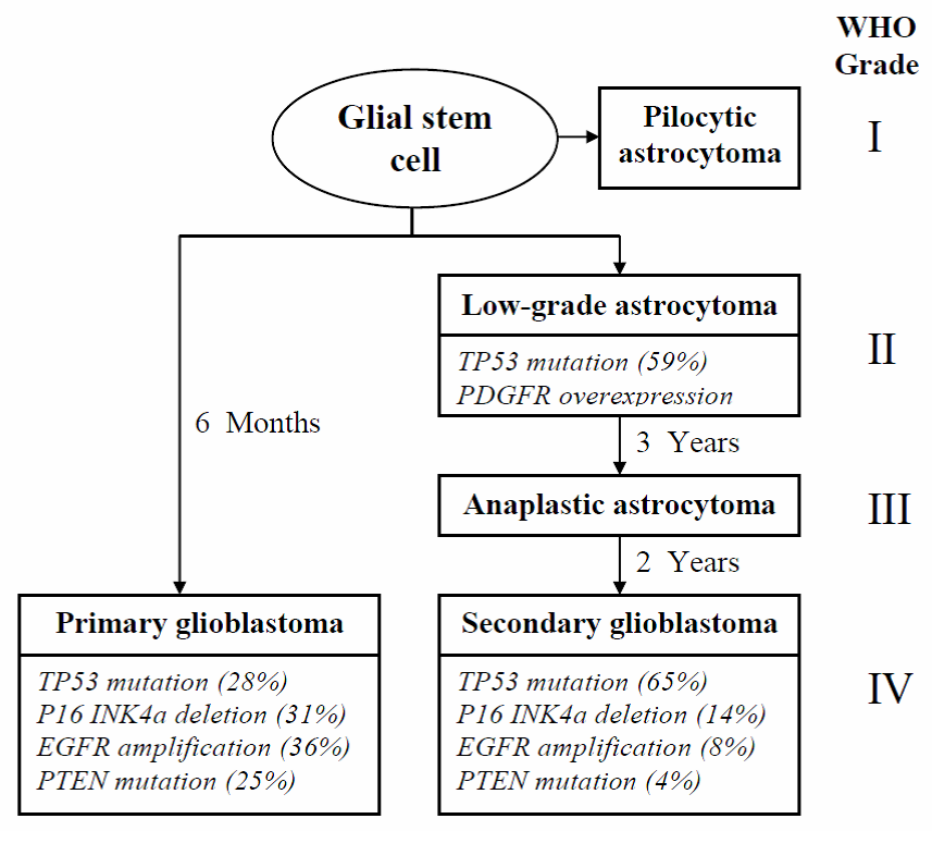

Fig 23-1 *The molecular oncogenesis of glioblastoma. Primary glioblastoma or de novo (95% of cases) arises directly from glial stem cells and the main gene alterations involve p16, EGFR and PTEN. Conversely, secondary glioblastoma (5% of cases) progresses stepwise from lower grade astrocytomas, with TP53 as the common and early gene mutation. Pilocytic astrocytoma is a stable tumor and does not progress to higher grade astrocytomas (Louis et al, 2007).*

benign meningioma is deletion of chromosome 22q, (the location of neurofibromatosis-2 gene (NF2, merlin) a tumor suppressor gene which controls cell proliferation. Progression of benign to atypical meningioma results from other deletions, especially 1p (ALPL gene), and malignant meningioma associated with loss of 9p (CDKN2A gene) and amplification of 17q. Expression of vascular endothelial growth factor (VEGF) is the cause of edema and invasive properties frequently observed with meningiomas.

Classification

Bailey and Cushing in 1920 introduced the first classification of brain tumors. They proposed that tumors arise from *embryonic cell remnants* which are arrested at various stages of development. However, at present it is generally accepted that cancer develops from *stem cells*, not from embryonic or adult cells, and that different phenotypes of tumors represent different differentiation lines of stem cells. The stem cell theory of cancer is applicable to brain tumors, in view of recent discovery of adult stem cells in the normal brain and malignant stem cells in glioblastoma. Recently, an *updated WHO classification* of brain tumors was reported (Louis et al, 2007) based upon the differentiation lineage of stem cells, with emphasis on the genetic and molecular changes in different tumor types.

A *conceptual approach* to the classification of brain tumors was also recently introduced (Orkin et al, 2009). Accordingly, brain tumors are classified into two main classes, namely: intrinsic and extrinsic. *Intrinsic* tumors are of neuroectodermal origin and hence their differentiation is native to the cells of the brain. Conversely, *extrinsic* tumors arise from stem cells which are foreign to the brain and reach the cranial cavity either through migration (e.g. germ cells and lymphoma), embryonic rests (e.g. craniopharyngioma) or come

Table 23-2 Classification of Brain Tumors According to Stem Cell Origin and Differentiation

Intrinsic Orgin

1. Gliomas
   Astrocytoma, oligodendroglioma, Ependymoma, choroid plexus tumors and astroblastoma
2. Neuronal tumors
   Ganglioneuroma
   Neurocytoma
3. Embryonal tumors
   Infratentorial PNET/Medulloblastoma
   Supratentorial PNET
   Atypical teratoid rhabdoid tumor
4. Mixed brain tumors
5. Meningeal brain tumors
   Meningioma,
   Melanocytic tumors,
   Hemangioblastoma,
   Hemangiopericytoma
6. Pineal tumors
7. Posterior pituitary tumors
8. Cranial nerve tumors

Extrinsic Origin

1. Craniopharyngeoma
2. Chordoma
3. Germ cell tumors
4. Lymphomas
5. Histiocytosis
6. Secondary tumors

Orkin et al, 2009/Louis et al, 2007)

from a distant primary malignancy (e.g. metastases). A *modified WHO classification* applying this concept is presented in (Table 23-2). Mixed brain tumors are compiled in separate group to facilitate their histologic recognition.

Frequency

Overall, gliomas account for about 60% of primary intracranial neoplasms, meningiomas 20% and all others 20%. However, the histologic profile of tumors varies strikingly in children as compared to adults (Table 23-3). Thus, in children, embryonic tumors predominate, whereas, secondaries, meningiomas and acoustic neuromas are exceedingly rare. Conversely, in adults, glioblast-oma, secondaries, meningioma and schwannoma are common.

The Foundation of Accurate Diagnosis

The precise diagnosis of a brain tumor is based on a triad of essential information (Fig 23-2). These are: the age of patient, location of tumor (determined by MRI), and pathologic study of tumor (either by tissue biopsy or cytologic smears).

1. Age: Tumor entities tend to develop in specific age intervals (Fig 23-3), hence, the diagnosis of a given tumor should conform with its age interval.

2. Site: Brain tumors also tend to develop at specific almost diagnostic sites (Fig 23-4 and Fig 23-5). Neuroimaging (CT or preferably MRI) will reveal both the location, as well as, the morphology of the tumor (gross pathology)

Table 23-3 Relative Frequency and Ranking of Brain Tumors in Children and Adults

Children	(%)	Adults	(%)
Astrocytoma		Astrocytoma	
(Low-grade)	37	(High-grade)	30
(High-grade)	8	(Low-grade)	10
Medulloblastoma	20	Secondary tumors	25
Ependymoma	10	Meningioma	15
Craniopharyngeoma	10	Schwannoma	10
Supratenterial PNET	5	Ependymoma	3
Secondary tumors	5	Oligodendroglioma	3
Choroid plexus tumors	3	Medulloblastoma	3
Germ cell tumors	2	Pineal tumors	1

Pizzo and Poplack, 2011/Louis et al, 2007/Stocker, 2002

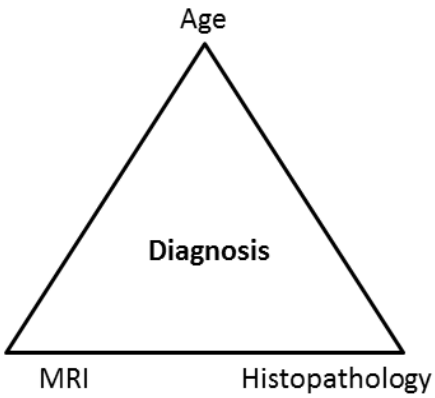

Fig 23-2 *The foundation of accurate diagnosis of brain tumors. A triad of essential information is needed, namely: age of patient, location of tumor (MRI) and histopathology.*

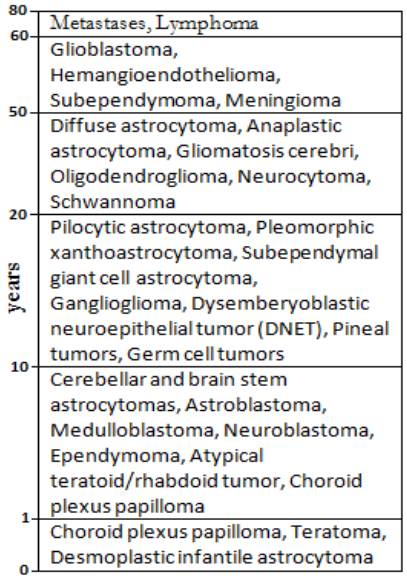

Fig 23-3 *Peak age incidence of brain tumors.*

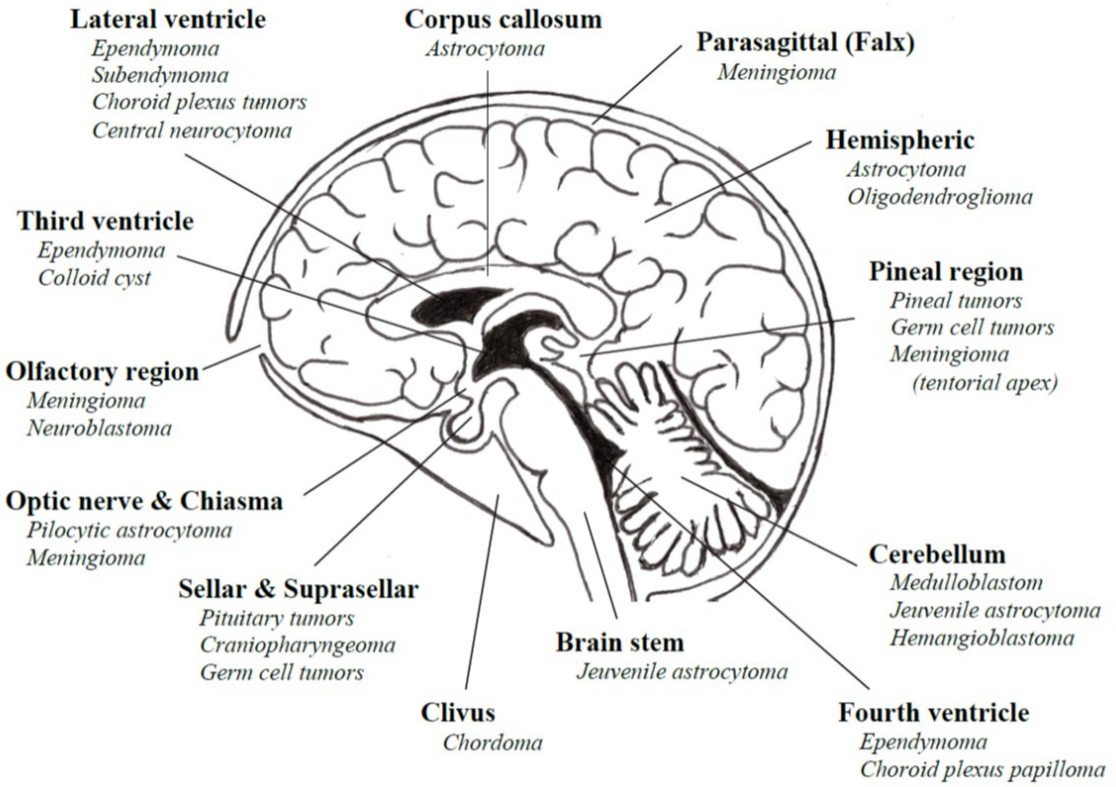

Fig 23-4 *Anatomic location of brain tumors in sagittal section. Midline brain tumors include, A. Supratentorial: olfactory neuroblastoma, olfactory meningioma, chiasmal astrocytoma, pituitary tumors, corpus callosum tumors, parasagittal meningioma, third ventricle tumors (ependymoma and neurocytoma) and pineal tumors. B. Infratentorial tumors include: brain stem astrocytoma, ependymoma of 4th ventricle and medulloblastoma of cerebellar vermis.*

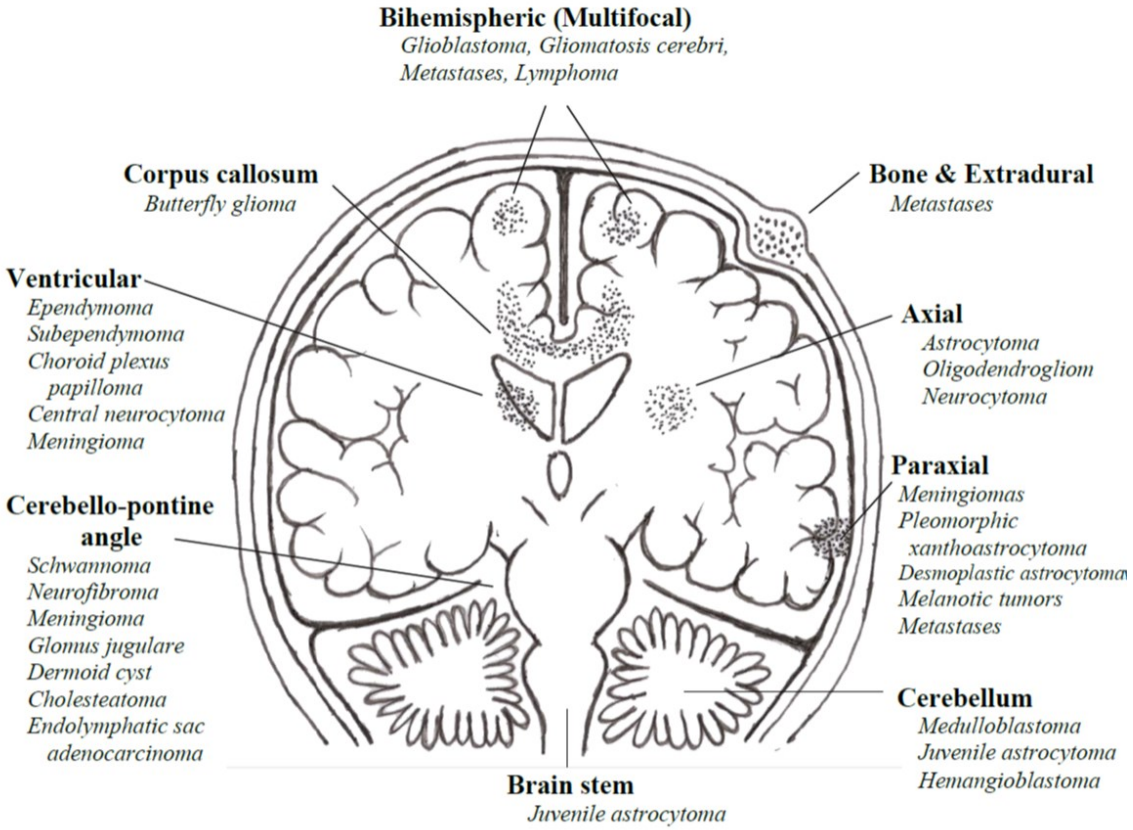

Fig 23-5 *Anatomic location of brain tumors in coronal section. A. Axial tumors are represented by diffuse astrocytomas and oligodendroglioma. B. Paraxial tumors (close to meninges) include meningioma, pleomorphic xanthoastrocytoma, metastases and melanotic tumors. C. Multiple and bilateral tumors are highly suggestive of metastases, lymphoma and glioblastoma.*

3. Pathology: This is essentially needed to confirm the diagnosis either preoperative (stereotactic tissue biopsy), or intraoperative frozen section and/or cytology smears (P 23-1 and P 23-2). This will assist the surgeon in locating the tumor and assure adequacy of surgical margins. The only contraindication of biopsy is brain stem tumors, since any traurmatic procedure in this location will end fatally from respiratory arrest.

Neuroimaging

Computerized tomography (CT) is usually the first imaging modality being rapid, inexpensive, efficient in identifying calcification and hemorrhage, as well as, applicable when MRI is contraindicated (patients with implanted electronic devices as cardiac pace makers or metallic foreign bodies).

Magnetic resonance imaging (MRI) represents the best imaging modality because of its high contrast resolution (better characterization of tissue), as well as, multiplaner capabilities (axial, sagittal and coronal images). Postoperative MRI done 3 days after operation will detect any residual tumor and follow up will detect recurrence.

MRI is based on the effect of a powerful magnetic field on water molecules which are a major constituent of human body. Each water molecule has two hydrogen nuclei or protons. When subjected to a magnetic field, water molecules align with the direction of the field. When the magnetic field is turned off, the excited protons return to their original position, and the difference in energy between the two states is released as radiophotons which are detected by a radioreceiving apparatus and used to create images. MRI can discriminate between water and fat. CSF, edema, hematoma and tumors are water rich, but, normal brain is water poor but fat rich.

Four standard images are necessary, namely: T1, T1-postcontrast, T2 and FLAIR.

1. T1WI (T1 weighted image). Water rich lesions as tumors appear darker than the fat rich normal brain which appears brighter. This image is good for anatomic localization of the lesion.

2. T1-post contrast. This postgodolinium image, because of break of blood-brain barrier in high-grade gliomas, enhancement of image is observed and hence diagnostic of high-grade tumors. Two low grade tumors are exception and show post-contrast enhancement, due to their vascularity, namely: pilocytic astrocytoma and pleomorphic xanthoastrocytoma.

3. T2 weighted image. Contrary to T1 image, water-rich tissues appear brighter than the water poor normal brain which appears darker. This image is ideal to determine morphology of the lesion.

4. FLAIR (fluid attenuated invasion recovery) image: this is best to identify the morphology of cystic lesions, since the lumen of the cyst appears black, whereas, the wall of the cyst or any mural nodule appears bright.

Illustrative examples of MRI images are shown in (P 23-3 and P 23-4). MRI can help to grade astrocytomas by T1-postcontrast imaging:

1. Grade I and II (Pilocytic astrocytoma and pleomorphic xanthoastrocytoma) appear either as a mural nodule in a cyst or a well-circumscribed enhancing lesion, but no peritumeral edema or shift of midline structures (no mass effect).

2. Grade II (Diffuse astrocytoma) this is a non-enhancing tumor, not associated with edema or mass effect.

3. Grade IV (Glioblastoma): shows post-contrast ring-shaped enhancement, peritumeral edema, infiltration of brain tissue, multicentricity in contralateral hemisphere and mass effect with shift of midline structures to the other side.

Magnetic resonance spectroscopy (MRS) is a special imaging method which measures the relative quantities of a variety of metabolites in a tumor compared to adjacent normal brain parenchyma or necrotic tissue. A glioblastoma typically shows elevated levels of choline (a marker for increased rate of cell turnover), whereas, in necrotic areas this metabolite is absent. MRS is useful to distinguish between viable and necrotic tissue of tumor after therapy.

Histopathology

Scherer in 1940 was the first to report on the importance of tumor pattern in the diagnosis of brain tumors. He described primary, secondary and tertiary structures in gliomas as follows:

1. Primary structure is an intrinsic histologic pattern of a tumor, unrelated or modified by the stromal environment. A classic example is rosette formation (Fig 23-6).

2. Secondary structures describe the modifications made on the tumor by its environment. Examples include focal aggregates of tumor cells in tissue interfaces or perineural spaces, usually resulting in change of shape of tumor cells to a spindle (bi-polar) form. Secondary structures are indicative of tumor invasiveness.

3. Tertiary structures describe the marked changes which occur in the tumor as a result of hemorrhage and necrosis and the subsequent healing tissue reaction. Tertiary structures are common causes of diagnostic difficulties.

The various *diagnostic histologic patterns* of brain tumors were recently collected and classified by Perry and Pratt (2010). Beside rosette formation (Fig 23-6), important patterns include: microcystic pattern in diffuse fibrillary astrocytoma, biphasic pattern in pilocytic astrocytoma, fried-egg pattern in oligodendroglioma, perivascular or angiocentric pattern in lymphoma, palisade pattern in acoustic schwannoma; whorled pattern in meningioma, nested pattern in paraganglioma and pleomorphic pattern in glioblastoma. To conclude, cell patterns are generally common in brain tumors, so, when a brain lesion lacks any pattern (patternless) a reactive gliosis must be suspected.

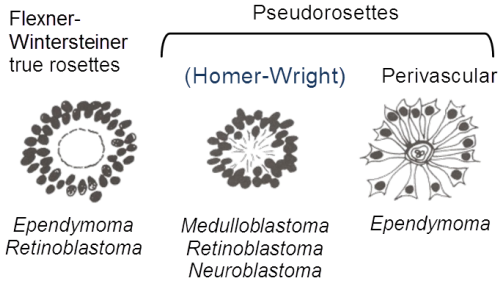

Fig 23-6 *Types of rosettes diagnostic of brain tumors (primary structures of Scherer). A true rosette of Flexner-Wintersteiner type shows a well-defined central lumen, whereas, in Homer-Wright psendorosette the central lumen contains fibrillary structures. In perivascular rosettes the nuclei are located away from basement membrane (suprabasilar).*

Grading

A four tiered grading system for astrocytomas was originally developed by Daumas-Duport (1988) based on objective criteria, namely: nuclear atypia, mitosis, microvascular proliferation and necrosis. Atypia was defined as variation of nuclear size and shape associated with hyperchromasia. The method results in a summary score which is translated into 4 grades as follows: 0 criteria = grade I, one criterion = grade II, two criteria = grade III and 3 or 4 criteria = grade IV (Table 23-4). These 4 grades generally correspond to the 4 histologic subtypes of astrocytomas (Fig 23-7). By lumping the grades, tumors may also be classified into two groups only, namely: low grade (includes grades I and II) and high grade (includes grades III and IV).

Recently, the WHO adopted this grading system (Louis et al, 2007) and applied it to all different types of gliomas (Table 23-5). This grading system serves as a useful guide to therapy. Thus, grade I gliomas are treated by complete surgical excision alone, whereas, grade II tumors (e.g. diffuse astrocytoma) is managed by surgery and postoperative radiotherapy. High grade (III and IV grades) tumors require radiochemotherapy.

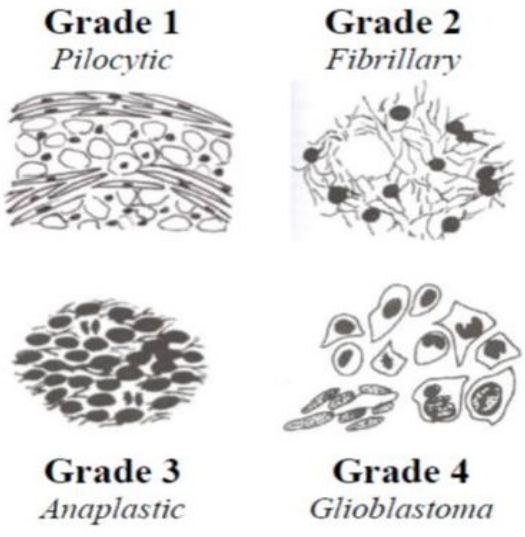

Fig 23-7 *Grades of the four main types of astrocytomas*

Immunohistochemistry

The following are helpful markers for immunophenotyping of tumors of CNS: glial fibrillary acid protein (GFAP) for gliomas, neurofilament protein (NFP), Neu N nuclear reactivity and synaptophysin for neuronal tumors, chromogranin and S-100 for paraganglioma, epithelial membrane antigen (EMA) for meningioma, vimentin and actin for mesenchymal tumors, placental alkaline phos-phatare (PLAP) for germ cell tumors, retinal S-antigen for pineal tumors and S-100 for acoustic schwannoma.

Since ependymomas and oligodendroglioma lack specific diagnostic immune stains, chromosomal studies are resorted to for characteristic deletions, namely: deletion of chromosome 22 in ependymoma and co-deletion of chromosomes 1 p and 19 q in oligodendroglioma.

Spread of Brain Tumors

1. *Local infiltration:* an important cause of early mortality if vital centers are affected.

2. CSF implantation occurs in 33% of gliomas specially ependymomas, choroid papilloma and medulloblastoma.

3. Distant spread outside CNS does not occur except in five situations: (a) medulloblastoma, to bones (10%) and lymph nodes; (b) extracranial growth of glioblastoma multiforme after craniotomy with metastases to lung and cervical lymph nodes; (c) meningothelial sarcoma to lungs and lymph nodes; (d) primary lymphoma of CNS to lymph nodes; and (e) peritoneal metastases of gliomas and medulloblastoma after ventriculoperitoneal shunts.

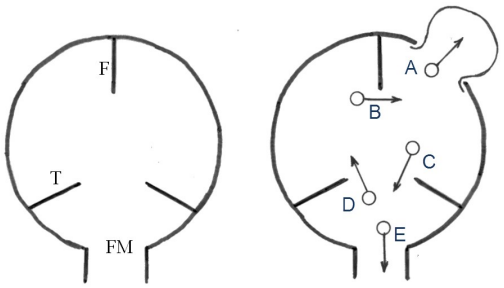

Fig 23-8 *Brain herniations due to tumors and their complications. A. Eternal B. Subfalx C. Tentoral D. Central upward E. Tonsillar. Three brain herniations cause morbidity only; including: the post craniectomy external herniation, the subfalx herniation will obstruct the anterior cerebral artery supplying the anterior lobe (loss of balance and coma), and tentorial herniation will damage the third cranial nerve (ocular paralysis). The other herniations are fatal, (D) will cause hemorrhage from basal artery and tonsillar herniation (E) result in medullary conization damaging the respiratory and cardiac centers. Abbreviations: F falx cerebri, T tentorium cerebelli and FM foramen magnum.*

Table 23-4 Histologic Criteria for WHO Grading of Gliomas

Grade	Atypia	Mitosis*	Vascular proliferation	Necrosis
I	-	-	-	-
II	+	-	-	-
III	+	+	-	-
IV	+	+	±**	±

(Daumas-Duport et al, 1988 and Louis et al, 2007)
*Mitosis may be quantitated by MIB-1 immunoreactivity to determine the KI nuclear labeling index (Grade I 1%, II<5%, III 5-10% and IV >10% up to 25%.
**Microvascular proliferation and /or necrosis is required for grade IV.

Table 23-5 WHO Grading of Gliomas

Low grade		**High grade**	
Grade I	**Grade II**	**Grade III**	**Grade IV**
Pilocytic astrocytoma	Diffuse astrocytoma	Anaplastic astrocytoma	Glioblastoma
Subependymal giant cell astrocytoma	Fibromyxoid astrocytoma	Anaplastic oligodendroglioma	Giant cell glioblastoma
Subependymoma Myxopapillary ependymoma	Pleomorphic Xanthoastrocytoma	Anaplastic oligoastrocytoma	Gliosarcoma
Choroid plexus papilloma	Oligodendroglioma Oligoastrocytoma	Anaplastic ependymoma	
Angiocentric glioma	Ependymoma		
Gangliocytoma Ganglioglioma	Atypical choroid plexus papilloma	Choroid plexus carcinoma	
Desmoplastic infantile astrocytoma	Chordoid glioma of third ventricle	Anaplastic Ganglioglioma	
Dysembyoplastic neuroepithelial tumor (DENT)			

(Louis et al, 2007)

Pathologic Effects

1. Focal changes: (a) intratumor hemorrhage (sudden increase in size), (b) destruction of adjacent vital neural centers and (c) epilepsy.

2. Regional changes: (a) increase of intracranial pressure due to tumor volume, edema, or obstruction of CSF circulation. This is manifested clinically by headache, nausea, vomiting, papilledema and coma. Systemic manifestations of raised intracranial pressure (hypertension, bradycardia and pulmonary edema) occur due to autonomic imbalance as a result of hypothalamic compression, and (b) hydrocephalus, pituitary infarction and bone erosion.

3. Brain herniations: (Fig 23-8) (A) external herniation through a bone defect; (B) subfalx contralateral cerebral herniation resulting in occlusion of anterior cerebral artery; and transtentorial lateral shift of midline brain structures may cause stretch injury of cranial nerves 3 and 6; (C) tentorial herniation with brain stem compression; (D) superior cerebellar hemiation and (E) inferior cerebellar herniation with medullary compression. Fatal brain herniations may be precipitated by withdrawing CSF at lumbar puncture.

Staging

There is no TNM staging classification, but SEER staging system (Table 23-6) and modified Chang staging (Table 23-7) are available. These systems depend on the extent of local spread and metastases as determined preoperatively by MRI.

Table 23-6 SEER Staging of Brain Tumors

Localized Supratentorial tumors confined to a cerebral hemisphere, or infratentorial limited to one site
Regional Tumors have crossed middle line, or involve more than one site of brain (cerebrum, ceredellum, brain stem or spinal cord), bone, meninges, major vessels or nerves
Distant CSF implants, or extension to pharynx or any extracranial site (postcraniotomy)

*SEER = Surveillance, Epidemiology and End Results Staging system, NCI, Bethesda, USA.

Table 23-7 Modified Chang Staging for Medulloblastoma by MRI

Stage	Features	5-year survival %
M0	No dissemination	70
M1	CSf cytology positive	57
M2	Cerebellar gross nodules	40
M3	Spinal nodules	
M4	Systemic metastases	

(Chang et al, 1989)

Table 23-8 Prognostic Groups of Primary Brain Tumors (Overall 5-year Survival with Recent Therapy)

Most Favorable (>80%)
Choroid plexus tumors (100%)
Pilocytic astrocytomas (95%)
Germ cell tumors (90%)
Pleomorphic xanthoastrocytoma (81%)
Meningioma grade I (81%)
Favorable (>50-80%)
Diffuse astrocytoma (80%)
Pineocytoma (80%)
Oligodendroglioma (72%)
Ependymoblastoma (70%)
Medulloblastoma (65%)
Unfavorable (>10-50%)
Pineoblastoma (50%)
Anaplastic astrocytoma (38%)
Most Unfavorable (0-10%)
Glioblastoma* (3-8%)
Anaplastic meningioma (0.0%)
Atypical teratoid / Rhabdoid tumor (0.0%)
Lymphoma (0.0%)
Metastases (0.0%)

*Occasional reports of higher survival of 30% (Hegi, 2005) and 16% (Baily and skinner/2010)

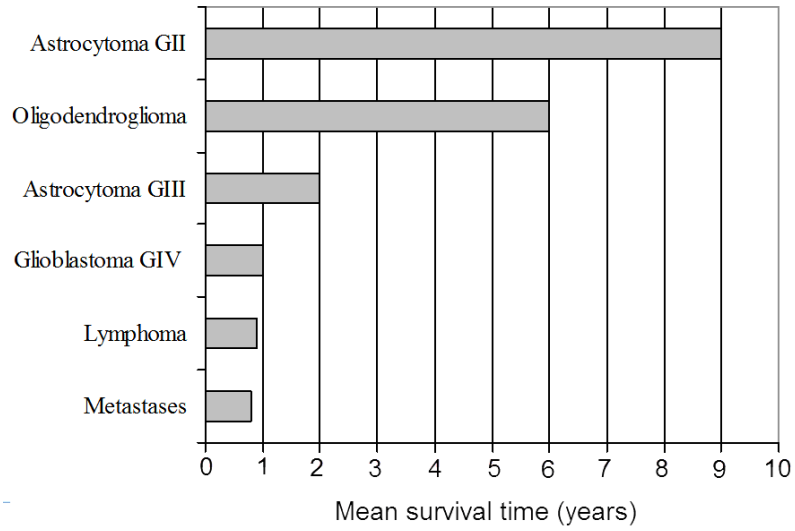

Fig 23-9 *Comparison of survival of brain tumors. The mean survival of ependymoma (not shown) is extremely variable (4 to 6 years) according to age and location, being more favorable in adults and 4th ventricle*

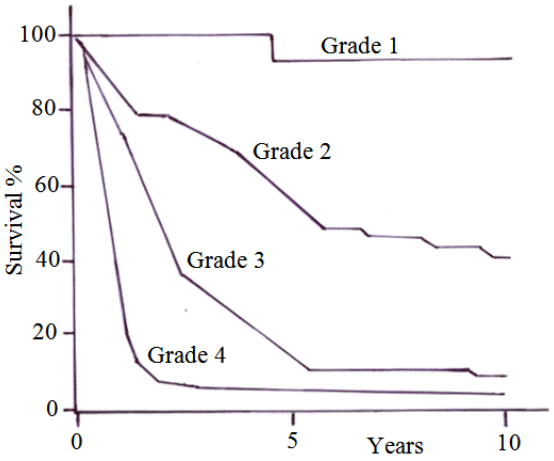

Fig 23-10 *Comparison of survival of astrocytomas in relation to WHO grades. The 5-year survival is about 95% in grade 1, 55% in grade 2, 40% in grade 3 and 3% in grade 4 in the pre -radiochemotherapy era (Daumas-Duport et al, 1988).*

Prognosis

The prognosis of brain tumors is dependent on several factors.

1. Histologic type: the mean survival time of the 6 common brain tumors is presented in (Fig 23-9). Glioblastoma, lymphoma and metastases are most unfavorable. Brain tumors can also be classified into 4 main groups according to their 5-year survival (Table 23-8).

2. Grade: survival curves of the four grades of astrocytomas demonstrate stratification of patients into four different survival patterns (Fig 23-10).

3. Site: tumors at midline or crossing the midline are unfavorable. Proximity to vital centers resulting in neurologic manifestation is also unfavorable feature.

4. Size: large tumors (>6 cm) are associated with poor prognosis.

5. Age: Adults patients (>40 years) have a poorer prognosis than pediatric patients.

6. Adequacy of surgical excision: this is a significant factor in ependymomas (survival is 70% with complete resection and <10% with incomplete excision). Also, in diffuse astrocytomas (grade II), survival is about 85% with complete excision and 67% with incomplete excision and postoperative radiation.

SPECIAL CONSIDERATIONS

INTRINSIC TUMORS

GLIOMAS

Astrocytoma

These are classified into low grade tumors (including diffuse astrocytomas, pilocytic astrocytoma and pleomorphic xanthroastrocytoma) and high grade astrocytomas (including anaplastic astrocytoma, glioblastoma and gliomatosis cerebri).

1. Diffuse astrocytoma (Grade II) is the most common type of astrocytomas (90%) with predilection of cerebral hemispheres in adults and brain stem in children. The median age is 35 years. Histologically, there is astroglial cell proliferation in a fibrillary stroma which often contains microcysts (P 23-5). The cells are not evenly distributed with frequent nuclear contact. Nuclear atypia (hyperchromasia and variability in shape) is evident but no mitotic activity. Special variants of astrocytomas include: gemistocytic astrocytoma (P 23-6), protoplasmic astrocytoma and mixed oligoastrocytoma.

2. Pilocytic astrocytoma (Grade l) is typically a tumor of childhood and adolescence which selectively affects the region of third ventricle, optic chiasma, thalamus and cerebellum. It differs from fibrillary astrocytoma in being relatively well circumscribed, may show cystic change and has no potential to malignant transformation. It is uncommon in cerebral hemisphere. Histologically, it is composed of elongated nuclei (hair-like pattern) with intervening loose fibrillary processes (P 23-7) and often containing Rosenthal fibers. Malformed blood vessels are present, but are lined by a single layer of endothelium. There is often calcification and microcystic change in the stroma. Pilomyxoid pilocytic astrocytoma (WHO grade II) is a special more aggressive variant.

3. Pleomorphic xanthoastrocytoma (Grade II) occurs most often in temporal or parietal lobe of young people (third or fourth decade). Usually there is prominent leptomeningeal involvement, underlying cyst formation with mural nodules. Histologically, the tumors are typically densely cellular and cytologically pleomorphic with inflammatory component. Tumor giant cells show lipid in the cytoplasm (P 23-8).

4. Anaplastic astrocytoma (Grade III) is an aggressive astrocytoma of adults (median age 45 years) arising in cerebral hemisphere. They may arise de novo or develop from grade 2 fibrillary astrocytoma. Histologically, it is characterized by high cellular density and mitotic activity (P 23-9). The stroma contains nonproliferative blood vessels and necrosis is absent.

5. Glioblastoma multiforme (Grade IV) is the most common type of astrocytomas constituting about 30-50% of cases in adults. The median age is 55 years and there is a slight male predilection. The tumors affect mainly the cerebral hemispheres and basal ganglia, rarely, the brain stem and cerebellum. They are multiple in 6% of cases. Histologically, in addition to cellular atypia and mitosis there are two more additional features (P 23-10), namely: (a) vascular proliferation, both endothelial and pericytes forming multilayer pattern, and (b) tumor necrosis with peripheral palisading of cells (P 23-11). Glioblastoma is associated with the worst prognosis (median survival is one year). Four variants are recognized: small cell glioblastoma, large cell glioblastoma (monstrocellular), gliosarcoma and gliomatosis cesebri (P 23-12).

6. Gliomatosis cerebri is a multifocal astroglial proliferation affecting the cerebral cortex. It occurs at any age and is rapidly fatal.

Other common Gliomas

1. Oligodendroglioma (Grade II-III) constitutes about 4% of CNS neoplasms and is predominantly a tumor of middle age (45 years). Sites of preference include the frontal, parietal and temporal lobes of the cerebral hemispheres, as well as, the thalamus, particularly in the young age group. They rarely affect the spinal cord or cerebellum. CSF seeding occurs in 5% of cases.

Histologically, it is composed of rounded cells with uniform nuclei and clear cytoplasm producing a halo or fried egg pattern and arborizing capillaries (Fig 23-11 and P 23-13). Calcification is common, detected radiographically in 40% of cases and histologically in 90%. The tumor may present as a pure form or mixed with astrocytoma (oligoastrocytoma), a combination with more favorable prognosis.

2. Ependymomas(grade II-III) represent about 4% of all intracranial tumors. They are primarily tumors of childhood and adolescence (median age 12 years). The preferred sites in descending order of frequency are: the fourth ventricle, lateral ventricles, third ventricle, Sylvian aqueduct, spinal cord, cauda equina and cerebellopontine angle. Due to its proximity to intraventricular location,

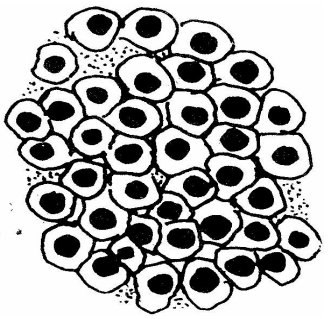

Fig 23-11 *Oligodendroglioma (fried egg appearance of tumor cells).*

obstruction to CSF flow and hydrocephalus is common, as well as, dissemination via the subarachnoid space. Histologically, the tumor shows characteristic perivascular pseudorosette pattern of ependymal cells (P 23-14 to P 23-16). Ependymomas are graded into low and high-grade. Three histologic variants are recognized: papillary ependymoma, myxopapillary and subependymoma. (P 23-17 and P 23-18). Myxopapillary ependymoma is a tumor of adults and commonly arises from spinal cord and cauda equina rather than brain. Ependymomas need adequate surgical excision, assisted by intraoperative pathologic examination in order to get the best prognosis.

Other Rare Gliomas

The WHO recognizes three tumors which exhibit glial phenotype (GFP positive), but obscure differentiation lineage. These are (1) astroblastoma, (2) choroid glioma of third ventricle (grade II) and (3) angiocentric (grade I). *Astroblastoma* is a supratentorial cerebral circumscribed glioma which may be of low or high grade. Histologically, the tumor shows perivascular pseudorosettes with fibrosis, simulating ependymoma, but, contrary to ependymoma it is extraven -tricular in location.

Choroid Plexus Tumors

These are ventricular papillary tumors derived from choroid plexus epithelium. These rare tumors (0.5% of brain tumors) usually affect young adolescent patients (<20 years). Benign choroid papilloma is covered by a single layer of pseudostratified columnar epithelium with vascular core (P 23-19). Mitotic activity is low (mean Ki-index 2%). Conversely, in choroid carcinoma, the epithelium is multilayered, anaplastic with high Ki-index (mean 14%).

Neuronal tumors

This includes two tumor types of different grades.

Gangliocytoma (ganglioneuroma), well-differentiated (grade I), composed of mature neurons. Common sites are posterior pituitary, cerebellum and spinal root ganglia.

Neurocytoma (grade II) account for 1% of brain tumors, composed of small relatively immature neurons of monotonous uniform cells simulating oligoastrocytoma (P 23-20). Neurocytomas may be located intraventricular or extraventricular.The characteristic immunoreactivity of neuronal tumors is strong reaction to synaptophysin, as well as, nerve filament protein (NFP), but GFAP is negative.

EMBRYONAL TUMORS

These are aggressive brain tumors (grade IV) that commonly affect pediatric patients during the first decade of life. They arise from a neuroectodermal stem cell that commonly remain in an undifferentiated state (chapter 4), hence the name primitive neuroectodermal tumor (PNET).

The molecular genetic structure of (PNET) is distinctively different from that of peripheral PNET (Ewing sarcoma). There is lack of t (11:22) and EWS/FLI-1 fusion gene, hence, the lack of immunoreactivity to CD99. However, central (PNET) express the classical neuronal phenotype (synaptophysin and neurofilament protein (NFP). Central PNET is classified anatomically into infratentorial and supratentorial types.

I. Infratentorial PNET

Medulloblastoma

Medulloblastoma is classified into a common classic or pediatric type (mean age 7 years) and a rare adult more favorable type or desmoplastic type. Grossly, the Juvenile type commonly affects the vermis of cerebellum and appears rather circumscribed with focal necrosis. Adult type affects cerebellar hemisphere.

Histologically, the classic or conventional type is composed of solid sheets of round cells with active mitosis and Homer-Wright rosettes (P 23-21). Other cell types may be encountered, reflecting the divergent differentiation potential of neuroectodermal stem cell, thus glial differentiation is present in 10% of cases and ganglion cells in 7%, four histologic variants are recognized

namely: desmoplastic, myoblastic (medullomyoblastoma), melanotic and large cell variant.

Staging is critical in planning treatment. A modified Chang preoperative staging system is generally used (Table 23-7) which emphasizes the extent of metastases. Survival with radiochemotherapy is 58% disease survival and 66% overall survival.

2. Supratentorial (PNET)

These embryonic tumors show a similar histology and immunophenotype to medulloblastoma and include: cerebral neuroblastoma, olfactory neuroblastoma, pineoblastoma, ependymoblastoma and medulloepithelioma with neural tube differentiation (P 23-22) characterized by the formation of tubular structures lined by primitive neuroepithelium.

Atypical Teratoid / Rhabdoid Tumor

This tumor shows multilineage differentiation including: rhabdoid cells, other mesenchymal cells, neuronal or glial cells and rarely glandular epithelium. It is highly aggressive, lethal in 1-2 years, with 1 year survival of only 20%.

Differential Diagnosis

The histology of some brain tumors is closely similar to that of other tumors or lesions, hence, leading to diagnostic pitfalls. The following are nine illustrative examples.

1. Diffuse astrocytoma and gliosis. The latter is a reactive process to infections, infarcts and demyelinating autoimmune disease as disseminating sclerosis (DS). In gliosis the nuclei of glial cells are uniform, evenly spaced and normochromatic (P 23-23). Their mitotic activity is low (Ki-index <1%) and negative for p53. The stroma is also rich in CD68 positive phagocytic cells.

2. Pleomorphic xanthoastrocytoma (PXA) and glioblastoma (GB). The peripheral location of PXA in relation to meninges is characteristic. There is lack of necrosis, mitosis and microvessel proliferation. Eosinophilic granular bodies (EGBs) are abundant in cells and matrix. Ki-index is <1% and p53 negative (P 23-8).

3. Small cell glioblastoma and non-Hodgkin lymphoma. The latter is perivascular in distribution and immunoreactive to LCA, CD20 or CD3.

4. Glioblastoma or ganglioneuroma from hamartomatous lesions of tuberous sclerosis. The latter shows multiple cortical or intraventricular subependymal lesions. The giant cells show double staining to glial and neuronal markers. Also, characteristic cutaneous lesions of the syndrome are evident.

*5. Neurocytoma (*P 23-20) *and oligodendroglioma*. Both show uniform round cells and arborizing blood vessels. Immunostains will differentiate, thus, neurocytoma is positive for synaptophysin, neurofilament protein and Neu N nuclear antigen, whereas, oligodendroglioma is GFAP positive.

6. Ependymoma and astroblastoma, both show perivascular pseudorosettes. However, the location of the tumors is different. Ependymomas are intraventricular, whereas, astroblastomas are located in cerebral parenchyma.

7. Choroidal carcinoma and metastases, both are positive for cytokeratin. However, metastases are negative for GFAP, multiple lesions in cerebral parenchyma and primary tumor evident by CT scans.

8. Medulloblastoma and metastases from small cell lung cancer, both show a similar histology and immunoreativity. The only way to distinguish between them is to identify a lung primary by CT scans.

9. Hemangioblastoma (P 23-35) and metastases from renal cell carcinoma (RCC). Both show perivascular clear cells rich in lipid and may be associated with VHL syndrome, but, RCC is positive for cytokeratin and abdominal CT scans will show a renal mass.

Mixed Tumors

Mixed brain tumors are classified according to the differentiation lineage of stem cells (Table 23-9). Oligoastrocytoma, the most common mixed glioma, shows two distinct neoplastic components of oligodendroglia and astrocytes (P 23-24). It arises from a glial progenitor cell with bipotential differentiation.

Glioneural tumors are biphasic tumors, readily recognizable by markers (positivity to both GFAP and synaptophysin). Dysembryoplastic neuroepithelial tumor (grade 1), shown in (P 23-26), is common in children (<15 years) and appears as nodules and cysts, extra-axial cortical in location. Histologically, it has three components, namely: oligodendroglia, neuronal ganglion like cells and dysplastic hamartomatous changes in the adjacent cartex. An example of gliomesenchymal differentiation is gliosarcoma (P 23-27). Atypical teratoid/ rhabdoid tumor (grade IV) represents a multilinear neuron-mesenchymal differentiation. Four differ-

Table 23-9 Mixed Brain Tumors and their WHO Grade

Class	Examples (grade)
Mixed gliomas (glio-glial)	Oligoastrocytoma (II)
Glio-neural	Ganglioglioma (I) Dysembryoplastic neuroepithelial tumor (I) Papillary glioneuronal tumor (I) Anaplastic ganglioglioma (II-IV)
Glio-mesenchymal	Gliosarcoma (IV)
Neurono-mesenchymal	Cerebellar liponeurocytoma (I)
Multilineage differentiation	Atypical teratoid/rhabdoid tumor (IV)

ent cell types are recognizable, namely: neuronal, glial, rhabdoid and glandular epithelium.

MENINGEAL TUMORS

1. Meningioma

Meningiomas arise from arachnoid cells of the leptomeninges, and is more common among spinal tumors (42%) than brain tumors (15%). It is multiple in 8% of cases (especially with NF-2 syndrome) and associated with a variable risk of local recurrence (9-40%) according to its WHO grade.

Meningiomas exhibit a remarkably wide range of histologic appearances, with a total of 15 variants. The common meningothelial type shows a characteristic whorly pattern (P 23-28) but other histiologic variants are encounted (P 23-28 to P 23 -33). The WHO classified meningioma variants into three grades (Louis et al, 2007) which correlate with the risk of recurrence, as well as survival (Table 23-10).

2. Melanocytic Tumors

These are rare aggressive tumors of adults, arising from melanocytes of the leptomeninges. They include the following: (1) Diffuse melanocytosis: a borderline diffuse tumor with invasion of underlying cortex, (2) melanocytoma: a localized tumor of borderline malignancy (P 23-34), and (3) malignant melanoma: a highly malignant tumor with obvious pleomorphic cells. All tumors are positive for HMB-45.

3. Hemangioblastoma

It represents less than 2% of brain tumors and can be either sporadic or syndromic associated with Von Hippel-Lindau (VHL) syndrome. The classic location is the cerebellum, but the medulla and spinal cord may be involved in syndromic cases. The histology is characterized by perivascular clear cells rich in lipid simulating clear cell renal cell carcinoma (P 23-35). The stromal clear cells have no specific immunostain, but may be reactive to a variety of markers (NSE, S-100, inhibin and VEGF).

4. Solitary Fibrous Tumor (Hemangiopericytoma)

This is the most commonly observed mesenchymal tumor related to cranial meninges. It affects adults, exhibit a high rate of local recurrence and late metastases. Histologically, it is composed of spindle cells arranged around thin-walled blood vessels of clefted or staghorn shape. Tumor cells have no specific immunostain, but, contrary to meningiomas it is negative for EMA, S-100 and cytokeratin, as well as, lacking any chromosomal abnormality.

PINEAL TUMORS

Pineal tumors constitute 0.5% of CNS tumors in adults, and 5% in children. There are three sources of origin: (1) parenchymal cells (neuroectodermal in origin) giving rise to pineoblastoma and pineocytoma (P 23-36), (2) ectopic inclusion cells: germ cells, glial, meningeal cells and melanocytes, and (3) metastases. Germ cell tumors are

Table 23-10 WHO Grading of Meningiomas, their recurrence Rate and Survival

Meningioma Variant	Grade	Frequency (%)	10-year	
			Recurrence (%)	Survival (%)
Meningothelial Fibrous Transitional Psammomatous Angiomatous Microcystic Secretory Lymphoplasmacyte rich Metaplastic	I benign	81	9	80
Chordoid Clear cell Atypical	II atypical	7	24	35
Rhabdoid Papillary Anaplastic *	III anaplastic	2	40	0.0

(Louis et al, 2007) *Median survival time only <2 years.
NB. Mean Ki-67 index 4% for grade I, 7% for grade 2 and 15% for grade III

the most common (germinoma 45% and teratoma 16%) and are histologically similar to gonadal germ cell tumors. Gliomas contribute 17% of cases and parenchymal tumors 15%.

Pineoblastoma (WHO grade IV). It is an aggressive tumor, common in children, and is an example of central PNET. Histologically (P 23-36 B), it is composed of embryonic cells which may form pseudorosettes, true rosettes or fleurette photoreceptors. It may be associated with bilateral retinoblastoma (then called trilateral retinoblastoma).

Pineocytoma (WHO grade I-III). It is a more favorable tumor affecting adults. The cells are more mature, lack mitosis and show a lobular organoid pattern with intervening stroma similar to the histology of the normal pineal gland (P 23-36 A). It may show pseudorosette pattern or ganglionic differentiation. The tumor cells are immunoreactive to NSE, S-100 and chromogranin.

The main pathologic effect of pineal tumors is increased intracranial pressure and hydrocephalus due to obstruction of aqueduct. The tumor spreads locally and by CSF seedling.

PITUITARY TUMORS

The anterior pituitary (derived from ectoderm) belongs to the endocrine system (chapter 19). However, the posterior pituitary (neuroectodermal in origin) belongs to the CNS and shows a similar profile of tumors (gangliocytomas and astrocytomas).

CRANIAL NERVE TUMORS

Two distinct types of nerve sheath (neurilemmal) tumors are recognized, namely: Schwannoma and neurofibroma.

1. Schwannomas

They characteristically involve sensory nerves (e.g. vestibular branch of eighth cranial nerve or trigeminal nerve), may be associated with (NF-2) Neurofibromatosis syndrome, commonly solitary and benign. Grossly, it appears circumscribed, displacing the nerve which could be easily recognized. Histologically, a palisade pattern of cell nuclei is common. Schwannomas immunostain, for both S-100 and calretinin.

2. Neurofiboma

It characteristically involve motor and autonomic nerves, and may be associated with (NF-1) neurofibromatosis syndrome. It may be multiple, and biologic behavior is variable (benign, precancerous or malignant). Grossly, it appears fusiform or plexiferm and the nerve of origin can not be distinguished from the tumor. The histology is characterized by a wavy serpentine pattern of cells. The tumor is immunoreactive to S-100 but negative for calretinin.

EXTRINSIC BRAIN TUMORS

Extrinsic brain tumors arise from stem cells which are foreign to the brain. The source of these cells may be embryonic remnants (e.g. craniopharyngioma and chordoma) or cells migrating from other parts of the body (e.g. germ cell tumors, lymphoma, histiocytosis and metastases).

1. Craniopharyngioma

Craniopharyngioma develops from remnants of Rathke pouch, which is an ectodermal diverticulum which gives rise to the anterior pituitary. The suprasellar region is the most common location (90%). Two histologic types are recognized, namely: (a) an adamantinoma-like pattern (90% of cases, affecting mainly children) and composed of peripheral palisaded columnar cells and central stellate cells which may undergo squamous differentiation, cystic change and calcification (P 23-37) and (b) a papillary variant (10% of cases, occurs in adults in third ventricle) and is composed of squamous epithelium without keratin formation or calcification. Craniopharyngeoma is a recurrent, but non-metastasizing tumor.

2. Chordoma

Chordomas arise from remnants of notochord. Commonly, intracranial chordomas represent spread of chordomas from basiocciput bone. However, chordomas may arise primarily in other intracranial locations from ectopic notochordal tissue. Histologically, the presence of vacuolated multinucleated giant cells (physaliferous cells) in a myxoid stroma is characteristic.

4. Germ Cell Tumors

These are most common in children (age <20 years) and usually arise in pineal or suprasellar regions. Four types may occur, namely: (a) germinoma or seminoma-like histology is the most common (45%), (b) mature and immature teratomas, (c) choriocarcinoma and yolk sac tumor, and (d) embryonal carcinoma. Yolk sac tumors are immunoreactive to placental alkaline phosphatase (PLAP and AFP).

5. Brain Lymphoma

Primary brain lymphoma accounts for 1 % of intracranial tumors, and they arise and grow within brain parenchyma. Conversely, secondary or systemic lymphoma of CNS invades mainly the meninges and CSF. Immunosuppressed patients (AIDS or iatrogenic) are at high risk to develop NHL, which is commonly large cell type and B-immunophenotype (P 23-38). The tumors are often multiple and perivascular in distribution. Tumor cells are positive to LCA and invariably contain the EBV genome. Differential diagnosis includes: PNET and metastases of small cell carcinoma (both are NSE positive). Extracranial dissemination to peripheral nodes and BM may occur late in the disease. Brain lymphomas arising in immunocompromised patients carry a very poor prognosis.

6. Histiocytosis

Histiocytosis, both Langerhans or non-Langerhans type (chapter 26) may affect the cranial cavity, the former being more common. Langerhans cell histiocytosis (LCH) in its multisystem disseminated form commonly damage the posterior pituitary , hence, diabetes insipidus is the most common initial presentation.

Ultimately in the chronic stage, anterior pituitary hormone deficiencies, as well as, paraneoplastic neurodegenerative syndromes become evident.

Metastatic Tumors

Secondary involvement of the CNS is a common complication of cancer patients, accounting for about 30% of malignant CNS tumors in neurosurgical series, and 84% in autopsy series (Laws, 1993). The mechanism of spread may be hematogenous or direct invasion.

Blood-borne metastasis is a common mechanism, since the brain receives 20% of the blood flow of the heart and the arteries of the brain have an "end artery" pattern which can trap malignant cells. The chief primary sites are the lung in males and breast in females (Table 23-11). Next in frequency are gastrointestinal tumors, renal cell carcinoma and melanoma. About 10%

are of unknown primary. In regard to the topographic distribution, metastases are most common in frontoparietal region of cerebral hemisphere (supplied by the middle cerebral artery), and they may be solitary in 50% of cases. The metastases are relatively superficial in location, at the gray-white junction of cerebral cortex (P 23-39). Another pattern of metastasis is diffuse perivascular involvement of periventricular tissue (leptomeningeal) observed in small cell lung cancer, lymphoma and melanoma.

The CNS may be also involved by direct spread from an intracranial tumor (pituitary), or extracranial tumors as glomus jugulare tumor, chordoma of basisphenoid, carcinoma of the ear, nasopharyngeal cancer and advanced basal cell carcinoma of the face.

Table 23-11 Metastatic Brain Tumors: Distribution by Primary Cancer

Primary site	%
Pulmonary	50
Breast	15
GIT	8
Genitourinary	6
Melanoma	6
Unknown	10
Others	5

(Laws, 1993)

SPINAL CORD TUMORS

Anatomy

In adults, the spinal cord usually ends at the level of lumbar disc (L1-L2) and the cord extends as cauda equina to the level of sacral disc (S1-S2). The cauda is composed of spinal nerves and filum terminale (the ependymal continuation of central canal of cord).

The meningeal coverings of the cord includes three layers, named from outside in: the dura, arachnoid and pia (or ependymal cells). Meningothelial cells are flat indistinct arachnoid cells that line the dura. The subarachnoid space contains CSF.

Contrary to cranial dura which is firmly attached to skull bone, spinal dura is loosely attached to bone creating an extradural space. This space is composed of loose fibroadipose tissue, which communicates through intervertebral foramina with mediastinum and retroperitoneum. All extradural tumors are either metastatic carcinomas which extends from vertebras, or lymphomas which spread through intervertebral foramina.

Pathology

Spinal cord neoplasms account for 15% of CNS tumors. Their relative frequency is presented in (Table 23-12). The profile of tumors is different from that of brain. Thus, in the spinal cord meningiomas, neurofibromas and ependymomas are more common than the brain, but, astrocytomas and metastases are less frequent.

Spinal cord tumors are classified into three main groups according to their location in relation to dura and cord (Fig 23-12). Extradural tumors are commonly malignant, whereas intradural tumors are commonly benign. The intradural extramedullary compartment is a common site of seeding from upper brain tumors, as well as, other benign tumors such as neurofibroma and meningiomas. Intramedullary tumors are commonly astrocytomas and ependymomas. The majority of myxopapillary ependymomas arise from the filum terminal of cauda equina at its termination in sacral region. This characteristic location of brain tumors helps in their pathologic diagnosis.

Table 23-12 Frequency of Primary Spinal Tumors

Histologic type	Frequency (%)
Meningioma	42
Schwannoma	22
Ependymoma	15
Astrocytoma	11
Other gliomas	2
Others	6

(Preston-Martin, 1990)

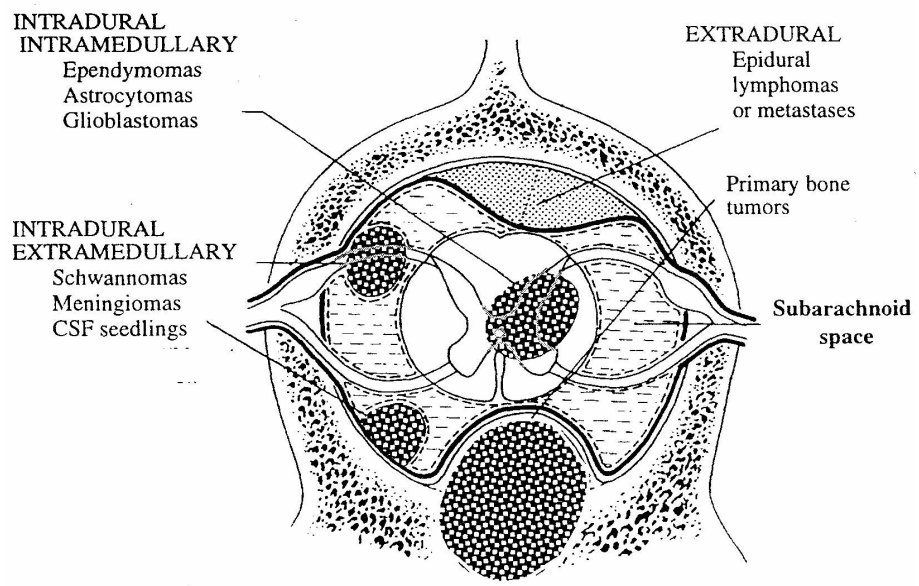

Fig 23-12 *Spinal cord tumors. Anatomic classification of tumors in relation to dura and cord. Extradural (metastatic carcinoma or lymphoma). Intramedullary tumors are also always malignant (astrocytoma or ependymoma). Intradural extramedullary tumors are either benign (neurofiboma and meningioma) or malignant (CSF seedling).*

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