

MR Imaging of Congenital CNS Anomalies

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The appearance of congenital brain anomalies is best understood in context of normal fetal brain development. At approximately 20 days gestation, the neural tube is formed with the coaptation of the primitive neural folds. Progressive closure of the tube ensues in a bi-directional fashion, both cranial and caudal. By 25 days, the anterior end closes, and by 28 days, the caudal or posterior end closes. Subsequent development of 3 components (vesicles) at the cranial portion of the neural tube constitutes formation of the prosencephalon, mesencephalon and the rhombencephalon. Between 5 and 10 weeks, there is further differentiation of these structures. The prosencephalon will eventually develop into the telencephalon (the precursor of the cerebrum) and the diencephalon. The rhombencephalon differentiates into the myelencephalon (which forms the pons and medulla) and the metencephalon, which forms the cerebellum. At 7 weeks, the germinal matrix forms, and during the second through the fifth month cellular proliferation and migration occur. After the fifth month, cortical organization and myelination transpire, and continue postpartum. Any insult which affects the brain during the crucial period of neuronal differentiation, migration and organization will have a relatively predictable impact on subsequent brain development. In fact, it is the timing of the insult, rather than the type of insult (vascular, infectious, traumatic, etc.) that primarily determines the subsequent malformation.

Magnetic resonance imaging has supplanted computed tomography (CT) as the modality of choice for most categories of central nervous system (CNS) pathology. The multiplanar capabilities of MRI provide unsurpassed visualization of brain structures. Its superior contrast resolution provided by the multiple sequences which are available exploit the various tissue characteristics of normal and pathologic structures. MR is exquisitely sensitive for the detection of both solid and cystic lesions within the brain, and for depicting aberrant anatomic structures. This allows accurate assessment of congenital malformations which affect the CNS.

HOLOPROSENCEPHALY

Holoprosencephaly results from failure of anatomic division of the primitive forebrain. The prosencephalon fails to divide and form the diencephalon and telencephalon. The

cerebral hemispheres don't form due to failure of cleavage of the telencephalon. This results in a grossly dysmorphic brain which is variable in severity. There are variable degrees of differentiation and division of the primitive brain structures which are encountered. A classification system proposed by DeMyer allows a general categorization of this entity, although these abnormalities describe spectrum of severity. Thus, a given patient may not display all of the characteristics of a single form of holoprosencephaly.

Alobar holoprosencephaly is the most severe form. There is complete failure of telencephalon cleavage to form the cerebral hemispheres. Thus the falx and interhemispheric fissure are absent. The thalami are fused, and therefore there is no intervening third ventricle. A holoventricle is seen adjacent to the small, deformed cerebrum. Severe midline facial anomalies accompany this form of holoprosencephaly.

Semilobar holoprosencephaly is a less severe cleavage deformity in which the dorsal portion of the cerebrum is divided into distinct hemispheres with an intervening fissure and falx. Likewise, there is partial separation of the thalami, between which there is usually a small, malformed third ventricle. The dorsal portion of the corpus callosum may be present as well.

Lobar holoprosencephaly is the least severe form of this group of anomalies. All but the most anterior portion of the interhemispheric fissure is present, where there is continuity of the frontal lobes. The septum pellucidum is absent, and there is variable formation of the anterior portion of the callosum. Patients with this mild form of holoprosencephaly may have normal facial features.

THE PHAKOMATOSES

The phakomatoses are disorders of histiogenesis associated with multiple neuroectodermal dysplasias. This diverse group of congenital syndromes is characterized by multiple lesions of the central nervous system and other organs. Multiple cutaneous findings are typically manifest as well. While a majority of these syndromes demonstrate a Mendelian inheritance pattern, sporadic cases are commonplace. Thus, in addition to diagnosis and serial monitoring of these patients, imagers provide information which facilitates genetic counseling. Although the

cutaneous manifestations often suggest the diagnosis clinically, clinicians rely on imagers to elucidate the central nervous system abnormalities and to monitor any changes over time.

There are a number of dyshistiogenic disorders to consider. In this section, the most common syndromes will be reviewed. These include neurofibromatosis, tuberous sclerosis, Von Hippel-Lindau disease and Sturge-Weber syndrome. Other important, albeit less common, syndromes such as neurocutaneous melanosis, Oslo-Weber-Rendu, Wyburn-Mason, Ataxia-telangiectasia and basal cell nevus syndrome may be referenced in most neuroimaging and neurological texts.

NEUROFIBROMATOSIS

Von Recklinghausen disease (NF type I) and central neurofibromatosis (NF type II) represent the two most common forms of neurofibromatosis. A small percentage of cases are represented by up to six additional subtypes which are much less common. Neurofibromatosis is a complex neural crest disorder which results in neoplastic and dysplastic lesions in the neural and cutaneous structures. The incidence of CNS tumors greatly exceeds that in the general population.

Neurofibromatosis type I is associated with a defect in chromosome number seventeen (table 1). The incidence is one in three to four thousand, making it the most common of the phakomatoses. The most common CNS manifestation of NF-1 is optic nerve gliomas. Peak incidence of this lesion is at four to five years of age. Gliomas may also occur in the remaining neural structures, especially the brainstem. Plexiform neurofibromas and ependymomas also occur with increased frequency in neurofibromatosis patients. Other ocular findings include Lisch nodules and buphthalmos.

The above lesions are best depicted with magnetic resonance imaging. The tumors are generally iso- to hypointense on T1 weighted images and hyperintense on long TR sequences. Optic nerve gliomas tend to show mild enhancement. Depending on histologic subtype, gliomas may be relatively nonenhancing, while pilocytic astrocytomas enhance intensely and may be associated with a cystic component. MR images also demonstrate hyperintensities on long TR images within the cerebellum and basal

ganglia in a majority of patients. These have been variably ascribed to hamartomatous change, heterotopias, glial rests and glial nodules. Previous reports describing these findings were based on the MR appearance, and not pathologic correlation. More recent pathologic studies have been performed showing that the basal ganglia and white matter foci of T2 prolongation, which may be transient in nature, represent spongioform myelinopathy or vacuolar changes within the myelin. There may be intramyelinic edema, which better explains the transient or evanescent nature of the MR findings.

The optic pathway lesions may also spontaneously regress, suggesting that not all enhancing tumefactive lesions represent gliomas. There is likely a spectrum of pathologic changes which range from benign hamartomatous dysplasia to malignant glioma, as suggested by Liu, et al. Patients with neurofibromatosis type I warrant a baseline MR during the first few years of life and a follow up exam to evaluate any neurologic changes, even minor complaints such as headache.

Central neurofibromatosis (NF-II) is much less common than NF type I. This distinct entity is associated with an abnormality involving chromosome 22. The incidence is 1 in 50,000. The prototypical CNS manifestation of central neurofibromatosis is the schwannoma, which primarily affects the cranial nerves. The vestibular component of the eighth cranial nerve is the most commonly effected. The presence of bilateral vestibular schwannomas (aka "acoustic neuromas") establishes the diagnosis of neurofibromatosis type II. A first degree relative with NF II and a vestibular schwannoma or another characteristic lesion such as neurofibroma, meningioma, glioma, or schwannoma also establishes the diagnosis. Schwannomas may also involve cranial nerves III-XII, with the fifth cranial nerve representing the second most common location. NF-II patients also harbor meningiomas and ependymomas with greater frequency than the general population. Spinal cord tumors are more common in patients with NF-II than NF-I. Spinal schwannomas, ependymomas and meningiomas may occur.

Imaging manifestations of the vestibular schwannomas include lesions originating within the internal auditory canal and extending into the cerebellopontine angle. Small intracanalicular lesions may be difficult to visualize without availability of enhanced MR. High resolution studies employing phased array coils and fast spin echo may obviate the need for contrast use

in this setting, but most workers feel more confident using an enhanced study to exclude intracanalicular lesions. Approximately 75% of vestibular schwannomas result in widening of the porus acusticus. The lesions demonstrate T1 and T2 prolongation and show intense enhancement following contrast administration. Cystic changes are seen in a significant minority of lesions. This is especially true of large lesions which may show central necrosis and/or associated adjacent arachnoid cysts. As with schwannomas, other tumors such as meningiomas, gliomas and ependymomas associated with neurofibromatosis have a similar imaging appearance as that seen in tumors in patients without the disease. NF-2 patients warrant annual MR follow up examination to monitor the progress of schwannomas and for the development of other changes.

TUBEROUS SCLEROSIS

Tuberous sclerosis is an autosomal dominant phakomatosis associated with multiple hamartomatous lesions of the brain, skin and thoracoabdominal organs. Chromosomes 11 and 9 have been implicated as the defective genetic substrate associated with this disorder. A majority of patients will have at least one of the following: adenoma sebaceum, seizures or mental retardation. The three comprise the clinical triad associated with tuberous sclerosis, but the complete troika is not present in a sufficient number of patients to make this a sensitive criteria for establishing

the diagnosis. Hypopigmented ash leaf spots are more common than adenoma sebaceum. Although inherited as an autosomal dominant pattern with variable penetrance, at least 50% of cases are sporadic.

Prior to the availability of cross sectional imaging, radiologists relied upon the presence of calcifications within the cerebral lesions which were dense enough to be detected radiographically. Alternatively, an irregular ependymal surface could be demonstrated via pneumoencephalography. CT and MR allow for much more accurate assessment of the central nervous system. The cortical tubers represent disordered glial tissue with heterotopic neurons and giant cells. These are hypodense on CT and hyperintense on long TR MR images. In the neonate, a confusing variant appearance has been reported: cortical tubers may be hyperattenuating and display T1 shortening on MR. This may mimic the appearance of a hemorrhagic lesion. Familiarization of this atypical appearance in neonates may avert misdiagnosis.

Subependymal glial nodules also occur, which are generally hyperintense on long TR images unless calcifications are present. Mild enhancement is occasionally demonstrated with these lesions. This in contrast to the intense enhancement demonstrated with the occasional subependymal giant cell astrocytoma. This potentially lethal lesion most commonly occurs at the foramen of Monroe. The potential to develop these lesions warrants an annual or at least biannual follow-up during the first two decades of life. The

Table 1. Neurofibromatosis Type I

Synonym	Von Recklinghausen disease
Inheritance pattern	Autosomal dominant / sporadic
Chromosome link	17
Incidence	1 : 3-4000
CNS manifestations	Optic nerve glioma Astrocytomas Ependymoma Plexiform neurofibroma Vacuolar myelin changes Lisch nodule, retinal phakoma, buphthalmos

Table 2. Neurofibromatosis Type II

Synonym	NF-2
Inheritance pattern	Autosomal dominant / sporadic
Chromosome link	22
Incidence	1 / 50,000
CNS manifestations	Schwannomas Meningiomas Ependymomas (cord)

parenchymal hamartomas and associated migration anomalies are best appreciated on MR imaging.

Multiple organs also demonstrate hamartomatous lesions in patients with tuberous sclerosis. Ocular hamartomas are seen in half of patients. Renal angiomyolipomas, cardiac rhabdomyomas, pulmonary cystic lymphangiomyomas and chronic fibrosis also occur. In the liver, leiomyomas and adenomas, and in the spleen and pancreas, adenomas are also noted with increased frequency. Cystic bone changes, subungual fibromas, and multiple bone islands within the calvarial diploic space are also harbored by tuberous sclerosis patients.

VON HIPPEL-LINDAU DISEASE

Von Hippel-Lindau (VHL) disease is also inherited in an autosomal dominant pattern. Chromosome 3 is implicated as the defective genetic site. These patients harbor potentially lethal tumors in multiple organ systems while demonstrating a paucity of cutaneous findings. In addition to neoplasms, cysts and angiomas are found in VHL patients.

The most common CNS lesion associated with VHL is a hemangioblastoma. These most commonly occur in the cerebellum, but are also found within the medulla and spine. If multiple hemangioblastomas are present, the diagnosis of Von Hippel-Lindau disease is established. Alternatively, a single hemangioblastoma with either a visceral manifestation or a family history will also establish the diagnosis. Hemangioblastomas tend to occur in the caudal cerebellum, but may occur in the superior aspect of the posterior fossa as well. Rarely, they involve the supratentorial compartment. Most lesions have a cystic component and an intensely enhancing mural nodule. However, a significant number of these tumors may be solid in appearance. The lesions tend to abut a pial surface. Prominent feeding vessels and draining veins are often demonstrated. The tumors demonstrate T1 and T2 prolongation on MR and are hypodense on CT. Retinal angioma or hemangioblastoma are seen in a majority of patients. These may be bilateral in up to half of cases. Associated intraocular hemorrhage may occur. Intense enhancement is demonstrated following contrast administration. Orbital hemangioblastomas have also been reported.

Organ manifestations including renal cell carcinoma, which is seen in up to a third of the patients. Renal tumors are the cause of death for a significant number of VHL

patients. Pheochromocytomas, as well as pancreatic and epididymal cysts and tumors may be associated with VHL. A baseline MR of the brain and spine is recommended. Serial exams every one to two years dictated by patients symptoms as recommended to assess for any progression of lesion in these patients.

STURGE-WEBER SYNDROME

Patients with Sturge-Weber syndrome may present with seizures, mental retardation, hemianopsia, hemiparesis and hemisensory defects. This phakomatosis demonstrates a sporadic rather than inherited pattern. It is characterized by facial and leptomeningeal angiomas. Typically a "port wine" vascular nevus involves the fifth cranial nerve distribution, most commonly the first division.

Intracranial manifestations are usually unilateral and are ipsilateral to the facial nevus. Rarely, the leptomeningeal angioma is contralateral to the cutaneous abnormality. Calcifications are frequently associated with the leptomeningeal angioma. There is a proclivity for affecting the posterior aspect of the hemisphere, often demonstrating ventral progression. Lesions may be bilateral in up to 20% of cases. Associated hemispheric atrophy and prominent diploic space are typical.

On MR, hyperintensity on long TR images is demonstrated within the adjacent white matter, possibly due to chronic ischemic change or disordered neuronal organization and myelination. Ipsilateral choroid plexus enlargement with intense enhancement is seen in a majority of cases, thought to represent angiomatous changes. Scleral telangiectasias and buphthalmos represent the ocular findings associated with this phakomatosis. Following contrast enhancement, prominent gyral enhancement is demonstrated, documenting the patency of the leptomeningeal malformation. Anomalous draining veins, and occasionally a venous angioma, are frequently associated with the hemispheric findings.

MIGRATION ANOMALIES

An insult which occurs during migration of neuroblasts from the germinal matrix to the cortical surface or during the subsequent organization of the cortical mantle may result in a number of (a wide range of) localized or widespread anomalous brain disorders. The severity of clinical manifestations are more closely correlated with the location and volume of brain tissue involved than the type of parenchymal anomaly.

Agyria / pachygyria (lissencephaly) is the most severe of the migration anomalies. Agyria (complete lack of cortical sulcation) and pachygyria (broad, flat gyri with shallow sulci) often coexist, and represent a spectrum of anomalous brain development. When they are both present, pachygyria is most commonly located in the frontotemporal distribution, while agyria is more commonly encountered in the posterior frontal and parietal lobes. Clinically, patients present with seizures, motor and developmental retardation and coexistent extra-CNS anomalies.

Imaging studies reveal smooth, thick gyri with no or sparse, shallow sulci. The Sylvian fissure is shallow. The brain essentially has the appearance of that of a second trimester fetus. Associated features include a hypoplastic brain stem and occasionally a small dorsal corpus callosum.

Polymicrogyria most often occurs in the middle cerebral artery territory near the posterior aspect of the Sylvian fissure. Grossly, it may appear similar to pachygyria, due to aggregation of small, malformed gyri at the brain surface. This imparts a thickened appearance to the cortical mantle. The presence of gliosis in the subjacent white matter may differentiate it from pachygyria which is not associated with this finding. Prominent vessels may be seen in conjunction with polymicrogyria, usually in the form of large, anomalous draining veins.

Unilateral megalencephaly may include localized regions of both polymicrogyria and pachygyria. In this condition, complete or partial hamartomatous overgrowth of a cerebral hemisphere is accompanied by migration defects, heterotopias and gliotic white matter changes. The involved cortex is

Table 3. Tuberous Sclerosis

Synonym	Bourneville disease
Inheritance pattern	Autosomal dominant / sporadic
Chromosome link	9, 11
Incidence	1 : 20 - 50,000
CNS Findings	Cortical tubers, subependymal nodules, subependymal giant cell astrocytomas, migration anomalies, retinal phakoma

Table 4. Von Hippel-Lindau Disease

Synonym	CNS angiomatosis
Inheritance pattern	Autosomal dominant
Chromosome link	3
CNS manifestations	Hemangioblastomas Retinal angiomas

nonfunctional, and unfortunately serves as a seizure focus in most patients. In addition to seizures, patients may present with hemiplegia (with or without hemihypertrophy). On imaging studies, the enlarged hemisphere demonstrates morphologic and signal abnormalities such that dysplastic cortex is relatively isointense with the abnormal underlying white matter. The lateral ventricle within the involved hemisphere is enlarged, with abnormal configuration of the frontal horn.

Schizencephaly describes a cleft in the brain which extends through one or both hemispheres from the lateral ventricle to the cortical surface. The fissure is lined with abnormal gray matter, and there may be close apposition of the bordering parenchyma (closed-lip schizencephaly). If there is intervening CSF between the gray matter-lined margins, it is termed open-lip schizencephaly. Bilateral involvement and an increase in volume of involved parenchyma portend a worse prognosis. Seizures and developmental delay are characteristic clinical features. On imaging studies, the gray matter lined cleft may show evidence of polymicrogyria or other morphological abnormalities. A small dimple in the lateral margin of the ventricle may provide a clue to an otherwise subtle close-lip defect. The septum pellucidum is usually absent.

SUMMARY

We have reviewed but some of the several hundred congenital CNS malformations which have been reported. Familiarity with brain development and the imaging manifestations of the anomalies which result when an insult occurs during formation of the brain (or on a genetic basis) is critical for the imager. This allows the accurate description of morphologic abnormalities and guides the acquisition and evaluation of

imaging studies. The multiplanar capabilities and superior contrast resolution of MRI provide the best noninvasive means for evaluating the anatomic features of these anomalies.

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choroid plexus in patient with Sturge-Weber

disease. *AJNR* 1986;7:623.

Table 4. Sturge-Weber Syndrome

Synonym	Encephalofacial angiomatosis
Inheritance pattern	Sporadic
CNS manifestations	Leptomeningeal angiomatosis, choroid plexus angioma, hemiatrophy, venous anomalies, scleral telangiectasia, buphthalmos, congenital glaucoma