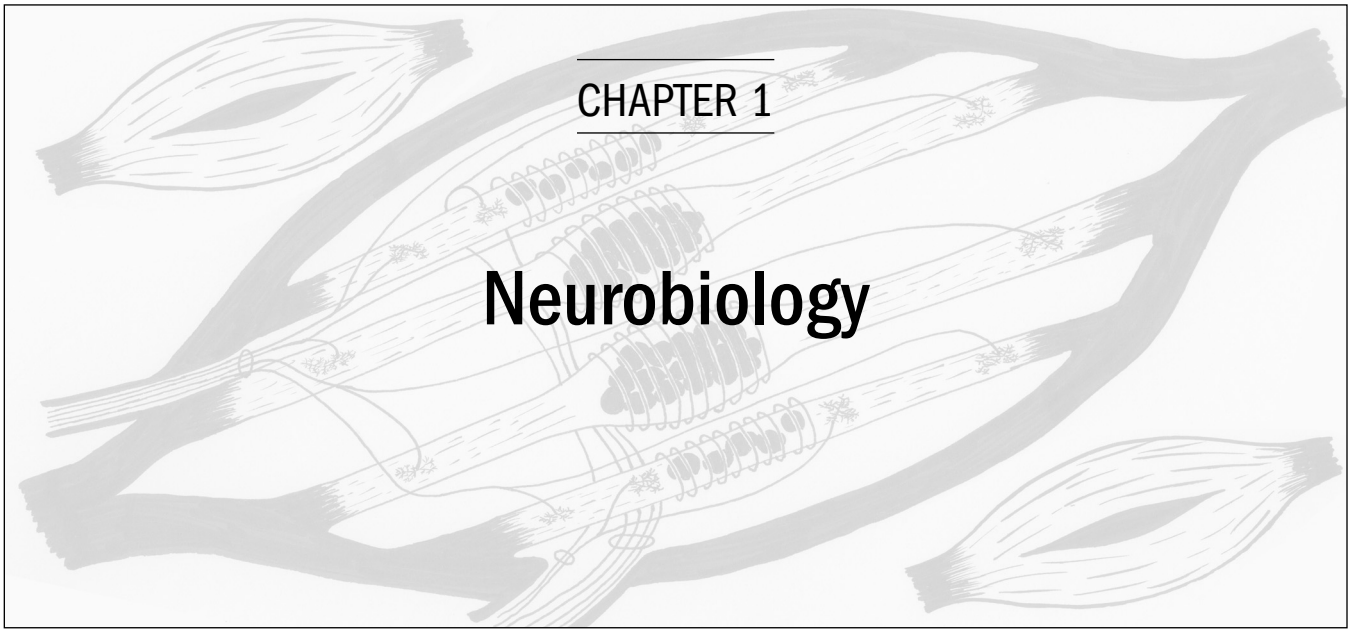


CHAPTER 1

Neurobiology

STRUCTURAL ORGANIZATION AND HISTOLOGY OF THE NERVOUS SYSTEM

Neuroglia

The nervous system is composed primarily of two classes of cells: glia and nerve cells. Neuroglia perform several important support functions, including myelination of neuronal axons, neurotransmitter uptake, neuronal growth factor synthesis, removal of extracellular debris, assistance with neuronal migration, and they also contribute to the structure of the blood-brain barrier. Neuroglia consist primarily of four distinct cell populations, including microglia, astrocytes, oligodendrocytes, and Schwann cells. Astrocytes are named for their star-shaped cell bodies and are essential to the structure and function of the central nervous system (CNS). Astrocytes regulate the balance of electrolytes in the extracellular space, primarily by sequestering potassium, which tends to accumulate in the extracellular space of depolarized neurons. The high permeability of the astrocyte cell membrane to potassium helps neurons maintain their responsiveness by facilitating repolarization. Astrocytes have long radial processes that project from the cell body with special terminations called end-feet. These end-feet provide nutrient support to neurons, and stimulate endothelial cells to form the tight junctions that compose the blood-brain barrier. Astrocytes also regulate the concentration of certain neurotransmitters, interact with the immune system, divide in response to injury (astrocytosis or gliosis), and have a limited phagocytic capacity. Grossly, astrocyte histology can be examined with heavy metal impregnation, and staining for a specific intermediate filament; namely, glial fibrillary acidic protein. There are two basic types of astrocytes: fibrous astrocytes, which are found primarily in white matter, and protoplasmic astrocytes, which reside primarily in gray matter. Specialized astrocytes include Bergmann cells, which surround and support the Purkinje cells of the cerebellum, and Müller cells of the retina. Oligodendrocytes reside solely in the central nervous system, and they are responsible for myelination of neuronal axons. A single oligodendrocyte can myelinate multiple axons. Schwann cells, in contrast, are found in the peripheral nervous system and they myelinate only a single internode of one axon. Microglia are derived from macrophages (mesodermal origin) and subsequently migrate into the CNS. They subserve a primary role of phagocytosis and antigen presentation and are activated with injury or infection (Kandel pp 19–21, 1288–1293).

Neurons

The neuron comprises the basic unit of the nervous system, but only accounts for approximately 10% of the total CNS cell population (glia account for the rest). Histologically, neurons have a nucleus, soma (cell body), dendrites, a single axon, and synaptic terminals. Neurons maintain high levels of metabolic activity, and thus have prominent ribosomes, rough endoplasmic reticulum (basophilic structure called Nissl substance), Golgi complexes, mitochondria, and lysosomes in their cytoplasm. The cytoskeleton of neurons is composed of microtubules, microfilaments, and neurofilaments. Large bundles of microtubules and neurofilaments are found at the bases of dendrites and axons. Dendrites represent the afferent component of the neuron, and they radiate out from the neuron

soma in highly variable and often extensive patterns. Dendrites are unmyelinated, in contrast to the axon, which is often myelinated. The neuron contains a single axon, which arises from the axon hillock of the soma and extends out in a tubular fashion. The axon hillock represents the most excitable portion of the neuron plasma membrane (due to a high concentration of sodium channels), and it is devoid of Nissl substance. The axon represents the efferent component of the neuron, and it conducts action potentials that are generated in the soma or axon hillock of the neuron. Action potentials often result in the release of neurotransmitters at the terminal end (presynaptic terminal) of the axon. Axons can synapse on neuronal dendrites, cell bodies, or even other axons, but often multiple axons synapse on both smooth and spiny portions along the dendrite. Neurons are often classified by their number of processes as unipolar (one process), bipolar (two processes), pseudounipolar (two processes that fuse into one), or multipolar (many processes). Unipolar neurons are the simplest and are found only in the autonomic nervous system in vertebrates. Bipolar neurons are associated with the special senses (vestibular, auditory, olfactory, and visual). Pseudounipolar neurons comprise sensory ganglia of cranial nerves and spinal nerves (e.g., dorsal root ganglia). Multipolar neurons are the most prevalent type of neuron in the nervous system, and they have multiple dendrites (Kandel pp 21–25, 72–75).

Ependyma

Ependymal cells line the surface of the ventricles of the brain and the central canal of the spinal cord. These cells have numerous apical cilia and microvilli, and are connected to each other by tight junctions at their apical (luminal) surfaces. Ependymal cells have absorptive and secretive functions, and their cilia facilitate cerebrospinal fluid (CSF) circulation within the ventricular system. The tight junctions that link ependymal cells together do not completely surround the cell. Therefore, large molecules are capable of traversing this space, which differentiates the CSF-brain barrier from the blood-brain barrier. The ependymal layer that lines the roof of the third and fourth ventricles, and the choroidal fissure of the lateral ventricles is called the tela choroidea. The tela choroidea is a specialized secretory epithelium (choroid plexus) that synthesizes approximately 70% of the CSF. The blood-brain barrier in the choroid plexus is also unique, in that it is primarily epithelial, in contrast to the endothelial blood-brain barrier that exists elsewhere (see Chapter 4, Neuropathology for basic neurohistology slides) (Kandel pp 1293, 1295–1297).

MOLECULAR BIOLOGY OF THE NEURON

Organelle Structure

Neurons have high levels of metabolic activity, which is reflected in their cytosolic structure. Neuronal cytoplasmic organelles include rough and smooth endoplasmic reticulum, endosomes, secretory vesicles, lysosomes, peroxisomes, mitochondria, and the Golgi apparatus. Proteins and phospholipids destined for secretion are initially synthesized in the rough endoplasmic reticulum (rER). These products are then transported to the Golgi apparatus via transport vesicles for processing (although N-linked glycosylation and glycolipid conjugation are initiated in the rER). The Golgi complex further modifies these proteins by adding polysaccharides, which can direct specific proteins to secretory vesicles, lysosomes, and the plasma membrane. Golgi processing includes glycosylation reactions (O-linked and N-linked glycosylation), proteoglycan formation, polysaccharide phosphorylation, attachment of fatty acids, and sulfation of tyrosine and sugar residues. This processing increases the hydrophilicity (solubility) of these proteins, increases their biologic activity, or helps delay their degradation by proteases. Clathrin coats facilitate the budding of vesicles from the Golgi complex. Secretory vesicles (dense core vesicles) are targeted primarily to axon terminals where they participate in calcium-regulated exocytosis after action potential propagation (Kandel pp 67–71, 94–97).

Axonal Transport

There are several types of axonal transport that facilitate trafficking of proteins and organelles to and from the axon terminal. Membranous organelles and secretory vesicles are transported to the axon terminal via fast anterograde axonal transport. This mode of transport is dependent on the protein kinesin and adenosine triphosphate (ATP), and occurs at a rate of greater than 400 mm per day. Kinesin binds the organelle or vesicle and then forms intermittent cross-bridges with tracks of microtubules, resulting in stepwise transport down the axon. Drugs that interfere with microtubule structure, such as vinblastine and colchicine, also disrupt fast anterograde transport. There are several types of slow anterograde axonal transport. Component A utilizes a protein called dynamin, is guanosine triphosphate (GTP)–dependent, and facilitates transport of cytosolic proteins and cytoskeletal elements. It is much slower than fast anterograde transport, occurring at a rate of 0.2 to 2.5 mm per day. Component B is slightly faster, at 2 to 4 mm per day, and uses an actin/myosin

CHAPTER 4

Neuropathology

Major Contributor: James L. Fishback

HISTOLOGY OF THE CENTRAL NERVOUS SYSTEM

The astrocyte is a star-shaped glial cell that performs several important functions in the CNS. Astrocytes contain long radial processes that provide support to surrounding neurons and endothelial cells that compose the blood-brain barrier. These cytoplasmic processes are numerous and highly-branched on protoplasmic astrocytes of the gray matter, and fewer in number and straight on fibrous astrocytes of the white matter. Astrocytes can be demonstrated in histologic sections with phosphotungstic acid-hematoxylin stains, Holzer stains, heavy metal impregnation techniques, and staining for the intermediate filament GFAP (Plates 1 A and B). Neurons in general have large cell bodies with prominent nuclei and nucleoli, basophilic granular cytoplasm, dispersed chromatin, a single axon, and many dendrites. Neurons can be demonstrated with routine hematoxylin and eosin stains, heavy metal impregnation techniques, and Nissl stains (Plate 2). The demonstration of neuronal cytoplasmic processes is more difficult, and often requires the use of heavy metal techniques, such as gold or silver impregnation (Plate 3). Oligodendrocytes are glial cells that myelinate axons within the CNS, and are often clustered around the soma of neurons. Oligodendrocytes usually have small condensed nuclei, which are often readily demonstrated with several different staining techniques (Plate 4). Ependymal cells are specialized glial cells that form a simple cuboidal or low columnar epithelial lining along the surfaces of the ventricles (Plate 5). Ependymal cells contain prominent cilia at their apical surfaces that facilitate the circulation of cerebrospinal fluid. The choroid plexus is a highly vascular structure that produces the vast majority of the cerebrospinal fluid and is located within the ventricular system of the brain. Choroid plexus is composed of a modified epithelial cell layer that surrounds a vascular stroma and exhibits a papillary configuration (Plate 6) (Wheaters pp 112–117, 130–134).

DEVELOPMENTAL DISORDERS

Hypoxic-Ischemic Fetal Lesions

Hypoxic-ischemic lesions are the most common etiologies of neuropathology in the pediatric population. Causes of hypoxic-ischemic lesions in the fetus include intrauterine infection, maternal disease (hypertension, diabetes mellitus, hypoxia), teratogens, smoking, trauma, placental abnormalities (cord tethering or knot formation), congenital heart disease, metabolic disease, and CNS malformations. Tissue repair in the CNS of the fetus during the first 20 weeks of gestation does not involve gliosis, which leaves a smooth-walled defect after resorption of necrotic tissue and can resemble malformations. Lesions that occur in the late weeks of gestation, however, are associated with prominent gliosis, which is more typical of acquired lesions. Porencephaly results from ischemic insults to the fetal or neonatal brain. Porencephalic cysts are usually found adjacent to the Sylvian fissures or central sulci, are often bilateral and symmetric, and are smooth-walled and lined with gliotic white

matter. Porencephaly is associated with mental retardation, congenital hemiplegia, chronic spasticity, and epilepsy. Schizencephaly is also a destructive lesion of the fetal or neonatal brain. Schizencephalic cysts are lined by heterotopic gray matter, extend from the ependymal surface of the brain to the pial surface, and their presentation and symptomatology is similar to that of porencephalic cysts. The cysts may be filled with CSF (open lip) or collapsed (closed lip). Arachnoid cysts are developmental abnormalities that are generated by the separation of the arachnoid membrane. The wall of an arachnoid cyst thickens with the deposition of collagen over time (Plate 7). Hemorrhage is also a relatively common cause of neuropathology in the brain of the fetus or neonate. Risk factors for hemorrhage in this population include perinatal distress, asphyxia, and immaturity. Hemorrhage in the brain of the fetus or neonate can be subarachnoid, subpial, intraventricular, parenchymal, or confined to the germinal matrix. Subependymal germinal matrix hemorrhage (SEH) usually occurs in premature infants (less than 34 weeks of gestation) with low birth weight, and is usually located adjacent to the head of the caudate nucleus or thalamus. SEH is the most common cause of intraventricular hemorrhage (IVH) in premature infants. Grade 1 SEH is confined to the germinal matrix, grade 2 extends into the lateral ventricle, grade 3 consists of IVH with hydrocephalus, and grade 4 involves extension of the hemorrhage into the brain parenchyma (Plate 8). The pathogenesis of SEH involves hypoxic injury to the fragile microcirculation of the germinal matrix, which leads to loss of autoregulation, overperfusion, and hemorrhage. The symptoms of SEH vary extensively depending upon the grade of the hemorrhage, and SEH is commonly associated with respiratory distress syndrome (hyaline membrane disease), coagulopathy, congenital heart disease, and hypernatremia. Choroid plexus hemorrhage (CPH) is the most common cause of IVH in the term neonate. CPH is usually asymptomatic, but large hemorrhages can result in hydrocephalus and increased intracranial pressure. White matter necrosis (periventricular leukomalacia) is usually located anterior to the frontal horns or adjacent to the lateral angles of the lateral ventricles, and results from impaired perfusion at the border between ventriculopetal and ventriculofugal arteries of the fetus (Plate 9). White matter necrosis (WMN) affects 5% of all newborns, and is diagnosed with ultrasound. The symptoms of WMN are usually non-specific, but most patients with WMN develop spastic motor dysfunction over time. Cerebral necrosis is more commonly observed in term infants than hemorrhage and white matter lesions, which are more common in premature infants. Cerebral necrosis can be related to intrapartum difficulties, congenital heart disease, and vascular collapse in the infant. Cerebral necrosis primarily involves the depths of sulci, and the necrosis can be laminar or pseudolaminar (Plate 10). Kernicterus results from the accumulation of bilirubin due to excessive production (hemolytic disease of the newborn) or insufficient excretion, and the unconjugated form of bilirubin exhibits neurotoxicity. Kernicterus often involves the globus pallidus, subthalamic nucleus, hippocampus, and lateral thalamus (Plate 11) (Ellison pp 2.1–2.15, 2.23, 3.54).

Malformations

CNS malformations account for a significant percentage of neuropathology in the pediatric population. Anencephaly is the most severe neural tube defect, and it results from failure of closure of the anterior neuropore. Anencephaly is not compatible with survival, is more common in females, and is usually detected in utero by ultrasound or increased maternal serum α-fetoprotein levels. The orbits are often well developed with anencephaly, but the cranial vault is hypoplastic and contains a mass of immature blood vessels known as the cerebrovasculosa (Plates 12 A and B). Encephalocele results from the herniation of brain tissue through defects in the cranial vault. Over 75% of all encephaloceles are occipital (Plates 13 A and B), with approximately 5–10% located in both the frontal and parietal areas. The contents of encephaloceles are variable, and the surrounding leptomeninges maintain fetal vasculature (plexus of thin-walled sinusoids). Transsphenoidal encephaloceles are rare and are associated with sellar anomalies, endocrine dysfunction, and agenesis of the corpus callosum. Sincipital encephaloceles are most common in Southeast Asians, and are rarely associated with other neural tube anomalies. Meckel-Gruber syndrome is a lethal autosomal recessive condition that consists of occipital encephalocele, hepatic fibrosis with bile duct proliferation, and polycystic kidneys. Chiari type 1 malformation consists of inferior herniation of the cerebellar tonsils through the foramen magnum (Plate 14). Chiari 1 is associated with syringomyelia, Klippel-Feil anomaly, platybasia, and suboccipital dysplasia. Chiari 1 can present with lower cranial nerve palsies, sleep apnea, ataxia, hydrocephalus, or long tract symptoms. Chiari type 2 malformation involves herniation of the cerebellar vermis, fusion of the inferior colliculi (beaked tectum), looping of the medulla over the cervical spinal cord, and abnormal lamination of the cerebral cortex. Almost all patients

cells. Pineocytomas are synaptophysin, neuron-specific enolase, and neurofilament positive, and occasionally S antigen positive. Germinomas are well-circumscribed primary germ cell tumors that can occur in the pineal (and suprasellar) region. Germinomas consist of round neoplastic cells with prominent clear cytoplasm and large nucleoli, occasionally with associated inflammation (T cell aggregates) (Plate 124). The reactive inflammation that is associated with germinomas can be pronounced and occasionally lead to granuloma formation. Germinomas label with antibodies to placental alkaline phosphatase. Germinomas are very sensitive to radiation, and they do not exhibit calcification or cysts. Embryonal carcinoma is a germ cell tumor that exhibits sheets of somewhat pleomorphic cells arranged in various patterns (glandular, papillary, cribriform) with prominent mitoses and necrosis (Plate 125). Embryonal carcinoma labels positive for cytokeratins, and occasionally placental alkaline phosphatase, β-HCG, and AFP. Yolk sac tumor is a germ cell tumor that exhibits loosely arranged cells with clear cytoplasm and prominent eosinophilic bodies (Plate 126). Yolk sac tumors are positive for AFP, and they often exhibit Schiller-Duval bodies. Choriocarcinomas are germ cell tumors that consist of syncytiotrophoblastic giant cells that are positive for β-HCG (Plate 127). Choriocarcinomas often exhibit necrosis, and they are commonly associated with hemorrhage. Teratomas are well-circumscribed, differentiated tumors that often contain ectodermal, endodermal, and mesodermal components (Plate 128). Mature teratomas are often cystic and exhibit a variety of tissue types, and they occasionally undergo malignant transformation to a carcinoma or sarcoma (Ellison pp 39.1–39.2, 39.5–39.8).

Choroid Plexus Neoplasms and Primary Central Nervous System Lymphoma

Choroid plexus papillomas (CPP) are well-circumscribed, vascular neoplasms that are usually located in the lateral ventricles in children and the fourth ventricle in adults. CPP consist of multiple papillae of columnar epithelium along a fibrovascular core (Plate 129). CPP exhibit mild nuclear pleomorphism, hyperchromasia, and occasional mitotic Figures. CPP are associated with Li-Fraumeni syndrome, and they are vimentin, GFAP, cytokeratin, and S100 positive. CPP also contain a prominent PAS positive basement membrane, and they are often lobulated and calcified. CPP can result in hydrocephalus secondary to increased CSF production or CSF pathway obstruction. Choroid plexus carcinoma (CPC) is an aggressive neoplasm that is characterized by increased pleomorphism, prominent mitoses, and necrosis. CPC is invasive, and is usually found in the lateral ventricles in children. Primary CNS lymphoma (PCNSL) most commonly involves the cerebrum, but it can also occur in the brainstem, cerebellum, or spinal cord. PCNSL is associated with immunodeficiency, and approximately 80% of all PCNSL exhibit diffuse large B cell morphology. PCNSL is usually found in a periventricular location, and it is often multifocal. Microscopically, PCNSL consists of small blue cells that form prominent perivascular aggregates with areas of necrosis (Plate 130). Perivascular reticulin is prominent in PCNSL secondary to expanded perivascular spaces. PCNSL tends to present earlier and act more aggressively in immunocompromised patients. PCNSL in the immunocompromised is also associated with Epstein-Barr virus (EBV), whereas PCNSL in the immunocompetent is EBV negative. PCNSL is CD20 and CD79a positive (B cell markers), and it carries a worse prognosis in immunocompromised patients, with an average survival of approximately 3 months, compared to 19 months in immunocompetent patients (Ellison pp 40.1–40.3, 41.1–41.5).

Peripheral Nerve Sheath Neoplasms

Schwannomas are indolent neoplasms that can arise from the dorsal roots of the spinal cord and various cranial nerves. Microscopically, schwannomas exhibit prominent fascicles of spindle-shaped cells (Antoni A areas) and adjacent regions of cells located in a myxoid stroma with prominent cytoplasmic processes and smaller nuclei (Antoni B areas) (Plate 131). Occasionally sequential nuclear palisading is observed, which is known as a Verocay body (Plate 132). Schwannomas are associated with neurofibromatosis type 2, and many sporadic schwannomas exhibit NF2 gene mutations (LOH 22q). Neurofibromas are tumors that involve peripheral nerves diffusely, and they can be cutaneous (dermal) or intraneural. Neurofibromas usually occur in the context of neurofibromatosis type 1, and plexiform neurofibromas are pathognomonic of NF1. Neurofibromas are slow-growing lesions that arise within the endoneurium and are rarely cystic or encapsulated. Microscopically, neurofibromas exhibit wavy, spindle-shaped cells in a mucoid matrix with abundant collagen (Plate 133). Neurofibromas are S-100 positive, and the presence of significant pleomorphism or nuclear hyperchromasia may imply progression to a malignant nerve sheath tumor, which is more common in plexiform neurofibromas in association with NF1. Malignant nerve sheath tumor (MNST) is a high-grade sarcoma that usually arises in the cervical or brachial plexuses. Intracranial MNST is

most commonly associated with the trigeminal nerve. MNSTs exhibit expansion of nerve trunks and infiltration of adjacent tissues, often with areas of necrosis and hemorrhage. Microscopically, MNST is characterized by fascicular and storiform cellular patterns with prominent mitoses, a high nuclear:cytoplasmic ratio, and necrosis (Plate 134). Metaplasia occurs in approximately 10% of MNSTs, and often consists of skeletal muscle (triton tumor), bone, or cartilage. MNSTs often contain melanin, and occasionally label with S-100 antibodies. MNST carries a poor prognosis, and approximately 50% of patients with this tumor have NF1 (Ellison pp 42.1–42.7).

Meningiomas

Meningiomas originate from arachnoid cap cells within the leptomeninges. The incidence of meningiomas increases with age, and they most commonly present in the fourth decade of life. Meningiomas are more common in females than males, and they are multiple in 10% of cases. Meningiomas are associated with estrogen-dependent neoplasms (breast cancer), radiation, NF2, Castleman's syndrome, and polyclonal gammopathies. The majority of meningiomas are supratentorial, 15% are infratentorial, 15% are intraspinal, and 2% are intraventricular. Approximately 15% of meningiomas recur after apparent complete resection. The most important histologic predictor of recurrence is the presence of brain infiltration. Some meningiomas grow as plaques within the dura (en plaque meningioma), and this is particularly common with lesions of the sphenoid ridge. The bone adjacent to meningiomas is often hyperostotic, even in the absence of invasion by the tumor. The microscopic appearance of meningiomas varies tremendously. The three most common variants are meningothelial, fibrous, and transitional. Meningothelial meningiomas are characterized by sheets or lobules of cells with indistinct cytoplasmic borders and small nuclei that may form whorls (Plate 135). Fibrous meningiomas are composed of spindle-shaped cells in a matrix of abundant collagen (Plate 136). Transitional meningiomas combine features of fibrous and meningothelial lesions, and also contain prominent whorls and occasional psammoma bodies (Plates 137 A and B). Foamy (xanthomatous) cells can often be observed in many of the meningioma variants. Psammomatous meningioma is characterized by a prominence of psammoma bodies, but there is no standard definition for the density of these structures that must be present to define this variant (Plate 138). Angiomatous meningioma exhibits prominent, thick-walled blood vessels among groups of neoplastic cells (Plate 139). Secretory meningiomas exhibit a meningothelial or transitional pattern, with prominent intracellular eosinophilic globules that are lined by microvilli (Plate 140). All of these meningioma variants are considered grade I tumors, and are usually well-circumscribed. The most common genetic abnormality in meningiomas is deletion of chromosome 22, which occurs in 60–90% of all cases. Other cytogenetic abnormalities include losses of chromosomes 11 and 18, and gains of chromosomes 6, 7, 17, and X. There are four histologic subtypes of meningiomas that are associated with more aggressive behavior. Clear cell meningiomas are grade II tumors that exhibit cells with glycogen-rich (clear) cytoplasm. Chordoid meningiomas are grade II tumors that resemble chordomas with eosinophilic cells in a myxoid matrix. Papillary meningiomas are grade III tumors that consist of perivascular aggregates of papillary-like structures. Rhabdoid meningiomas are also grade III lesions, and they contain prominent intermediate filaments within their cytoplasm. Atypical meningiomas exhibit increased mitoses, high nuclear:cytoplasmic ratios, prominent nucleoli, sheet-like growth patterns, and occasional foci of necrosis. Atypical meningiomas are grade II tumors, and they are more likely to recur than benign variants. Anaplastic meningiomas are frankly malignant lesions (grade III) that often exhibit brain invasion, metastasis, or a marked increase in the number of mitoses. Atypical and anaplastic meningiomas often exhibit allelic losses on chromosomes 1p, 10, and 14q, and higher Ki-67 labeling indices. Meningiomas in general are immunoreactive for vimentin and epithelial membrane antigen, and more than 75% of these lesions express progesterone receptors. Some meningiomas are also immunoreactive for S-100 and cytokeratins (Ellison pp 43.1–43.14; Laws pp 78–79).

Parasellar and Intrasellar Neoplasms

There are many different neoplasms that can occur in the region of the pituitary gland, including pituitary adenomas, craniopharyngiomas, astrocytomas, metastatic carcinomas, meningiomas, and germinomas. Pituitary adenomas are derived from cells of the adenohypophysis, and some adenomas secrete hormones in an unregulated fashion that can lead to endocrine disturbances. Pituitary adenomas are composed of a population of monomorphic cells, and they are more common in females than males. Pituitary adenomas are associated with multiple endocrine neoplasia type 1, and mutations of H-*ras*, *gsp*, and protein kinase C have been identified in some adenomas. Approximately 40% of growth hormone-secreting adenomas exhibit *gsp* mutations. Microscopically,

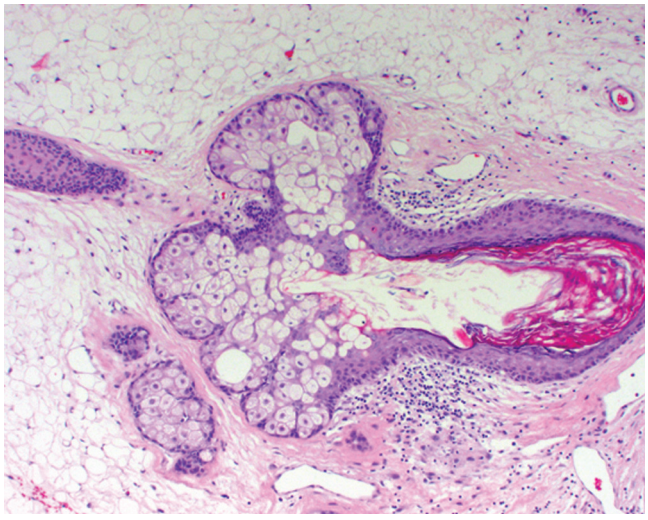


PLATE 128 Teratoma. Note the wide variety of tissue types present in this mature teratoma.

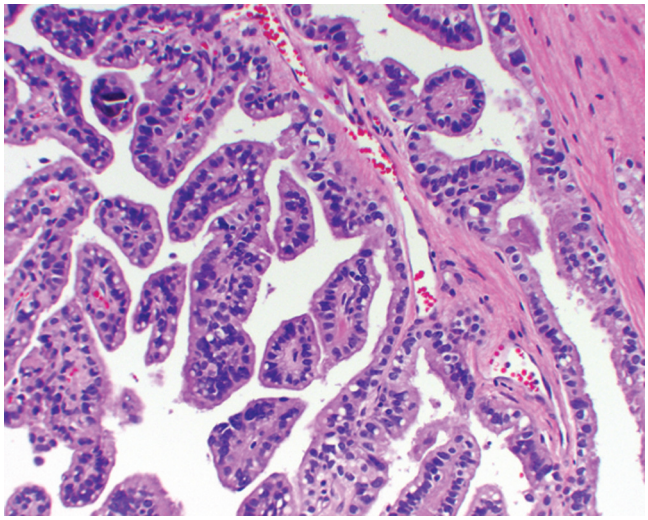


PLATE 129 Choroid plexus papilloma. Note the layer of columnar epithelium with mild nuclear pleomorphism surrounding a fibrovascular stroma.

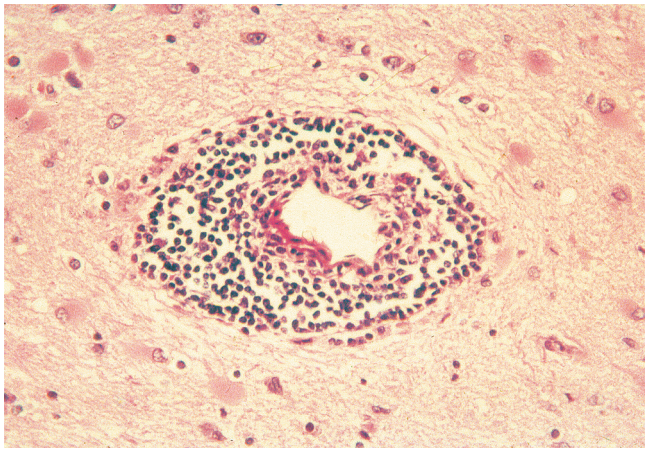


PLATE 130 PCNSL. Note the perivascular location of these neoplastic cells with a few interspersed reactive lymphocytes.

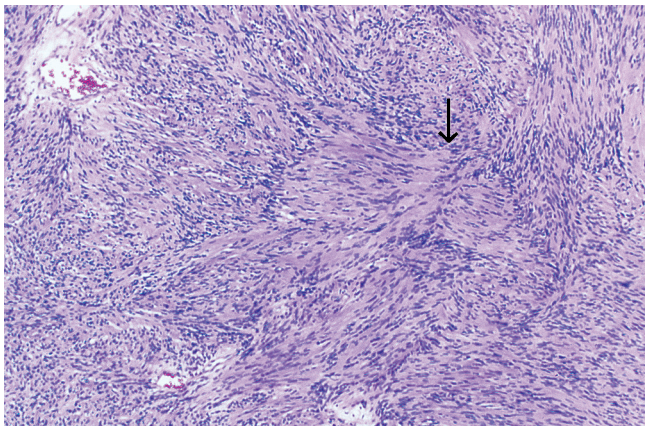


PLATE 132 Verocay body. Note the sequential palisading of nuclei adjacent to an anuclear area (*arrow*).

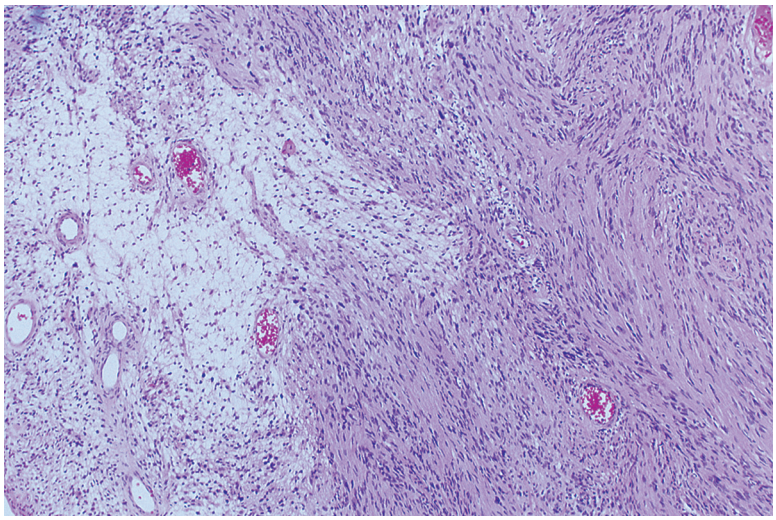


PLATE 131 Schwannoma. Note the presence of Antoni A areas (*right*) with compact, interlaced fascicles of cells, and Antoni B areas (*left*) with spindle cells arranged in a loose myxoid stroma.

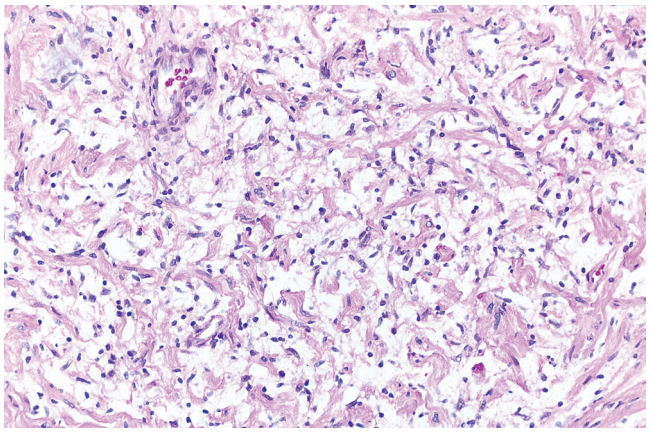


PLATE 133 Neurofibroma. Note the randomly-arranged spindle cells with wavy nuclei and a prominent matrix of mucin and collagen.

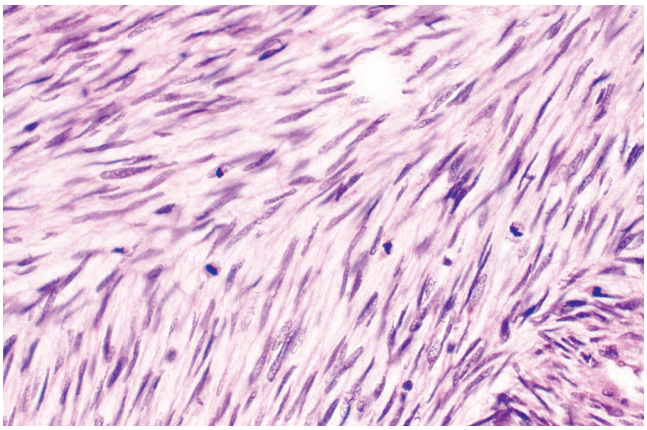


PLATE 134 MNST. Note the fascicular arrangement of these neoplastic cells that exhibit a high nuclear:cytoplasmic ratio and prominent mitoses.

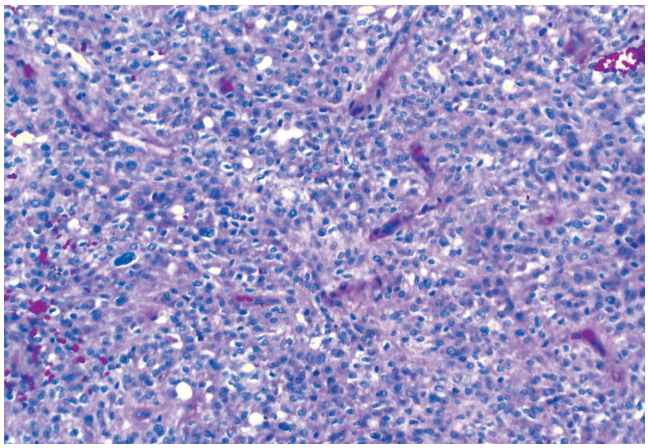


PLATE 135 Meningothelial meningioma. Note the presence of oval cells with prominent nucleoli in a syncytial arrangement.

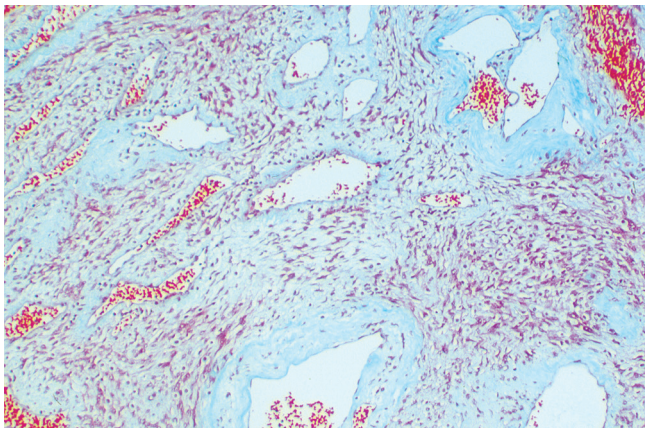
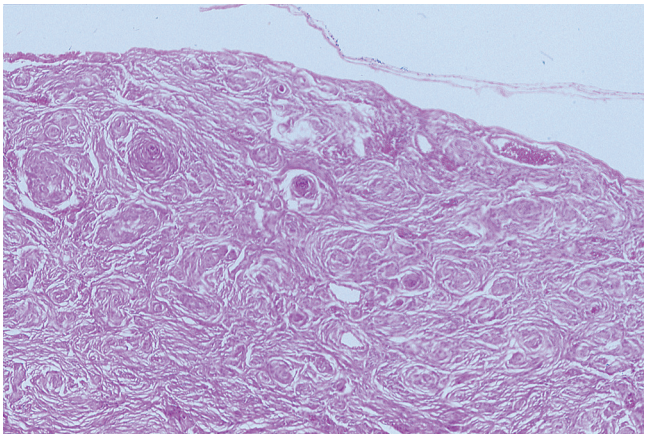
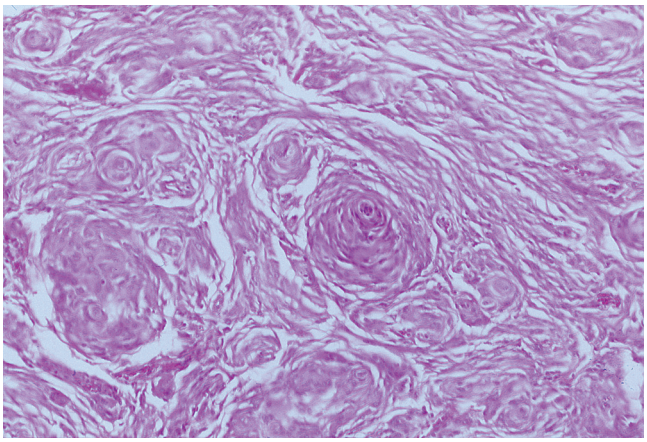


PLATE 136 Fibrous meningioma. Note the presence of elongated neoplastic spindle cells and occasional hyalinized blood vessels.



(A)



(B)

PLATE 137 Transitional meningioma. This meningioma variant exhibits prominent cords and whorls of neoplastic cells. *A*, low power; *B*, high power.

CHAPTER 5

Neuroradiology

DEVELOPMENTAL DISORDERS

Chiari malformations result from various abnormalities in the development of the hindbrain. The Chiari type I malformation consists of the inferior displacement of the cerebellar tonsils through the foramen magnum (Figure 5.1). The distance of inferior displacement of the cerebellar tonsils that is required to be considered a Chiari I varies with age. In the first decade, 6 mm of displacement is required, which decreases to 5 mm by the second and third decades, and 4 mm in the fourth to eighth decades. Chiari I malformations may result in long-tract signs or lower cranial nerve palsies, but many of these lesions are asymptomatic. Chiari I malformations are associated with a syrinx in approximately 20–40% of all cases (Figure 5.2). The best method of identifying Chiari I malformations is on sagittal T1- and T2-weighted magnetic resonance (MR) images. Chiari II malformations involve abnormalities of the brain, skull, spinal cord, and the meninges. The skull may exhibit lacunar changes (lückenschädel) secondary to alterations in the radial growth of the calvarium in patients with Chiari II malformations who are younger than 6 months of age (Figure 5.3). The posterior fossa is also reduced in size with Chiari II, and the torcular herophili occupies a low position. The medulla and cerebellum are displaced inferiorly with Chiari II, and the cervicomedullary junction is often "kinked." With Chiari II malformations, the fourth ventricle is often elongated, the tectum is "beaked," and there may be associated colpocephaly, polymicrogyria, and agenesis of the corpus callosum (Figure 5.4). Myelomeningoceles are almost always associated with Chiari II malformations, and syringomyelia is also frequently observed. Chiari III malformations consist of the presence of occipital encephaloceles with other features of Chiari II malformations (Figure 5.5). Agenesis of the corpus callosum can occur in isolation or in association with other developmental anomalies,

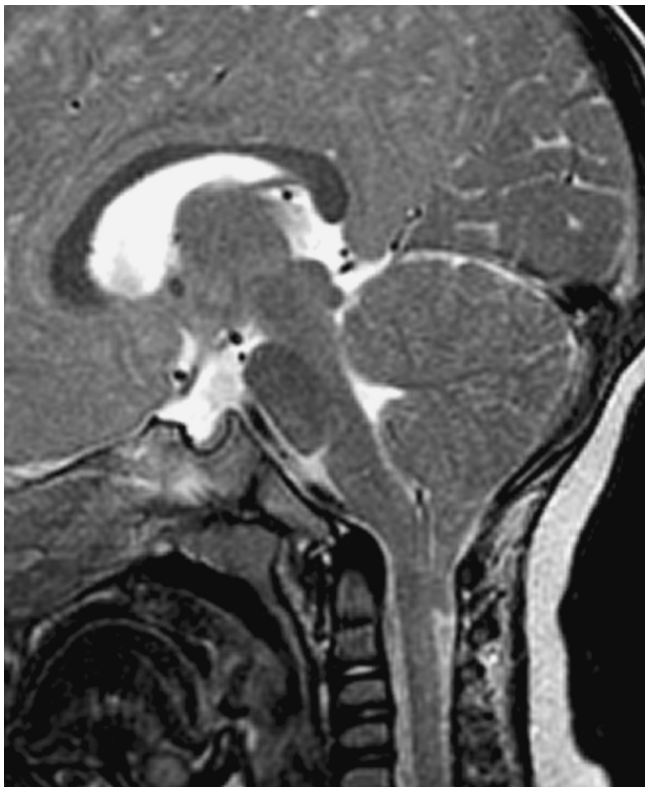


FIGURE 5.1 Chiari I. Note the prominent extension of the cerebellar tonsils below the foramen magnum (sagittal T2WI).

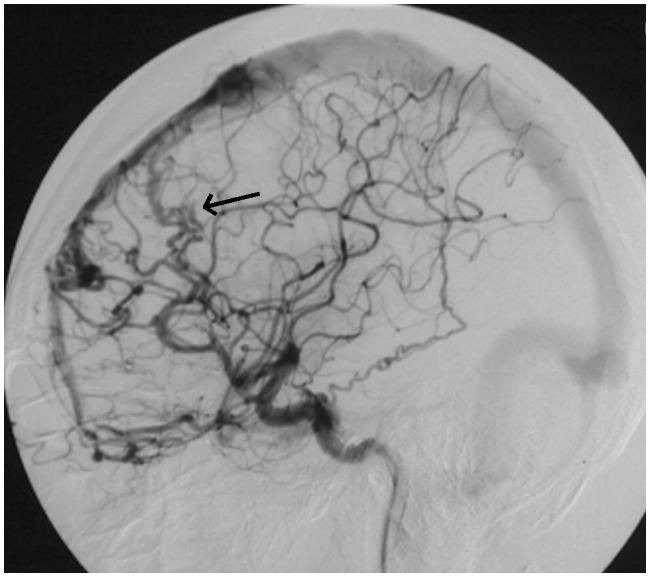


FIGURE 5.65 DAVF. Note the presence of prominent retrograde cortical venous drainage (*arrow*) that results in early filling of the superior sagittal sinus on this lateral angiogram. This lesion is associated with a high rate of subarachnoid hemorrhage.

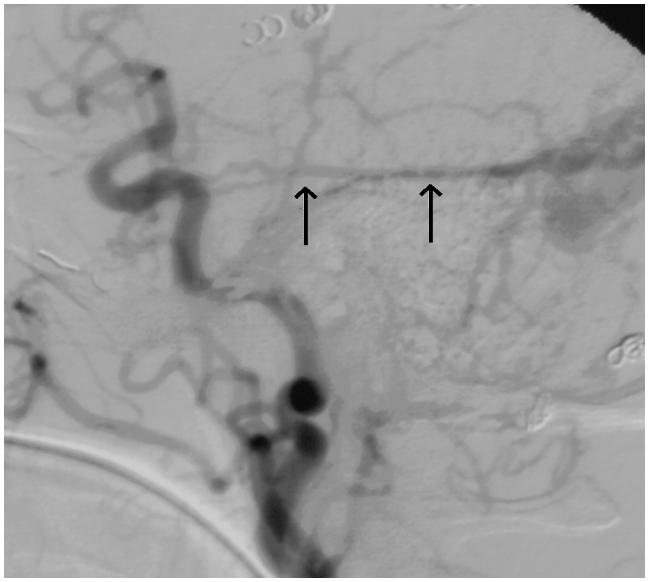


FIGURE 5.66 DAVF. Note the prominent Italian artery (*arrows*) feeding the tentorial DAVF on this lateral angiogram.

vessels of the AVM will appear as flow voids on T1- and T2-weighted images, and AVMs typically lack any mass effect, unless they have recently hemorrhaged. Dural arteriovenous fistulae (DAVFs) represent vascular malformations that are located within the wall of a venous sinus, and they are often associated with venous sinus stenosis or occlusion. The majority of DAVFs, in contrast to true parenchymal AVMs, are acquired lesions that result from venous sinus recanalization after sinus thrombosis. DAVFs are most commonly associated with the cavernous, transverse, and sigmoid sinuses, and their symptoms vary with location. The presence of retrograde cortical venous drainage is ominous in DAVFs, and it is associated with a high rate of subarachnoid hemorrhage. Therefore, the presence of retrograde cortical venous drainage mandates the treatment of the DAVF. Six-vessel angiography is usually required to completely delineate the anatomy of a DAVF, because these lesions are often fed by branches of the internal and external carotid arteries (Figure 5.65). Tentorial DAVFs are often fed by an enlarged tentorial artery, which is a branch of the meningohypophyseal trunk of the cavernous ICA, and is also known as the artery of Bernasconi and Cassinari (Figure 5.66). This artery was originally described as a feeder to an intracranial meningioma, however. Capillary telangiectasias are small vascular anomalies that are often located in the pons or cerebellum (Figure 5.67). These lesions are

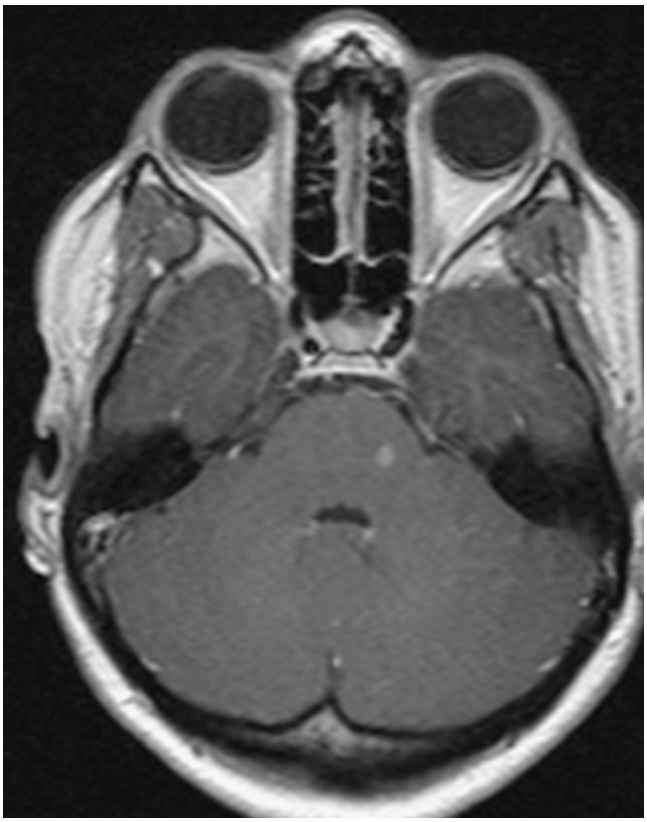


FIGURE 5.67 Capillary telangiectasia. Note the small lesion located in the left lateral pons on this contrasted axial T1WI.

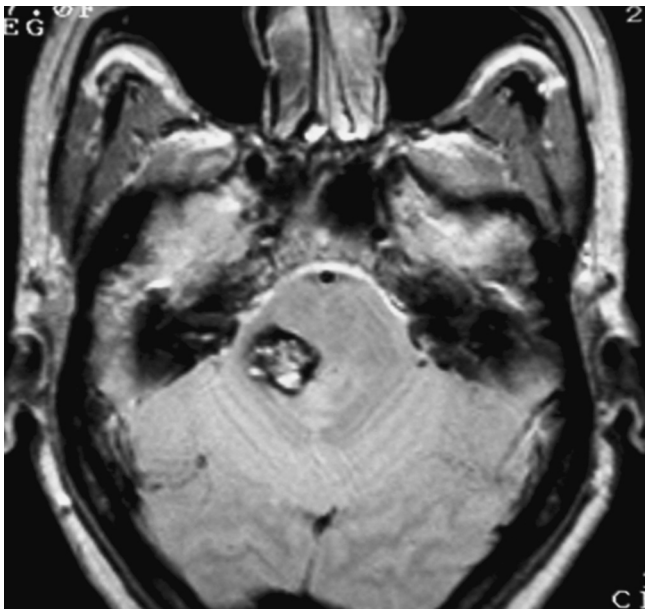


FIGURE 5.68 Cavernoma. Note the classic "reticulated core" and surrounding rim of hemosiderin associated with this cavernoma (axial T2WI).

usually identified at autopsy, and are rarely associated with hemorrhage. Cavernous angiomas (cavernomas) are discrete, multilobulated lesions that can be located anywhere throughout the brain and spinal cord. These lesions often exhibit various ages of hemorrhage simultaneously, which gives them a "popcorn-like" (reticulated core) appearance on T2-weighted MRI (Figure 5.68). Cavernomas are often surrounded by a hemosiderin rim of low signal, and gradient echo sequences are the most sensitive MR sequences for the identification of these lesions. Cavernomas are usually angiographically occult as well. Cavernomas commonly present with seizures, hemorrhage, and focal neurologic deficits. Familial cavernomas are inherited in an autosomal dominant fashion, are more common in Hispanic families, and are often associated with the presence of multiple lesions (Figure 5.69). Venous angiomas are benign developmental anomalies that consist of dilated anomalous veins that drain into a transcortical vein in a radial fashion (Figure 5.70). Venous angiomas are most commonly located in the deep white matter of the cerebrum or cerebellum. Venous angiomas are occasionally associated with cavernous malformations. If hemorrhage has occurred adjacent to a venous angioma, it is usually due to a concomitant cavernoma. Angiography is diagnostic of venous angiomas, and the appearance is often referred to as "caput medusae" (Figure 5.71). Vein of Galen malformations (VOGM) are congenital vascular malformations that involve aneurysmal dilatation of

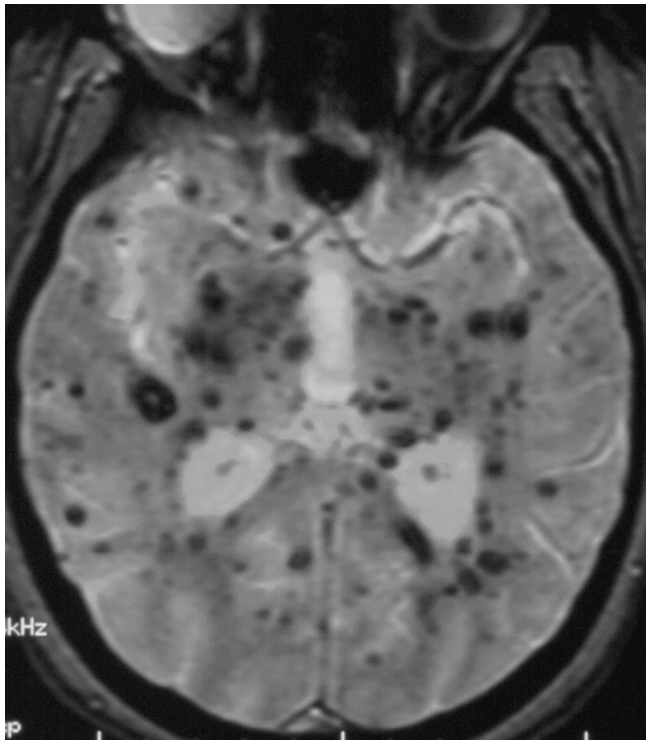


FIGURE 5.69 Cavernoma. Note the presence of innumerable cavernomas in this patient with familial cavernomas (axial GRE sequence).

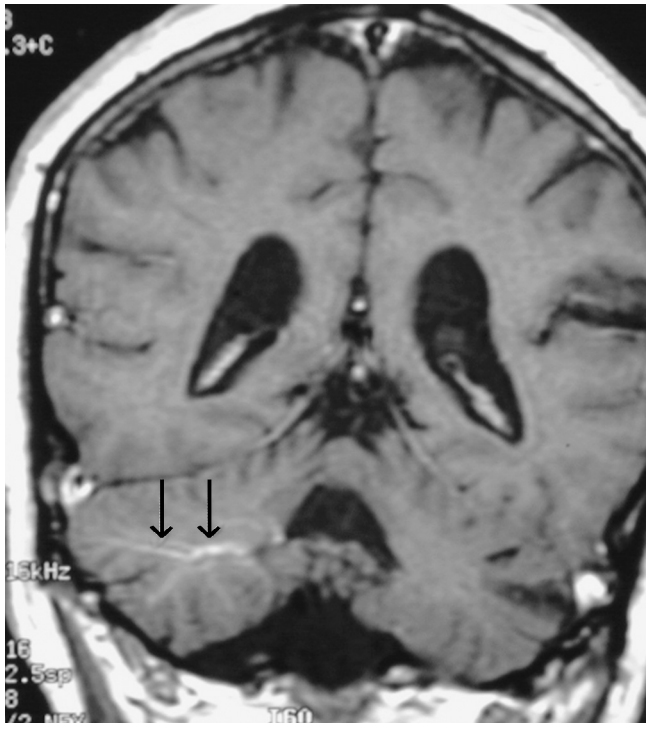


FIGURE 5.70 Venous angioma. Note the presence of a benign venous angioma of the right cerebellar hemisphere (*arrows*) on this contrasted coronal T1WI.