A Practical Approach to Supratentorial Brain Malformations

What Radiologists Should Know

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KEYWORDS

• Brain malformation • Holoprosencephaly • Callosal dysgenesis • Lissencephaly • Pachygyria • Focal cortical dysplasia • Polymicrogyria • Cobblestone malformation

KEY POINTS

- The number of genetically elucidated brain malformations has dramatically increased in recent years. However, a morphologic approach based on an understanding of embryology remains essential to correctly recognizing these malformations and placing them in a mechanistic context.
- Errors in hemispheric cleavage and neuronal migration/organization explain the most common cerebral malformations encountered in clinical practice.
- Cerebral malformations frequently co-occur with abnormalities in the deep gray matter structures, corpus callosum, and overall brain size. These associated features help narrow the differential diagnosis.

INTRODUCTION

Congenital brain malformations are a major contributor to neurodevelopmental disability potentially manifesting as epilepsy, cerebral palsy, developmental delay, or as part of a broader genetic syndrome.[1–5] Therefore, brain malformations should be considered a focal point in the imaging evaluation of children with developmental delay and seizure, along with evidence of prior injury and metabolic disorders. Even in general radiology practice, these malformations are encountered periodically on obstetric imaging or as an incidental finding, making a basic understanding of brain malformations essential to all radiologists.

Correct classification of brain malformations is critical in guiding the appropriate work-up for these pediatric patients and setting expectations for prognosis. This classification can be particularly challenging for supratentorial malformations, which can have overlapping morphologic features or multiple abnormalities. To complicate the matter further, an enormous body of work has defined the genetic etiologies of many brain malformations over the past several years, making brain malformations an increasingly intimidating subject even for those who deal with such malformations routinely.[1,6]

In this review, a practical approach to supratentorial brain malformations is discussed based on a standard framework used by pediatric neurologists and neuroradiologists.[7] Fundamental to this approach is an understanding of the embryologic steps necessary to create the morphologically normal brain and optimal imaging technique for recognizing structural abnormalities, both of which are reviewed. Once this foundation is established,

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major categories of supratentorial brain malformation can be placed into a mechanistic context, including disorders of hemispheric cleavage (ie, holoprosencephaly [HPE]) and disorders of neuronal migration/organization (eg, gray matter heterotopia, lissencephaly/pachygyria, cortical dysplasia, polymicrogyria [PMG], and cobblestone malformation). Although nonspecific, callosal abnormalities also deserve discussion along with these supratentorial malformations due to their frequency in supratentorial brain malformations and their role as a sentinel sign for more widespread abnormalities. Finally, the issues of specificity that arise once a particular cerebral malformation is identified are briefly discussed.

EMBRYOLOGIC CONSIDERATIONS

The morphologically normal supratentorial brain or cerebrum has several obvious features. To begin with, there are 2 cerebral hemispheres of equal size separated by the interhemispheric fissure as well as the falx cerebri and joined by the major interhemispheric commissural tract, the corpus callosum, which suspends the septum pellucidum at the midline. In each cerebral hemisphere, there is an orderly arborization of the cerebral white matter peripherally. Overlying the subcortical white matter, there is cortical gray matter 2 mm to 4 mm thick, which is sharply defined from the white matter and seemingly uniform in thickness in any one region.[8] Although not visible on standard MR imaging, the cortex has 6 histologically recognizable layers.

This complex morphology of the cerebral hemispheres arises through embryologic transformations that far exceed what can be summarized briefly. But for the purpose of this article, the embryogenesis of the cerebral hemispheres can be viewed schematically as a series of steps (**Fig. 1**).[7,9,10] The first step is folding of the neural tube and closure of the tube at each end near the fourth week postconception, a process known as neurulation. By the 6th week, 2 separate vesicles arise from the primitive neuronal matrix at the anterior neural tube setting the stage for 2 separate cerebral hemispheres (ie, hemispheric separation). Between the 6th week and 16th week, neuronal precursor proliferation occurs deep within the cerebral hemispheres in the ventricular zone and subventricular zone, the ventricular zone representing what is later recognized as germinal matrix on imaging.[11–13] These neuronal precursors then undergo neuronal migration by moving radially outward between 8 weeks and 24 weeks postconception, populating the cortex with neurons and eventually organizing into 6 layers. As this migration occurs, there is also crossing of fiber tracts at sites of acquired fusion in the midline. Although initially at the anterior midline, the largest of these commissures, the corpus callosum, fuses with the hippocampal commissure located slightly posterior, and it progressively expands posteriorly between weeks 13 to 20 (discussed later).[14]

By the end of this schematized process through the 24th week postconception, the brain still has a primitive appearance with only minimal gyral convolution (see **Fig. 1**F–H), and the process described above omits certain key details, such as the presence of tangential as well as radial/centrifugal migration of neurons.[15,16] Nonetheless, the steps described above set the basic architectural plan for the brain and can explain the congenital brain malformations, described later. During the remainder of fetal life (24+ weeks), the brain assumes dramatically greater size/weight and increasing gyral complexity.[9] These later transformations, however, build on the foundation established earlier in gestation.

IMAGING TECHNIQUES

High-quality brain MR imaging is essential for an accurate analysis of brain malformations. Although a variety of technical parameters can provide good results,[17] pediatric patients at the authors' hospital for whom a structural brain abnormality is suspected (eg, medically intractable epilepsy) are imaged on a 3T MR instrument with a 32-channel or 64-channel head coil according to the imaging protocol, summarized in **Box 1**. This protocol includes isotropic (0.9-mm) T1-weighted and fluid-attenuated inversion recovery (FLAIR) MR imaging as well as high-resolution T2-weighted MR imaging in the axial and coronal planes, as shown in **Fig. 2**. Magnetization prepared T1-weighted MR imaging at isotropic resolution beautifully depicts gray-white matter interfaces with any regional abnormality easily compared with multiple cortical ribbons seen elsewhere in the same slice. The volumetric FLAIR MR imaging accentuates subtle signal abnormalities (cortical as well as white matter) that can indicate a cortical dysplasia; some institutions supplement this sequence with magnetization transfer imaging.[18] Finally, diffusion-weighted MR imaging can complement other imaging sequences in characterizing suspected gray matter heterotopias because heterotopias should follow gray matter sequences on all sequences, including diffusion-weighted sequences.