An Imaging Approach to Diffuse White Matter Changes

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KEYWORDS

• Diffuse • Leukodystrophy • Leukoencephalopathy • MRI • T2 • White matter

KEY POINTS

- Diffuse white matter abnormalities encompass a large number of congenital and acquired disorders.
- Clinical history is paramount to honing the differential in diffuse leukoencephalopathies.
- Approaching white matter disorders categorically and then individually in a standardized fashion will aid greatly in procuring a reasonable differential diagnosis.

INTRODUCTION

White matter disorders represent a large, heterogeneous group of disorders that span the continuum of congenital metabolic disorders (typically presenting early in infancy) to acquired processes, such as chronic ischemic microvascular white matter disease (typically manifesting in the late stages of life). Magnetic resonance (MR) imaging has dramatically revolutionized the diagnostic evaluation of patients with these disease processes, proving to be far more sensitive than any other imaging modality in detecting white matter disease.[1] Furthermore, in those suffering from the same malady, the patterns of MR imaging findings are often objectively similar, greatly aiding diagnosis of such patients even with confounding clinical signs and symptoms that may cloud the diagnosis. Unfortunately, however, imaging patterns of many white matter disorders may overlap, especially in their end stages, posing significant challenges for radiologists. A disciplined, systematic imaging approach to diagnosing white matter disorders is therefore paramount in deriving accurate, complete differentials that will serve to hone the initial clinical workup of these complex patients and possibly, in some cases, even provide a single diagnosis. An initial helpful imaging approach to white matter disease is to first separate focal from diffuse white matter disorders, while remembering that any focal process may progress to eventually become diffuse. For the purposes of this article, a diffuse white matter disorder is defined as any entity that involves the entirety or vast majority of the supratentorial and/or infratentorial white matter as a unit rather than as an isolated, random location within the brain. Also included in this definition, and briefly discussed, are those disorders that characteristically involve typical, symmetric large regions of white matter in persons afflicted with the same disorder. Discussed in this review is the imaging approach to diffuse pediatric and adult white matter disorders.

DEFINITIONS

Terminology in white matter disorders may be quite confusing as different authors commonly use the same terms with slightly different meaning and yet still use various nomenclature

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interchangeably, further complicating the matter. The terminology used in this discussion coincides with that used in the text by Dr Marjo S. van der Knaap and Dr Jaap Valk in *Magnetic Resonance of Myelination and Myelin Disorders, third edition*, given its authoritative presence in the field and more so, the consistent use of white matter language contained within the text.[2] Briefly, "white matter disorders" and "leukoencephalopathy" are interchangeable umbrella terms that encompass all disorders, no matter the cause, that exclusively or predominately affect the white matter.[2] "Hypomyelination" and "amyelination" are terms that refer to the near complete or complete permanent absence of myelination, respectively, without inclusion of diseases that result in destruction of myelin or the presence of abnormal myelin.[2] "Dysmyelination" is representative of disorders in which dysfunctional myelination results in some degree of abnormal myelin within the white matter with or without the presence of demyelination.[2] "Demyelination" is simply the loss of myelin by whatever insult. Delayed, but progressive myelination is referred to as "retarded myelination" and is typically the result of chronic, reversible, or irreversible diseases that impair timely, but otherwise normal myelination.[2] A more complete discussion of white matter terminology can be found in the article by Guleria and Kelly elsewhere in this issue.

IMAGING TECHNIQUE

Computed Tomography

Computed tomography (CT) of the head is often a first-line modality that patients presenting emergently with diffuse white matter pathology may encounter when the diagnosis of a white matter disorder has not been previously made. It remains a gross survey tool and should primarily act as a screening tool for acute pathologic abnormalities, such as mass lesions, hemorrhage, profound hypoxic ischemic encephalopathy (HIE), and so on, for which immediate attention is typically necessary. Although in some instances CT may serve as a terminal imaging modality, it more commonly acts as a bridge to definitive imaging with MR imaging given CT's poor sensitivity and specificity in evaluating white matter disorders even with the administration of intravenous contrast.[1] CT technique for all indications is commonly performed using axial technique at peak kilovolt of 120 and milliamperes of 250 to 350 with modern multislice scanners, allowing for source slice thicknesses on the order of 0.625 mm, usually reconstructed at 2.5 to 3.0 mm in both brain and algorithm. Pediatric doses are typically lower with common peak kilovolts ranging from 100 to 120 and milliamperes ranging from 100 to 250.

MR Imaging

Conventional sequences including T1-weighted spin-echo-based or inversion recovery, T2-weighted fast spin-echo, and T2-fluid attenuated inversion recovery (FLAIR) at all ages remain the gold standard in and of themselves in evaluating white matter disorders. Diffusion-weighted imaging and postcontrast T1-weighted sequences may also prove helpful in some cases and probably should routinely be performed in patients suspected of having a leukoencephalopathy. When available, it is advisable that multivoxel MR spectroscopy (see the article by Bray and Mullins elsewhere in this issue), at both short and intermediate echo times (TE = 20–30 ms and TE = 135–144 ms, respectively) and diffusion tensor imaging be performed, as the former may aid in the differential diagnosis and both may be helpful in monitoring disease status with or without treatment (see the articles by Bray and Choudhri elsewhere in this issue). Although conventional sequences may offer limited advantages from 1.5 T to 3.0 T, because advanced imaging modalities like MR spectroscopy and diffusion tensor imaging benefit greatly from high-field strength, it is generally advisable that all patients suspected to have a leukoencephalopathy be evaluated at 3.0 T whenever possible.

CLINICAL HISTORY

As challenging as white matter disorders may be, an initial interrogation of the clinical history may be quite helpful in children and adults suspected of having a white matter disorder. In children, family history, birth history, head circumference, psychomotor retardation including issues of speech, motor, or global developmental delay, psychomotor regression, tonicity, seizures, and even results of ophthalmologic examination are all potentially helpful in categorically refining the differential. For both children and adults, age, gender, known toxic exposure including history of radiotherapy, time of onset (ie, infancy vs childhood vs adulthood), acuity or chronicity of sign and symptom onset, and immune status may all be helpful. For example, a child presenting in the infantile period with hypotonia, psychomotor retardation, and macrocephaly may clue the radiologist into the possibility of Canavan or Alexander disease as opposed to an acquired leukoencephalopathy or acute demyelinating inflammatory process, such as acute disseminated encephalomyelitis.