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Congenital Brain Malformations in the Neonatal and Early Infancy Period

Christine Kim, MD,* Kristen W. Yeom, MD,* and Michael Iv, MD†

Congenital brain malformations are a major cause of morbidity and mortality in pediatric patients who are younger than 2 years. Optimization of patient care requires accurate diagnosis, which can be challenging as congenital brain malformations include an extensive variety of anomalies. Radiologic imaging helps to identify the malformations and to guide management. Understanding radiologic findings necessitates knowledge of central nervous system embryogenesis. This review discusses the imaging of congenital brain malformations encountered in patients who are younger than 2 years in the context of brain development.

Introduction

Congenital brain malformations are a major cause of morbidity and mortality. Neural tube defects alone occur in 1 in 1000 live births and in as many as 1 in 250 conceptuses.[1] Because of the intricacy of brain development, congenital brain malformations also encompass a wide variety of anomalies. Therefore, recognizing specific malformation types can be challenging, but it is essential for optimal management.

Imaging evaluation helps to identify congenital brain malformations and guide management. Understanding and classifying structural abnormalities requires knowledge of central nervous system embryogenesis, including formation of the neural tube and its differentiation into the brain and spinal cord. This review discusses embryogenesis of the central nervous system and the imaging findings of congenital brain malformations that may be encountered in patients who are younger than 2 years, which are classified by the phases of development during which defects occur: dorsal induction, ventral induction, cerebral corticogenesis, and cerebellar formation. We also highlight the clinical presentation and treatment options available for many of these lesions.

*Department of Radiology, Lucile Packard Children's Hospital, Stanford University, Stanford, CA.
†Department of Radiology, Stanford University and Stanford University Medical Center, Stanford, CA.
Address reprint requests to Christine Kim, MD, Department of Neuroradiology, Stanford Medical Center, 300 Pasteur Dr, Room S047, Stanford, CA 94305. E-mail: christi6@stanford.edu

Embryogenesis

Development of the central nervous system involves a number of complex molecular and cellular interactions during the prenatal and postnatal periods. A detailed description is beyond the scope of this review, but in brief, development begins with gastrulation. Gastrulation refers to the transition of the blastula, a single-layer sphere of cells, into the gastrula, which contains 3 germ cell layers: the ectoderm, mesoderm, and endoderm.[2,3]

The ectoderm, which becomes the epidermis and nervous system, gives rise to the central nervous system through the processes of dorsal induction and ventral induction. Many congenital brain anomalies can be categorized by disturbances during these processes.

Dorsal Induction

Dorsal induction encompasses the formation of the neural plate, notochord, neural groove, neural folds, and neural tube. In a 2-step process called neurulation, the neural plate develops into the neural tube, which is the precursor of the central nervous system. Neurulation begins at approximately 17-19 days of gestation and is completed by day 28.[2,4] Primary neurulation refers to the formation of the part of the neural tube that becomes the brain and most of the spinal cord. The formation of the lower lumbar, sacral, and coccygeal portions occurs during secondary neurulation.[2,5]

In primary neurulation, the lateral aspects of the neural plate elevate fold over the midline to become apposed and fuse to form a tube with a central patent lumen. Fusion is thought to

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be multisite and bidirectional. The adjacent ectoderm then migrates to become the overlying skin. The neural tube separates from the overlying ectoderm in a process called disjunction.[2,4,5]

Primary neurulation defects are typically due to disruption of tube closure or mesoderm development. These anomalies include exencephaly, anencephaly, cephalocele, and Chiari malformation. Defects of secondary neurulation involve the lumbosacral spine.[4,5]

Causes of neural tube defects may be genetic, environmental, or a combination of both. Extrinsic risk factors include maternal diabetes, folic acid deficiency, and anticonvulsant medications.[4]

Malformations of Dorsal Induction

Exencephaly and Anencephaly

When the anterior neuropore does not close, the developing forebrain, called the prosencephalon, remains exposed to amniotic fluid. This is known as exencephaly. Anencephaly occurs when the exposed forebrain subsequently degenerates. Consequently, the brain and overlying skull are at least partially absent, though the brainstem and cerebellum may be preserved.[4,5]

The brain parenchyma in exencephaly and anencephaly is composed of disorganized masses of vascular neural tissue containing multiple cerebrospinal fluid–filled cavities and fibrosis called cerebrovasculosa. Because exposure to amniotic fluid promotes rapid brain necrosis, exencephaly is rarely seen in humans. Meroacrania refers to anencephaly primarily affecting the rostral brain and skull. In the severest forms of anencephaly, the defect extends to the foramen magnum and is known as holoacrania.[4,5]

The incidence of anencephaly is 1:1000, with a 4:1 female to male predilection. Diagnosis is often made antenatally by evaluation of elevated maternal serum alpha fetoprotein level and prenatal ultrasound, which is nearly 100% sensitive by 14 weeks of gestation. Ultrasound may detect anencephaly as early as 11 weeks. Sonographic findings include absent tissue and calvarium above the level of the orbits and a short crown-rump length. The absent calvarium and prominent orbits may form a “frog-eye” or “Mickey-Mouse” sign on coronal imaging. Polyhydramnios is also often present because of impaired swallowing.[6,7]

Inadequate folic acid intake has been well established as a risk factor for anencephaly. In general, anencephaly is rarely encountered because of improvements in nutrition, antenatal diagnosis, and subsequent pregnancy termination.[3,4] Because neonates are stillborn or survive for only a few days, postnatal imaging is rarely performed.[4]

Anencephaly is usually associated with other congenital anomalies, including other neural tube defects, cleft lip or palate, congenital heart defects, skeletal anomalies, and gastrointestinal and urinary tract abnormalities. Spine defects, such as segmental anomalies, absent spinal cord, or dysplastic spinal cord, always accompany anencephaly.[4]

Congenital Cephaloceles

Congenital cephaloceles are protrusions of intracranial contents through congenital skull defects. Defects are midline and covered by epithelium, suggesting disruption of neural tube closure during the postneurulation period. An explanation involves failed disjunction of the neural tube from the overlying ectoderm. Consequently, mesoderm cannot form between the neural tube and ectoderm, producing a defect in the skull and dura.[4,8]

The incidence of cephalocele is 0.8-3 per 100,000 live births. Specific types of defects have sex, race, and geographic predilection. Several classifications of cephaloceles exist, including categorization by the contents of the cephaloceles or whether the skull base is involved. Clinically, cephaloceles are defined by the site of bony defect. Using this method, the types of cephaloceles are occipital, nasal (frontoethmoidal and basal), parietal, temporal, and atretic.[4,8]

Except for basal cephaloceles, most cephaloceles are diagnosed on prenatal ultrasound. Postnatally, the bony defect may be seen on computed tomography (CT), though magnetic resonance imaging (MRI) best evaluates the contents that have herniated through the defect.[4,8]

Occipital Cephalocele

Occipital cephaloceles comprise 70%-80% of cases and are most common in female infants of North America, Europe, and Australia.

Depending on the contents of the cephalocele sac, imaging characteristics vary. Leptomeninges and cerebrospinal fluid herniate through the defect, with a variable amount of infratentorial or supratentorial brain parenchyma, which may be normal or dysplastic (Fig. 1). Traction distorts and displaces the brain structures remaining in the cranium. If a cerebral hemisphere is pulled into the cephalocele preferentially, the contralateral cerebral hemisphere may cross the midline and occupy the bilateral anterior cranial fossae. Alternatively, the frontal lobes may occupy the middle cranial fossae, displacing the temporal lobes posteriorly to the petrous ridge.[4]

The ventricles and brainstem may also herniate into the cephalocele. Depending on where the cerebrospinal fluid spaces are narrowed, hydrocephalus of the ventricles may develop intracranially or within the cephalocele. Vascular compression at the neck of the cephalocele may cause ischemia or hemorrhage or a combination of both. The falx is hypoplastic and may herniate into the cephalocele. The tentorium is also often hypoplastic and inserts inferiorly to the petrous ridge, decreasing the size of the posterior fossa. Cervicooccipital cephaloceles are rare and involve defects of the inferior occipital bone and the posterior elements of the upper cervical spine.[4]

Occipital cephaloceles may be associated with a variety of other brain malformations, most commonly absence of the anterior commissure, septum pellucidum, and fornices.[4]