Images in Clinical Medicine Congenital Neural Malformations Related to Their Embryological Background

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Abstract: Congenital neural malformations are complex anomalies, which stem from an abnormality in the embryological development of the nervous system. The development of the nervous system begins by the formation of the neural tube and its subsequent closure. The failure of closure results in neural tube defects (NTD). Defect in the formation of prosencehalon or rhombencephalon will result in holoprosencephaly or Dandy walker complex respectively. The formation of neuroblasts and their migration to cerebral cortex may be altered by many neuronal migration disorders. Lissencephaly, schizencephaly, and heterotopic gray matter are the most prominent.

Conclusion: The objective of the study is relating congenital neural malformations to their corresponding embryological background, and so helping in better understanding the time and the way of the occurrence of such anomalies.

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Introduction

The congenital anomalies of the nervous system are a frequent cause of fetal and neonatal morbidity and mortality. Understanding the complex nature of the embryological development of the nervous system is mandatory in order to better recognize the different neural malformations.

For simplicity, we can discuss the subject in terms of various stages.

Stage of Neural Tube Formation

The nervous system develops from the neural plate. The formation of the neural tube (process called neurulation) begins during the early part of the 4th week of development.

The fusion of neural folds proceeds in cranial and caudal directions. The lumen of neural tube (the neural canal) communicates freely with the amniotic cavity. The cranial and caudal opening (rostral and caudal neuropores) close at the 25th and 27th days. The walls of the neural tube thicken to form the brain and spinal cord. The neural tube cranial to the 4th part of somites will develop into the brain, while the neural canal is converted into the ventricular system of the brain (cranially) and the central canal of spinal cord distally [1, 2]. The congenital defects related to this stage include the following.

Spinal dysraphism

It is a broad term encompassing a heterogeneous group of congenital spinal anomalies, which result from the defective closure of the neural tube early in fetal life and the anomalous development of the caudal cell mass.

It can be sub-classified into the following types: a) Spina-bifida occuta, and b) Spina bifida cystica, which is more severe and associated with meningeal herniation (meningocele) or meningomyelocele (Fig. 1) if associated herniation of neural elements occurred [2, 22].

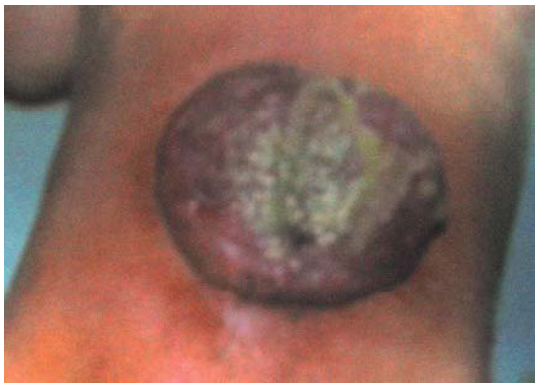


Fig. 1. Source: Moore's "Before We are Born". Neonate with lumabr meningocele.

Encephalocele

Encephalocele represents one end of the spectrum of open neural tube diagnoses. The diagnosis is based on the herniation of a spherical fluid-filled structure, more correctly diagnosed as a meningocele or brain parenchyma (encephalocele) beyond the calvarial confines. The herniation occurs through a calvarial defect. An encephalocele is the result of the failure of the surface ectoderm to separate from the neuroectoderm. This results in a bony defect in the skull table, which allows the herniation of the meninges (cranial meningocele) or the herniation of the brain tissue (Figs. 2 and 3). It is often associated with Dandy-Walker malformation and Arnold-Chiari II malformation [3, 20, 21, 23].

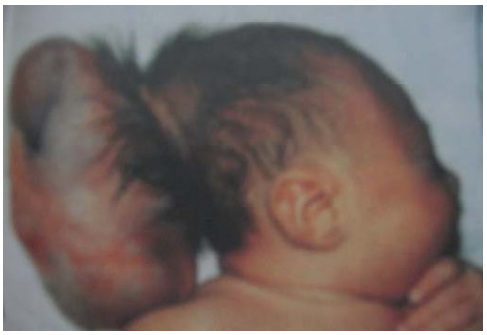


Fig. 2. Source: Moore's "Before We are Born". Neonate with encephalocele.

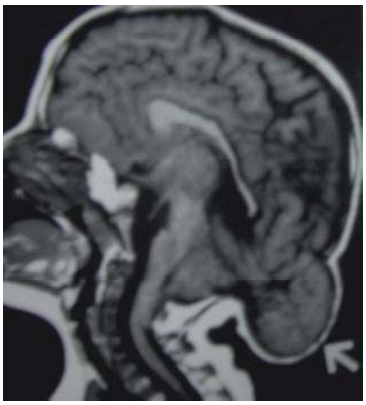


Fig. 3. Encephalocele. MRI-T1WI-arrow pointing to an occipital encephalocele (note herniated brain).

Stage of Diverticulation

Three distinct vesicles—primary brain vesicles—are formed from the rostral end of the neural tube: the forebrain (prosencephalon), the midbrain (mesencephalon) and the hindbrain (rhombencephalon) (Fig. 4). These will give rise to secondary brain vesicles, wherein the forebrain will give rise to the telencephalon and diencephalon.

In this stage, the following congenital defects are recognized.

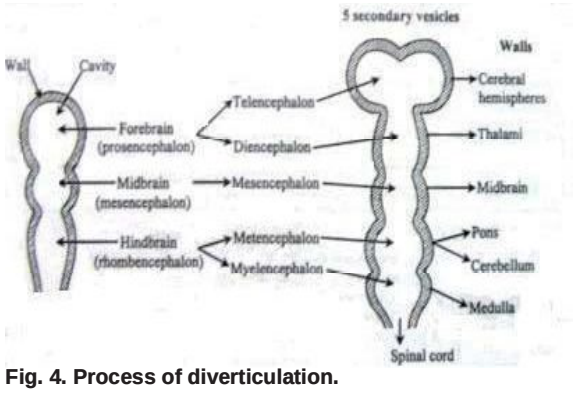


Fig. 4. Process of diverticulation.

Holoprosencephaly

Holoprosencephaly denotes an incomplete or an absent division of the embryonic forebrain (prosencephalon) into distinct lateral cerebral hemispheres. De Myer categorized holoprosencephaly into three types (from the most the severe to least severe): Alobar holoprosencephaly, or complete absence of midline forebrain division resulting in a monoventricle and fused cerebral hemispheres; semilobar holoprosencephaly, or incomplete forebrain division resulting in a partial separation of cerebral hemispheres, typically posteriorly; and lobar holoprosencephaly, or complete ventricular separation with focal areas of incomplete cortical division or anterior falcine hypoplasia (Fig. 5) [4, 25, 26].

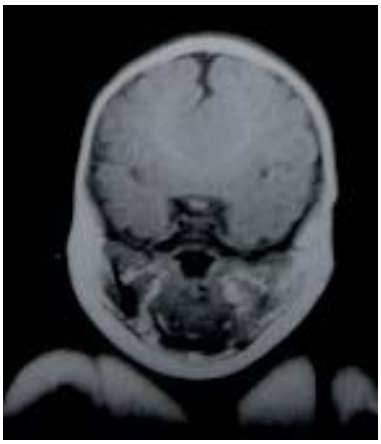


Fig. 5. Holoprosencephaly (MRI-T1WI). Note the fusion of both frontal lobes. Lobar holoprosencephaly.

Anencephaly

Most of the brain and cranial vault are absent due to the failure of the closure of anterior neuropore, and non-developed cephalic part of neural tube (Fig. 6) [2].

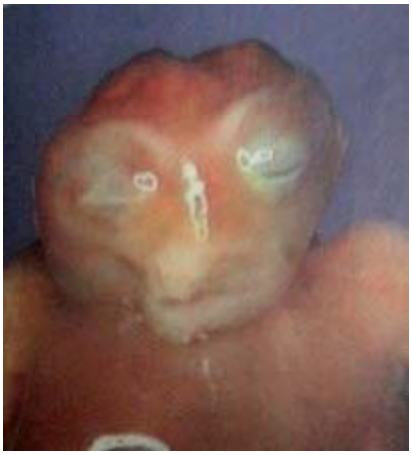


Fig. 6. Moore's "Before We are Born". A still-birth anencephalic fetus.

Stage of Metencephalon Formation

The walls of metencephalon form the pons and cerebellum, and its cavity forms the superior part of the 4th ventricle [1, 2]. In this stage, the following congenital defects are recognized.

Dandy-Walker complex

Dandy-Walker malformation, variant, and mega cisterna magna are currently believed to represent a continuum of developmental anomalies on a spectrum that has been termed the Dandy-Walker complex.

The Dandy-Walker complex is characterized by an enlarged posterior fossa, a high position of tentorium with upward displacement of the lateral sinuses, torcular herophili associated with varying degrees of vermian aplasia or hypoplasia, and a cystic dilatation of the 4th ventricle that nearly fills the entire posterior fossa [5]. This includes the following.

Dandy-Walker malformation:

The rationale of this congenital defect is in the form of dysembryogenesis involving the hindbrain. An insult leads to a developmental arrest in the formation of the hindbrain, with a lack of the fusion of the cerebellum in the midline (at the 7th and the 10th gestational weeks). This results in a blockage or atresia of the foramina of Magendie and Luschka. This, in turn, results in a cystic transformation of the roof of the 4th ventricle and in an obstructive (non-communicating) hydrocephalus, in which a cyst arises from the compromised absorption of CS (Fig. 7). The condition is characterized by the agenesis or hypoplasia of the cerebellar vermis, cystic dilatation of the 4th ventricle, and the enlargement of the posterior fossa. Approximately 70-90% of patients have hydrocephalus [5, 6].

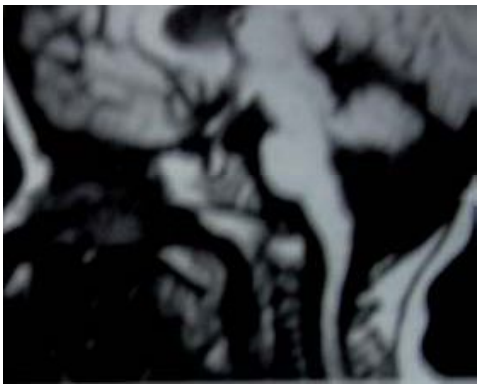


Fig. 7. Differential diagnosis in MRI-MRI-T1WI. A cyst in a large posterior fossa with cerebellar atrophy. Dandy-Walker cyst. (Source: Buergener F, et al.).

Dandy-Walker variants:

Dandy-Walker variants consist of vermian hypoplasia and cystic dilatation of the 4th ventricle without enlargement of the posterior fossa.

Mega cisterna magna:

The mega cisterna magna consists of an enlarged posterior fossa, secondary to an enlarged cisterna magna, but a normal cerebellar vermis and 4th ventricle.

Arnold-Chiari malformation (type II)

The Chiari II malformation is a complex anomaly with skull, dural, brain, spinal, and spinal cord manifestations. The hindbrain findings of Chiari II malformation are best explained ith the theory of McLone and Knepper, which allows the hindbrain disorder to be conceptualized as resulting from a normal-sized cerebellum developing in an abnormally small posterior fossa with a low tentorial attachment. Associated anomalies include: Lumbar myelomeningocele (88-100%), dysgenesis of corpus callosum (80-90%), obstructive hydrocephalus following the closure of myelomeningocele (50-98%), syringohydromyelia (50-90%), aqueductal stenosis (70%), and the absence of septum pellucidum (40%) [7, 8].

Stage of Commisural Formation

As the cerebral hemispheres grow, groups of fibers-called commisures connect corresponding the areas of cerebral hemispheres with one another. The largest is the corpus callosum [2]. The only congenital defect is the agenesis of corpus callosum.

Agenesis of corpus callosum
Development and anatomy:

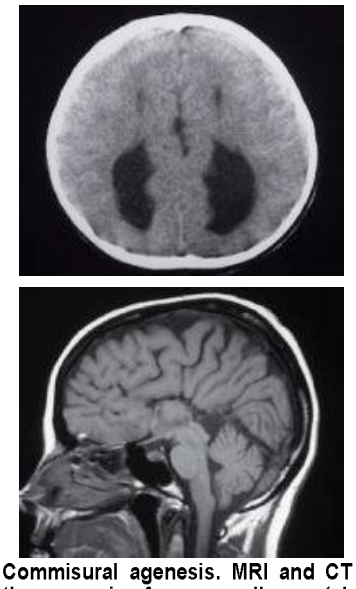
The corpus callosum develops from the lamina reuniens in the telencephalon, and it begins to appear between the anterior and hippocampal commissures at about 10.5 weeks. The adult form of the corpus callosum is achieved by 17 weeks of gestational age. The initial formation of the corpus callosum occurs in the genu and the body, progressing posteriorly. The anterior genu and rostrum develops last, folding back under the genu. The callosum thickens with increasing myelination.

The fibers of the corpus callosum normally arise from the superficial layers of the cerebral cortex and they project to the homotypic region of the contralateral cortex by passing through the corpus callosum while crossing the midline.

The disturbance of embryogenesis in the first trimester of gestation by some unknown insult leads to the failure of the callosal axons to pass across the midline. These arrested axons form the longitudinally oriented bundles of Probst that are located medial to the lateral ventricles in patients with agenesis.

Imaging particulars:

When the corpus callosum is absent, the third ventricle is often high riding, extending superiorly between the lateral ventricles. On coronal imaging, a candelabra appearance occurs, with the third ventricle forming the central vertical portion and the lateral ventricles the peripheral arms of the candelabra. On axial imaging, the lateral ventricles are parallel (Figs. 8 and 9) [9].



Figs. 8+9. Commisural agenesis. MRI and CT findings in the agenesis of corpus callosum (absent corpus callosum in MRI, parallel lateral ventricles in CT).

Stage of Histogenesis

Emryological background

The neuroblasts are formed in the germinal matrix, present in caudothalamic groove. Then, they migrate to the cerebral cortex. The newly formed cells migrate through the already migrated layer to reach the superficial part of the cerebral cortex (i.e. the more recent are more superficial) until the six layers of the cerebral cortex are formed. The defect of the neuronal migration is the base of many congenital anomalies [1, 2].

Unilateral hemimegalencephaly

Hamartomatous overgrowth of the involved hemisphere, nodular or multinodular gray matter heterotopia, with associated enlargement of ipsilateral lateral ventricle ad hemisphere [11].

Lissencephaly

The severe disorder of neuronal migration (7^{th}-16^{th} week) with absent (agyria) or incomplete formation of gyri, sulci, and sylvian fissures. Abnormal thick cortex, gray matter heterotopia, with smooth gray/white mater interface (Fig. 10) [11].

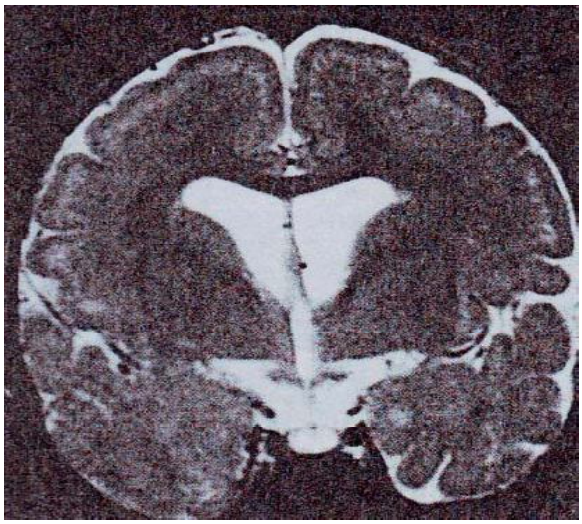


Fig. 10. Differential diagnosis in MRI MRI-T2WI. Note the abnormally flat Gyria: Pachygyria (Source: Buergener F, et al.).

Schizencephaly:

Schizencephaly is an uncommon disorder of neuronal migrational characterized by a cerebrospinal fluid–filled cleft, which is lined by gray matter. The cleft extends across the entire cerebral hemisphere, from the ventricular surface (ependyma) to the periphery (pial surface) of the brain. The clefts may be unilateral or bilateral and may be closed (fused lips), as in schizencephaly type I, or separated (open lips), as in schizencephaly type II (Fig. 11) [11, 12, 28, 29].

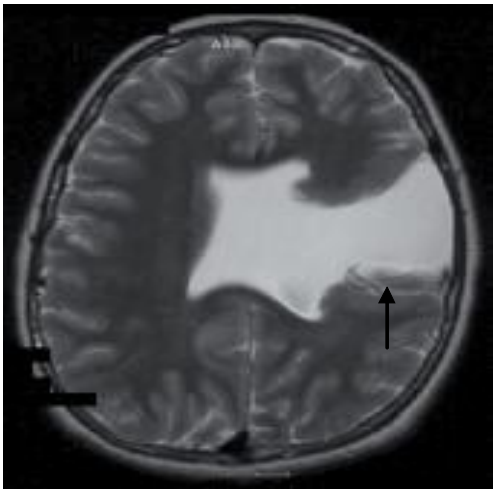


Fig. 11. Schizencephaly MRI-T2WI. Wide cleft lined by gray matter and filled by CSF: Open lip schizencephaly.

Heterotopic gray matter (nodular/laminar):

Gray-matter heterotopia means the collections of gray matter in abnormal locations. It can be:

- Nodular: Nodules of gray matter along the ventricles or within white matter (Fig. 12).
- Laminnar: Bands of gray matter within white matter [11, 27].

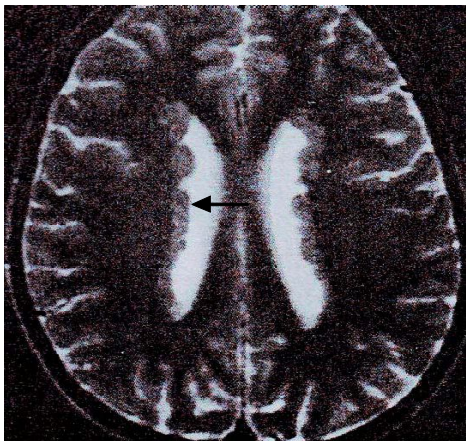


Fig. 12. Differential diagnosis in MRI MRI-T2WI. Note the nodularities on the wall of both lateral ventricles isointense to gray matter, Nodular heterotopia (Source: Buergener F, et al.).

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