CHAPTER 15

Neoplasms of the Nervous System

A neoplasm is an abnormal mass (tumor) of tissue produced by a disturbance of cell growth caused by an autonomous proliferation of cells. The lack of lymphatics and paucity of connective tissue in central nervous system (CNS) modifies spreading and cell growth of these lesions. Site of the lesion (medulla versus frontal lobe) and growth kinetics of neoplasm are more important than traditional distinction between histologically benign and malignant neoplasms. These neoplasms grow in a closed space and cause increased intracranial pressure and herniation syndromes (transientorial, tonsillar).

CNS tumors can originate within intracranial cavity if they are found above foramen magnum or within spinal canal if they are found below the foramen magnum. The distinction between intracranial and intraspinal is important because they differ in their clinical manifestations, frequency, and prognosis. More than 50% of intracranial tumors are histologically malignant and surgically not feasibly resectable, whereas more than 50% of intraspinal tumors are histologically benign and surgically resectable. Unfortunately, 85% of CNS tumors originate above foramen magnum.

INTRACRANIAL TUMORS

Primary intracranial tumors can arise in brain tissue itself (intraparenchymal or intraaxial), most of them being gliomas, or they can originate in tissues outside brain tissue (extraparenchymal or extra-axial) such as meninges (meningiomas), cranial nerves (schwannomas), pituitary gland (adenomas), or bony structures (osteomas, sarcomas). Secondary tumors originate in other organs and can reach the CNS by direct extension (nasopharynx) or by bloodstream (hematogenous metatases). Extra-axial tumors can compress brain tissue and when surgically removed, brain can re-expand without underlying tissue injury. Intra-axial tumors can invade or infiltrate the underlying brain tissue. Metastases invade brain tissue and usually arrive by hematogenous dissemination. Primary malignant brain neoplasms arise de novo in the brain and infiltrate brain tissue extending along white matter pathways and it is not possible for surgeon to obtain tissue plane between normal and neoplastic tissue. For metastatic neoplasms, it is possible to obtain tissue plane between normal and neoplastic tissue; however, due to hematogenous dissemination, there may be multiple lesions even though only one may cause clinical symptoms and others are clinically “silent”.

The incidence of CNS tumors seen in a given hospital differs greatly and depends on whether the hospital has neurosurgical service, type of clinical facility, and availability of specialists (neurosurgeons, neurooncologists). Autopsy figures vary according to the thoroughness with which the brain is examined. Also, incidence of tumors has changed with time. An increase in the incidence of brain tumors is the result of prolonged longevity. An increase in brain metastasis is the result of improvement in the treatment of primary systemic tumors and longer survival of cancer patients. Primary CNS lymphomas have increased because of high frequency in human immunodeficiency virus-infected patients. It is possible for intracranial tumors to be asymptomatic and be found incidentally at autopsy. In adult admissions to general
hospitals, metastatic tumors are probably the most common intracranial neoplasm, followed by
the gliomas. Both groups combined make up 60% of all intracranial neoplasms. Meningioma is
the third most frequent tumor, followed by the schwannomas of the acoustic nerve. The
incidence of pituitary adenomas varies in the different surveys, but they are fourth most frequent
intracranial tumors in adults. Pinealomas and midline embryologic nest tumors (teratomas and
cranioopharyngiomas) are rare tumors of childhood, whereas medulloblastomas/primitive
neuroectodermal tumors (PNT) and gliomas are frequent childhood tumors. The distribution of
intracranial gliomas shows a preponderance of 2:1 in males, whereas meningiomas occur 2:1 in
females.

Age is important factor for the type and localization of intracranial tumors. CNS is the
second most common site of primary tumors in children. In this age-group, 70% of intracranial
tumors are infratentorial (posterior fossa). Early in childhood (first decade) cerebellar
medulloblastomas/PNTs are the most frequent tumors followed by cerebellar astrocytomas.
Brain stem gliomas are seen in adolescents, whereas ependymomas of fourth ventricle are usu-
ally seen in children and young adults. The supratentorial tumors in childhood include
cranioopharyngiomas and pinealomas followed by astrocytomas.

Tumors in adults are chiefly supratentorial (located above the tentorium) and include
metastasis and glioblastoma multiforme followed by the meningiomas and pituitary adenomas
and other gliomas. The infratentorial (located below the tentorium including the cerebellum,
brain stem or fourth ventricle) posterior fossa tumors in adults include acoustic neuromas
(schwannomas) and cerebellar hemangioblastomas followed by gliomas, meningiomas, and other
rare tumors (Table 15-1).

The accuracy of the histologic diagnosis and the safety of diagnostic brain biopsies have
improved with the combination of better imaging resolution, immunocytopathology, and
stereotactic needle biopsies. Close cooperation and communication between neurosurgeons,
radiologists, and pathologists optimize the use and accuracy of needle biopsies for brain tumors.
The intraoperative use of the microscope, technological surgical advances, and presurgical
embolization of highly vascular tumors have improved the postoperative outcome.

**Symptomatology**

Intracranial neoplasms cause signs and symptoms by their general or local brain effects. General
effects are due to space occupation by the tumor, obstruction of cerebrospinal fluid (CSF) flow,
and edema of adjacent cerebral tissue. These effects produce increased intracranial pressure and
manifest clinically by headache, vomiting, and papilledema. Intracranial hypertension is not always
present in CNS tumors and correlates better with rapidity of tumor growth or obstruction
of CSF pathways rather than with presence or size of tumors. Benign, slowly growing tumors
such as meningiomas, pituitary adenomas, or slowly growing infiltrating gliomas give signs of
increased intracranial pressure very late in their course. The headache of tumor is frequently
intermittent, usually worse in the morning hours, with tendency toward increasing frequency and
severity. It is aggravated by straining, coughing, and change in posture and can be localized to
the site of the tumor. Nausea and vomiting are rare features and more frequently noted in
patients with cerebellar tumors. Papilledema, when present, is evidence of increased intracranial
pressure.

The local effects can be irritative and produce focal or generalized seizures. Onset of
seizures in nonalcoholic or nondrug abusers older than 30 years of age suggests intracranial mass
of which neoplasm is most common etiology. Seizures can occur in both intraaxial or extraaxial hemispheric neoplasms. Effects of tissue destruction by the neoplasm are loss of function (focal weakness) at the level of the lesion and liberation of lower centers (spasticity and hyperreflexia). Frequently onset of symptoms is non-acute and the clinical course progressive. If neurological symptomatology develops rapidly, mechanism is most likely vascular (ischemia, hemorrhage) but if nonacute, with progressive worsening (due to continued tumor growth and development of vasogenic edema due to breakdown of blood-brain) over a course of days, weeks or few months, consider neoplasm. Bleeding into the substance of a necrotic tumor such as a metastatic tumor or a glioblastoma, however, can appear as a sudden catastrophic illness (strokelike onset), particularly if tumors have grown "silently" in areas such as the frontal or temporal lobes. Certain rapidly growing malignant tumors such as glioblastoma multiforme or metastasis can also evolve clinically in a few days. Also, certain metastatic neoplasms (melanoma, lung, and renal cancer, choriocarcinoma) may bleed to cause brain hemorrhage. Also, pituitary neoplasm may cause tumoral bleeding “apoplexy”.

NEOPLASMS OF CHILDHOOD

Infratentorial Tumors

Medulloblastomas and Primitive Neuroectodermal Tumors (PNT)

Medulloblastomas, also known as primitive neuroectodermal tumors (PNT), are highly malignant; rapidly growing tumors derived from nests of small-undifferentiated cells located in the fetal external granular cells of cerebellum. A specific chromosome abnormality (17q duplication or deletion) may be found in some cases. They are predominantly found in infants and young children and arise in vermis of cerebellum. As they grow, these tumors occupy fourth ventricle. In older patients tumor arises laterally in cerebellar hemispheres (circumscribed desmoplastic medulloblastomas/PNT). Seeding by tumor cells in subarachnoid spaces and cerebral hemispheres is frequent. Clinical signs are due to cerebellar lesions and are primarily truncal ataxia and increased intracranial pressure because of obstructive hydrocephalus (compression of fourth ventricle). CT detects presence of posterior fossa tumor; however, MRI is more sensitive to show tumor extent in axial, coronal and sagittal sections. Treatment consists of radical surgical removal and shunting for correction of hydrocephalus followed by maximal radiation therapy because of radiosensitivity of medulloblastoma. Chemotherapy can be helpful for recurrent tumors. Some therapeutic protocols have reported a 50% to 60% incidence of long-term, disease-free survival.

Cystic Cerebellar Astrocytomas

Most cerebellar astrocytomas are cystic, slowly growing, benign, well-differentiated tumors. They are found predominantly in children. They usually arise laterally in cerebellar hemispheres. Frequently they are large cystic lesions containing mural nodule. Clinical findings are homolateral appendicular (limb) ataxia and head tilting to same side as the lesion. Signs of increased intracranial pressure are caused by compression of fourth ventricle. Treatment consists of cyst drainage with resection of mural nodule. Radiation and chemotherapy are not usually indicated. The prognosis is usually good, with long survivals even after partial resections.
Brain Stem Gliomas

Brain stem gliomas are tumors arising from astrocytes, usually in the pons, with a variable degree of cell differentiation. Most are fibrillary or diffuse in type, but glioblastomatous degeneration can occur. The higher the location in brain stem, more undifferentiated tumors are likely to be. These tumors are found predominantly in late childhood and adolescence and manifest clinically as slowly progressive long pyramidal tract signs and multiple cranial nerve involvement. Papilledema and other signs of intracranial hypertension are very late because of infiltrative growth up and down brain stem axis rather than direct neural tissue compression. These neoplasms usually originate in midpons. They can grow upward into midbrain and thalamus or downward into medulla or can extend exophytically into cerebellopontine angle cisterns. Survival is short in children who have cranial nerve palsies, patients who have a hypodense tumor on noncontrast CT/MRI, or patients with tumors involving entire brain stem as visualized on CT/MRI. Biopsy and partial resection can be done in tumors with exophytic extension. Surgical drainage of cysts found on imaging studies helps some patients. The majority of infiltrative neoplasms are not amenable to surgery. Radiation therapy can prolong survival in some patients. The full extent of these lesions is seen with MRI, especially on sagittal sections. These gliomas have worst prognosis of all childhood brain neoplasms and are usually fatal within 24 months.

Ependymomas

Ependymomas are benign, slowly growing, well-circumscribed intraventricular tumors derived from ependymal cells. The fourth ventricle is most common site (70%), but ependymomas can be found anywhere in ventricular system. When localized in fourth ventricle, they are most common in first two decades. Because tumor grows into ventricular cavity, clinical symptoms are late. Changes in mental status and frontal lobe signs are due to progressive hydrocephalus, as are signs of intracranial hypertension. Although histologically benign, they are difficult to resect completely because of their location. Partial surgical resection, shunting, and irradiation are palliative treatments.

Supratentorial Tumors

Supratentorial tumors in children are rare. The most frequent supratentorial tumors are craniopharyngioma and pinealoma. Also, solid, diffuse, well-differentiated astrocytoma can be seen. Gliomas (astrocytomas) of optic nerves and hypothalamus are seen more frequently in patients with neurofibromatosis. Gliomas (astrocytomas) can also arise in thalamic region or cerebral hemispheres in children and young adults.

Craniopharyngiomas

Craniopharyngiomas (adamantinomatous type) originate from squamous cell nests believed to be remnants of Rathke's pouch or from metaplastic cells from adenohypophysis. One of most frequent supratentorial tumors of childhood, craniopharyngioma is benign, slowly growing lesion that calcifies and adheres to surrounding neural tissue. Parasellar in location, it is usually suprachiasmatic, producing compression of hypothalamus and chiasm (Figure 15-1). Clinical manifestations are those of visual field defects (bitemporal caused by chiasmal compression) and hypothalamic syndrome (short stature, failure to thrive, delay in sexual development, diabetes insipidus). Suprasellar calcifications can be detected on plain skull roentgenography, and they
are well delineated by CT and MRI. Because of their location and the fact that they can adhere to neural tissue, total surgical removal without removing adjacent brain tissue is usually impossible. Craniopharyngioma has another peak of prevalence around the fourth and fifth decades. Calcification in this age-group is less frequent. Symptoms are visual defects caused by chiasmal compression or endocrine deficiencies caused by hypothalamic compression.

**Pineal Tumors**

The most frequent form of tumor in pineal region and third ventricle is germinoma (atypical teratoma). This is malignant and infiltrative tumor derived from primitive germ cells identical to those seen in the gonads. Because tumor grows within third ventricle, tumor cells frequently seed into ventricular system and subarachnoid spaces. The tumor can originate within pineal gland (true pinealoma) or in parasellar area (ectopic pinealoma). Symptoms may be due to 3 mechanisms: 1) intracranial hypertension caused by hydrocephalus and posterior third ventricular obstruction; 2) direct neural compression of diencephalon-midbrain (paralysis of vertical gaze and Parinaud syndrome); 3) endocrine dysfunction due to hypothalamic involvement (including diabetes insipidus, precocious puberty). It predominantly affects young adolescent males. Symptoms in pineal area tumors consist of compression of quadrigeminal plate and posterior commissure, giving origin to Parinaud's syndrome (vertical, mainly upward gaze palsy, papillary irregularity with nonreactivity to light) and compression of aqueduct producing hydrocephalus. Diabetes insipidus, visual field defects, and hypothalamic pituitary failure can be seen in lesions situated in anterior third ventricle. CT and MRI show presence of tumor; however, MRI in sagittal plane shows relationship of tumor to surrounding normal neural structures. Determination of alpha-fetal-protein and beta human-choriogonadotrophic levels indicates if malignant germ cell elements are present. These are most radiosensitive CNS tumors. Radiation therapy should include entire CNS axis because of CSF seeding. Survivals of more than 20 years after radiation therapy have been reported. Benign pineal tumors are best treated with surgery alone, whereas malignant tumors require radio- and chemotherapy. Other rare pineal tumors are teratomas. These tumors are usually benign with a range of well-differentiated tissue elements derived from three germ layers. Although they are benign tumors histologically, they are difficult to resect completely. Other tumors of pineal parenchyma are pineocytoma and pineoblastoma/PNT.

**NEOPLASMS OF ADULTHOOD**

Most of adult neoplasms (70%) are supratentorial. The two most frequent tumors are the metastatic type and glioblastoma multiforme followed by meningiomas, pituitary adenomas, and other gliomas. Glioblastomas and brain metastasis are very close in frequency, and together they constitute 60% of adult brain tumors. There are predominantly two posterior fossa neoplasms seen in adults: schwannoma of cranial nerve and cerebellar hemangioblastoma. Clivus meningiomas, chordomas, and epidermoid cysts are rare posterior fossa lesions in adults.

**Supratentorial Tumors**

**Metastatic Tumors**

Intracranial (brain, leptomeningeal) metastases are increasing in frequency because of longer survival of patients with other visceral primary tumors and more effective treatment of systemic cancer. Eighty-one percent of metastases are supratentorial, 16% are cerebellar, and only 3% are
found in brain stem. Neurologic symptoms can be first manifestation of some systemic neoplasms, most commonly lung cancer. Signs of increased intracranial pressure, seizures, dementia, or focal motor or sensory deficit are seen (Figure 15-2). Symptomatology is usually progressive, but acute onset (strokelike) can be seen in some tumors that bleed or spread by hematogenous dissemination (tumor embolus) (Figure 15-3). Brain tumor headache is frequently morning in occurrence due to intracranial hypertension. Lateralizing neurological signs are due to location of metastatic lesion. If there are multiple lesions, clinical features may be diffuse and encephalopathy from bilateral hemispheric dysfunction may occur. CT/MRI with contrast is most sensitive study to detect metastatic lesions; however, they lack specificity to determine precise pathology of lesion(s). Lumbar puncture with CSF cytology is necessary if leptomeningeal metastases are suspected which may coexist with parenchymal lesions. A triphasic clinical course (sudden onset, stabilization sometimes with improvement, followed by progressive worsening) can be seen in metastatic neoplasms or with glioblastoma multiforme. The most frequent primary sources of metastasis are lung tumors in both sexes followed by breast tumors in females. Both tumors are followed in frequency by melanoma and colon tumors. Multiple brain lesions are frequent and are likely to be associated with lung cancer and melanomas. Colon, breast, and renal cell (clear cell) tumors have a tendency to produce solitary lesions. Diagnosis of solitary lesion is important because of its resectability if found in surgically accessible (superficial) brain area; however, even if CT/MRI show only single macroscopic lesion, there may be multiple microscopic lesions. Most hemispheric lesions are found in arterial border zones, predominantly in parietal lobe. Although most lesions are intraparenchymal nodules, dura can be infiltrated and thickened in hemorrhagic subdural seeding. Also, diffuse infiltration of the meninges (meningeal carcinomatosis) is predominantly seen with gastrointestinal and breast adenocarcinomas. Vasogenic edema surrounding metastases is a constant feature. The edema is frequently severe and can cause cerebral herniation but edema responds dramatically to corticosteroid therapy. Irradiation therapy and corticosteroids are palliative measures for both intracranial and intraspinal metastases. Chemotherapy is useful in some patients.

**Paraneoplastic Syndromes (Remote Effects of Cancer on the Nervous System)**

There is a group of neurologic disorders that occur in patients with carcinoma, but that are not due to direct infiltration of nervous system by neoplastic cells. Everyone of these conditions can appear before the malignancy is diagnosed, during its course, or at a time when the malignancy is thought to be in remission. These disorders are characterized pathologically by destruction of neurons and by perivascular lymphocytic cuffs in affected regions. The histopathologic findings, presence of antineuronal antibodies in the CSF and serum of affected patients, synthesis of specific antibodies within the CNS, detection of intraneuronal IgG within patient's brains, and response to immunosuppressive therapies suggest autoimmune mechanism. Commercially available determination of Hu and Yo paraneoplastic autoantibodies can confirm the autoimmune cause for neurologic symptoms associated with the syndromes. Box 15-1 shows neurologic syndromes, which can occur singly or in combination.
Glioblastoma Multiforme
Glioblastoma multiforme is highly malignant, rapidly growing tumor of glial cell origin that usually arises de novo but occasionally can start as astrocytoma or oligodendroglioma. It is most frequent primary tumor in adults and is found mainly in frontal and temporal lobes but can arise in any part of the CNS including brain stem (Figure 15-4). It predominantly affects males in fourth and fifth decade, but it can be found in young patients. Symptoms are usually progressive but of short duration, and, when discovered, tumors are usually large and infiltrate into normal neural tissue. Because lesions are highly necrotic and vascular, they have tendency to bleed and can present as apoplectic episode (strokelike onset). In some cases, patients present with seizure (focal or partial) disorder. The initial diagnostic studies, CT/MRI, usually visualize the lesion but can rarely be negative; and if initially negative subsequent studies then show the neoplasm. CT/MRI show irregularly shaped, mixed density lesion, which is maximally seen in deep cerebral white matter with infiltrating portions. Enhancement pattern is irregular and heterogeneous and usually ring-like in shape. The tumor spreads along white matter pathways such as corpus callosum. Lack of enhancement should eliminate likelihood of malignant glioma. These neoplasms infiltrate into normal neural structures and make treatment difficult. Even after radical resection, radiation therapy, and chemotherapy, mortality is still high, with neurologic deterioration and death occurring within 2 years. Treatment protocols have prolonged survivals by only few months. Novel treatment strategies (inhibition of signal transduction pathways) are being developed to enhance survival.

Meningiomas
Meningiomas are benign, slowly growing, extraaxial tumors derived from arachnoidal cells, chiefly those in arachnoidal villi, hence their tendency to arise along venous sinuses. They are extra-axial and well circumscribed. They compress but do not invade neural structures as constrained with gliomas. They are the third most common tumor seen in adults, and majority occur in females (2:1). The most frequent site is in parasagittal region, with some of arising from falx cerebri (Figure 15-5). Other sites are sphenoid ridge and tuberculum sella; more unusual locations are tentorium cerebelli, foramen magnum, clivus, and within ventricular system. When seen in the clivus, they can compress brain stem. The neoplasm grows outside, displacing and compressing, rather than infiltrating, nervous tissue. The neurologic findings, when present, depend on site of tumor. Headache, focal or generalized seizures, dementia, and progressive ocular and motor deficits can be clinical signs dependent upon meningioma location. Papilledema is not a frequent finding because the tumors grow slowly. CT/MRI demonstrates sharply margined, homogeneously enhanced lesion. Hemorrhages and cysts within tumor are rare; however, psammoma body calcifications are common throughout meningioma. Angiography demonstrates tumor's blood supply. Estrogen receptors are present on meningiomas and may stimulate growth. There is higher incidence in woman and increased association with breast cancer. Because most of the tumors are highly vascularized and their circulation is derived from dural vessels, enlargement of vascular marking and hyperostosis caused by reaction to infiltration by the tumor on adjacent skull can be seen on plain skull roentgenograms. Preoperative embolization of tumor facilitates resectability. Treatment consists of surgical resection, which is not always successful because of tumor location in inaccessible area or

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infiltration into the venous sinuses. The tumor can recur if it is not completely resected and may undergo sarcomatous malignant degeneration.

**Pituitary tumors**

Most pituitary neoplasms arise from anterior lobe portion of gland, hence the name pituitary adenoma. They may be small and asymptomatic and may be incidental lesions detected by skull radiogram, CT or MRI. Radioimmunoassay techniques measure increased serum hormone levels (prolactin, growth hormone, adrenocorticotropic hormone). Certain small microadenomas (less than 10 mm) which are incidental or secrete high hormone levels) can be demonstrated with CT/MRI especially when pituitary gland is visualized in coronal sections. When pituitary biopsy is done it is possible to demonstrate hormone granules within the tumor cells by immunocytochemical staining (immunoperoxidase). Pituitary adenomas are classified according to hormonal secretions and cytoplasmic granules stained by immunocytochemistry. In the past, pituitary adenomas were classified as acidophilic, basophilic, chromophobic as determined by staining properties with hematoxylin and eosin. These lesions include prolactin cell adenoma (prolactinoma), growth hormone cell adenoma, mixed prolactin and growth hormone adenoma, corticotropic cell adenoma, and acidophilic stem cell adenoma. Forty-one percent of the adenomas are prolactinomas, 19.5% are growth hormone producing, and 16.7% are adrenocorticotropic hormone (ACTH) producing. Nonsecreting hormone neoplasms (null cell or oncocytomas) are rare. Prolactinomas can cause amenorrhea, galactorrhea, and infertility in young females; in males they can cause impotence. Serum prolactin levels are usually elevated. CT/MRI shows enlarged size sella and small hypodense lesion in slightly enlarged gland (microadenoma). MRI scanning is more sensitive in detecting these small tumors and these are best visualized on coronal imaging sections. Prolactinomas can also grow to erode and enlarge sella and can compress optic chiasm (initial growth and compression is on undersurface of optic chiasm), producing bitemporal superior quadrantanopia and later bitemporal hemianopsia. Macroadenomas are larger than 10 mm in size. As tumor enlarges, symptoms of panhypopituitarism can appear. Bleeding within tumor (pituitary apoplexy) can produce acute onset of blindness and signs of subarachnoid hemorrhage. The tumor can also extend laterally into cavernous sinus to compress abducens, oculomotor, trochlear, ophthalmic division of trigeminal nerve, internal carotid artery) or grow down into the sphenoidal sinus to cause CSF rhinorrhea. Also, tumor can grow anteriorly into optic nerve(s) or frontal lobe or posteriorly into brain stem: headache result from stretching of diaphragma sella and contiguous dural structures which transmit impulses through ophthalmic branch of trigeminal nerve. Adenoma can be resected transsphenoidally or by bifrontal craniotomy. Bromocriptine can reduce prolactin level but tumor size when medication is discontinued hormone level rises and symptoms recur. Adenomas are radiosensitive tumors. Growth hormone-secreting tumors appear in adults as enlargement of hands, feet, jaws, and frontal bones (acromegaly) or as gigantism in children. Endocrinologic studies show elevated serum growth hormone levels. Surgical resection is always necessary. ACTH-secreting adenomas are usually small (microadenomas) and appear as Cushing's disease, manifested by "moon faces," hirsutism, hypertension, osteoporosis, "buffalo hump," and diabetes mellitus. Endocrinologic studies confirm presence of hypercortisolism. Most frequent cause of Cushing's syndrome is iatrogenic use of corticosteroid, and it also can be produced by primary adrenal disease but search to visualize pituitary tumor should be done in
selected cases. Transphenoidal microsurgical exploration is procedure of choice in ACTH-producing pituitary microadenoma.

Other Supratentorial Tumors
Other less common supratentorial tumors include oligodendrogliomas, astrocytomas, and lymphomas (microgliomas). Oligodendrogliomas are rare tumors derived from oligodendroglial cells. They are predominantly seen in adults, frequently in frontal lobes. Frequently they are calcified (28%) and can also bleed. Papilledema, paresis, and seizures are frequent symptoms. Calcification, cysts and necrosis are common pathological features. CT shows calcified and cystic features and infiltrative and malignant feature of neoplasm. Treatment depends upon pathological features as to whether neoplasm is “low-grade” or “high-grade”. If high grade, surgery, radio, or chemotherapy is warranted. Astrocytomas can also be found in adults and are usually low-grade infiltrative tumors. Gemistocytic astrocytomas are seen in temporal lobe of young adults and have a tendency to become anaplastic astrocytomas. Primary CNS lymphomas (microgliomas) or reticulum cell sarcomas of brain are tumors derived from B-lymphocytes. They are frequently multicentric and are most frequent in patients on immunosuppressive therapy, but may also be seen in immunocompetent patients. They are multifocal intra-axial periventricular tumors which may have diffuse leptomeningeal involvement. Eye (uveal or vitreous) lesions may be initial manifestations of lymphoma. Pathological examination of CSF (cytology) aqueous humor (by vitreous examination) or brain biopsy establishes the lymphoma diagnosis. Diagnosis requires brain biopsy and is of importance because tumor may respond to a combination of radiation and chemotherapy. Primary CNS lymphoma is the most frequent CNS tumor in patients with acquired immune deficiency syndrome (AIDS) and in these patients carries a poor prognosis regardless of therapy (surgery, irradiation, chemotherapy, corticosteroids). Meningeal lymphomatous infiltration produces multiple cranial nerve involvement.

Infratentorial Tumors
There are two main tumors in adults that originate in posterior fossa structures: schwannoma of cranial nerves and cerebellar hemangioblastoma.

Schwannoma of Cranial Nerves
Schwannomas are benign, slowly growing tumors found in peripheral nerves, usually sensory roots, and are derived from Schwann cells and fibroblasts. They frequently arise from intracanalicular portion of eighth nerve, frequently vestibular branch (acoustic neuroma), but can also originate from fifth or seventh nerve. Bilateral tumors are found in patients with von Recklinghausen's disease. Earliest clinical symptom is hearing loss, especially speech discrimination, followed by symptoms caused by compression of structures in pontocerebellar angle with homolateral cerebellar dysfunction, facial weakness or facial sensory deficit, and long tract signs if tumor has compressed pons. CT/MRI in coronal plane shows enlargement of intracanalicular portion of internal acoustic canal with homogeneously enhancing round lesion seen within acoustic canal. Brain stem (auditory) evoked potentials are usually abnormal in patients with acoustic neuromas. Treatment consists of resection of lesion attempting to spare
acoustic and facial nerve. Other tumors occupying cerebellopontine angle area include meningiomas, chordomas (arising from clivus), and epidermoid cysts (cholesteatomas).

Cerebellar Hemangioblastoma
Cerebellar hemangioblastoma is a benign, slowly growing tumor composed of mixture of endothelial cells and stromal (foam) cells of obscure origin. The tumors are usually cystic with mural nodule but can be solid hemorrhagic lesions. They are found in young and middle-aged adults. In approximately 20% of the cases the tumor is familial (Lindau's disease) and can be associated with tumors in spinal cord, retinal angiomas, pancreatic and hepatic cysts, and renal tumors (von Hippel-Lindau disease). Clinical symptoms are those of cerebellar deficit associated with polycythemia as result of release of erythropoietin by tumor or one of its precursors. Signs of increased intracranial pressure may be evident because of displacement of fourth ventricle. CT/MRI studies differentiate these lesions from other neoplasms, except from cystic cerebellar astrocytomas. Treatment consists of surgical resection.

Chordoma
This is a rare posterior fossa, destructive, slowly growing tumor of notochordal origin seen predominantly in young adult males that arises in the clivus area and can compress the brain stem. This tumor develops from remnants of embryonic notochord and resembles cartilage. They are locally infiltrative and injure contiguous cranial nerves. These patients clinically present with multiple, progressive cranial nerve dysfunction. Skull radiogram shows destructive bone lesions at skull base and sagittal MRI may demonstrate the lesion. The chordomas are also seen in the lumbosacral spine.

Colloid Cyst
This epithelial cyst predominantly appears in anterior third ventricle and can produce intermittent hydrocephalus by blocking foramina of Monro. The main symptom is intermittent headache occurring over a period of several years, sometimes relieved by changing position of head. Neurological examination may show papilledema and lateral rectus paresis only. This may simulate idiopathic intracranial hypertension; however, CT/MRI may show the lesion at anterior third ventricle causing obstructive hydrocephalus. Sudden death is frequent and is result of herniation. Treatment consists of surgical resection or CT/MRI-guided aspiration of the cyst.

Epidermoid and Dermoid Cysts
These cysts, also known as pearly tumors, are not true neoplasms. They grow by desquamation of keratin from well-differentiated squamous epithelium that lines inner portion of the cyst's wall. The dermoid cyst also contains adnexal appendages. These lesions are predominantly found in posterior fossa in cerebellopontine angle, parapontine region or within fourth ventricle. Clinical features are those of compression of cerebellum or brain stem. CT shows very low density lesion and occasional peripheral calcification whereas this appears as hyperintense lesion on MRI. The treatment consists of surgical resection of the cyst.
Intraspinal Tumors

Intraspinal tumors can best be understood if they are related to the dura (see Figure 15.6). Imaging studies (CT/MRI) have improved diagnostic accuracy. The most common intraspinal tumors are the extradural (epidural) tumors, which are very frequently metastatic to vertebral bone and produce signs because of compression of nerve roots or spinal cord.

Epidural spinal metastases originate from vertebral bodies. Initial symptoms are back pain which is worse at night and not relieved by rest (as contrasted to pattern seen in patients with myofascial pain). On clinical exam, there is exquisite localized pain when pressure is applied to involved vertebral body. The metastatic lesion may extend to contiguous nerve root to cause radiculopathy and with further extension there is epidural spinal cord compression. This causes motor, sensory and autonomic (bladder and bowel dysfunction) at and below the level of spinal cord compression. Osteolytic and osteoblastic lesion can be detected by spine radiogram, isotope bone scan and CT. MRI is most sensitive imaging technique to detect complete length of cord compression. This is seen with sagittal views. Treatment of epidural spinal cord compression depends upon patient clinical condition (clinical state, age, extent of primary neoplasm, tumor pathology). Surgical decompression may be warranted especially if tumor is radiation resistant. Patients with advanced systemic disease are poor surgical risks. A combination of high dose steroids and radiotherapy is best therapeutic approach.

Tumors that are intradural may be extra- (outside of substance of cord) or intramedullary (within substance of the cord). Intradural extra-medullary (within the dura but outside the cord) tumors include meningiomas, neurofibromas, schwannomas, and may compress one-half of the cord (hemisection or Brown-Sequard syndrome with ipsilateral motor and proprioceptive deficit and contralateral pin-temperature and loss with autonomic dysfunction). Intradural intramedullary tumors include astrocytoma, ependymoma. Clinical features include shawl-like sensory loss due to initial involvement of spinothalamic fibers which cross or decussate in the central portion of spinal cord. As tumor expands, cervical-thoracic and lumbar fibers are involved, but sacral area is usually spared as these fibers are most lateral. Syringohydromyelic may simulate presentation of intradural intramedullary neoplasm. Myelography, with post-myelogram, CT or MRI may detect spinal tumor.

Most of the intradural tumors are primary (Figure 15-6). The intradural tumors can arise within spinal cord tissue (intramedullary), most of them being gliomas, or they can originate outside cord in nerve roots (schwannomas) or arachnoid (meningiomas). Meningiomas, schwannomas, and ependymomas are in most cases surgically resectable. The level at which tumor originates is important because most of cervical tumors are astrocytomas, most thoracic tumors are meningiomas, most lumbar area tumors are schwannomas, and most sacral and filum terminale tumors are ependymomas. The most frequent spinal tumor is extradural metastatic tumor. The most frequent intramedullary tumor is the ependymoma.

SUMMARY

Neoplasms of the nervous system are abnormal masses produced by a disturbance of cell growth caused by an autonomous proliferation of cells. Neoplasms can be primary if they arise from intracranial and intraspinal tissues or secondary if they originate outside brain and spine and invade CNS (metastasis). Primary tumors can originate from brain parenchyma (gliomas) or from meninges (meningiomas), pineal gland (pinealomas), or pituitary gland (pituitary adenomas). Age, sex, and location of tumor are important factors in diagnosis of these lesions.
Most tumors in children are infratentorial, meningiomas are more frequent in females and rare in children, and glioblastomas are more frequent in adult males. Systemic cancer can affect CNS and PNS by producing not only metastasis but also paraneoplastic syndromes due to autoimmune phenomena. New developments in imaging techniques have improved detection and improved complete delineation of these lesions. Innovations and refinements in surgical procedures have improved surgical treatment of some of these tumors.


**Suggested Readings**

**General**

**Acoustic Neuromas**

**Gliomas**

**Lymphoma**

**Meningiomas**
Metastases

Pituitary Neoplasms

Pineal Neoplasms

Spinal Cord Neoplasms

Paraneoplastic Syndromes
BOX 15-1

1. Cerebellar degeneration. This represents pancerebellar disturbance with gait and truncal ataxia occurring along with ataxia of arm and legs. The patients can also be dysarthric and have horizontal nystagmus. This disorder is most commonly associated with lung and ovarian carcinoma and lymphoma. Cerebellar dysfunction does not improve despite tumor removal, but clinical improvement has been reported after successful tumor treatment. Antibodies to the Yo antigen are most common paraneoplastic antibodies to Purkinje cells found in these patients.

2. Peripheral neuropathy and sensory neuronopathy. Subacute or chronic mixed sensorimotor neuropathy is most frequent type of neuropathy associated with neoplasia. Neuropathy is usually seen in adult males and appears as distal numbness, dysesthesias, and paresthesias. It is most common with carcinoma of lung, but it can be associated with cancer of gastrointestinal system and with multiple myeloma. It is important to remember that sensorimotor neuropathies are also a common complication of certain antineoplastic drugs (e.g., vincristine, cisplatin). Sensory neuronopathy consists of paresthesias, pain, and unsteadiness (especially in dark environment) and severe sensory ataxia associated with small cell bronchogenic carcinoma. The pathologic features, which explain clinical findings in sensory neuropathies, are degenerative changes in dorsal root ganglia with secondary changes ascending into posterior columns of spinal cord. Several tests to detect autoantibodies are commercially available to identify cause of the patient's neuropathy.

3. Subacute necrotizing myelopathy. This rare condition is characterized by rapidly progressive necrotizing myelopathy. Initial symptoms are paresthesias and weakness in feet which rapidly spread to legs, trunk, and arms. These patients have loss of bladder and bowel function and develop paraplegia with bilateral Babinski signs. Pathologic findings are necrotic lesions in both gray and white matter of spinal cord. Diagnostic tests, including imaging studies, are necessary to differentiate this remote effect from spinal epidural metastases.

4. Encephalomyelitis. This condition has usually been associated with oat-cell bronchogenic carcinoma. This inflammatory disorder can affect all levels of neural axis (cerebral hemispheres, brain stem, spinal cord) with predominant involvement of gray matter. Pathologically there is destruction of neurons, microglial proliferation, and perivascular lymphocytic cuffing. If cerebral hemispheres are involved, there is predilection for limbic system (i.e. limbic encephalitis). These patients show neurobehavioral abnormalities (confusion, memory loss, anxiety, depression, hallucinations). CSF shows sterile lymphocytic pleocytosis (without neoplastic cells) and elevated protein content.

5. Motor neuron disease. A form of motor neuron disease associated with neoplasia has been recognized; however, there is only one reported case in which the symptoms of amyotrophic lateral sclerosis remitted following successful treatment of neoplasm. Both motor neuron disease and carcinoma cause weight loss, weakness, muscle wasting, and cachexia and occur most commonly in patients older than 50 years old, so association may be more apparent than real. Not all patients with symptoms of motor neuron disease require a complete search for an occult neoplasm.

6. Dermatomyositis. When seen in adults, particularly in males, this can be associated with occult neoplasm.

7. Eaton-Lambert myasthenic syndrome. This is characteristically seen in adults, predominantly males. The fatigue caused by this syndrome rarely affects the eye muscles and is associated with areflexia that returns after exercising the tested muscle. Patients may also complain of a metallic taste in the mouth. Autonomic dysfunction is common with this condition.

8. Progressive multifocal leukoencephalopathy. This is a viral infection produced by JC virus. It was first described in patients with systemic lymphomas and is seen predominantly in immunosuppressed patients. It is now an infection frequently seen in AIDS patients.
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FIGURE 15-1. CT scan of brain with contrast showing a mid-line suprasellar (area of third ventricle) multicystic calcified craniopharyngioma.

FIGURE 15-2. CT scan with enhancement showing multiple bilateral round metastases surrounded by edema (low-density areas).
FIGURE 15-3. Brain and cerebellum showing well-circumscribed metastatic lesions with hemorrhage.

FIGURE 15-4. A. Coronal section of a brain showing a glioblastoma multiforme. Note infiltration of the tumor across the corpus callosum and areas of hemorrhagic necrosis. B. CT scan with enhancement showing a glioblastoma multiforme surrounded by edema (lucent area).
FIGURE 15-5. A. Coronal section of brain showing a convexity meningioma. Upper arrow shows displaced cortex and surrounding edema. Ventricle is compressed on same side. Lower arrow shows hippocampal herniation. B. CT scan with enhancement showing a parasagittal meningioma surrounded by edema (lucent area).

FIGURE 15-6. Intraspinal tumors.