Pediatric Multiple Sclerosis
Distinguishing Clinical and MR Imaging Features

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KEYWORDS

• Pediatric multiple sclerosis • Diagnostic criteria • MR imaging
• Acute disseminated encephalomyelitis • Neuromyelitis optica
• Acquired demyelinating syndromes • Children

KEY POINTS

- Overall, 3% to 10% of patients with multiple sclerosis (MS) show their first clinical event during childhood.
- Children with MS have higher relapse rates compared with adult-onset MS.
- As in adult patients, pediatric MS diagnosis requires dissemination in space and time, clinically or by MR imaging findings.
- Alternative diagnoses such as acute disseminating encephalomyelitis and neuromyelitis optica spectrum disorder must be differentiated from MS.
- Revised MR imaging criteria are a useful tool to discriminate between pediatric MS and mimickers.

INTRODUCTION

Although multiple sclerosis (MS) occurs most commonly in adults, its onset in childhood and adolescence is now increasingly recognized. It has been estimated that pediatric-onset MS accounts for 3% to 10% of all MS patients,[1–4] whereas disease onset before the age of 10 years has been reported in 17% of all pediatric MS patients.[5] Nevertheless, diagnosing MS in a child or adolescent continues to be challenging due to the higher frequency of transient demyelinating events and other disorders with similar symptoms and neuroimaging findings.

In this article, the author gives an overview of the current diagnostic criteria of pediatric MS, key characteristics for differential diagnosis, and distinguishing features of pediatric-onset MS compared with the typical adult-onset disease.

DIAGNOSTIC CRITERIA OF PEDIATRIC MULTIPLE SCLEROSIS

In 2007, the International Pediatric Multiple Sclerosis Study Group (IPMSSG) met to propose consensus definitions for pediatric-onset acquired inflammatory demyelinating disorders of the central nervous system (CNS), including acute

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disseminated encephalomyelitis (ADEM), neuromyelitis optica (NMO), clinically isolated syndromes (CIS), and MS.[6] These definitions were developed to improve consistency in terminology, avoid misclassification, and facilitate epidemiologic studies and clinical research in children.

The diagnosis of MS in childhood, as in adult patients, requires evidence of CNS demyelination with dissemination in space (DIS) and time (DIT). Accordingly, the 2007 criteria for pediatric MS incorporated and expanded the 2005 McDonald criteria for adult-onset MS by including children of all ages and introducing a caveat for an ADEM-like initial event. In this situation, a second non-ADEM event should be accompanied by further evidence of DIT, either with new MR imaging T2 lesions $\geq$3 months from the second event or with a new clinical relapse.[6]

Several MR imaging criteria specific to pediatric-onset MS were developed to improve the ability to predict a subsequent MS diagnosis in children with acute CNS demyelination, and they are listed in **Table 1**. The French Kid Sclerose en Plaques Study Group identified 2 MR imaging features on baseline MR imaging that could predict subsequent MS diagnosis. The proposed MS criteria for "Kids with MS" (KIDMUS) were at least one lesion perpendicular to the long axis of the corpus callosum, and the sole presence of well-defined white matter (WM) lesions.[7] Another study that evaluated the KIDMUS criteria and the 2005 McDonald criteria for DIS in a pediatric cohort with acute demyelination demonstrated that both criteria had a high positive predictive value (PPV) and specificity, but low sensitivity, particularly in the youngest patients.[8] Therefore, a study was conducted using a standardized scoring tool, which was applied to MR imaging scans performed in a longitudinal pediatric cohort with CNS demyelination.[9] One set of pediatric criteria was developed to distinguish patients with MS from those with a non-demyelinating disease (migraine and CNS lupus) on baseline MR imaging (see **Table 1**).[10] Another set of pediatric criteria was developed by the same study group to improve the ability to discriminate between children with monophasic ADEM and those destined for MS (sensitivity 81%, specificity 95%, PPV 95%, negative predictive value 79%)[11] (see **Table 1**). The performance of these criteria has been replicated in an independent pediatric cohort, particularly focused on children presenting with an ADEM phenotype.[12]

In 2010, the McDonald criteria were further revised by an International Panel in an attempt to simplify neuroimaging requirements necessary in the diagnosis of MS (**Table 2**). This revision of the McDonald criteria formally addressed the diagnosis of MS in the pediatric population, considering that most pediatric patients with MS

Table 1
Pediatric MR imaging criteria for multiple sclerosis diagnosis

References	Pediatric-Onset MS
Mikaeloff et al,[7] 2004	MR imaging prognostic factors for MS in children with acute demyelination: Two of the following: 1. T2 lesions perpendicular to the long axis of the corpus callosum 2. Sole presence of well-defined T2 lesions
Callen et al,[10] 2009	MR imaging criteria to distinguish pediatric MS from relapsing non-demyelinating disorders Two of the following: 1. >5 T2 lesions 2. >2 T2 periventricular lesions 3. >1 T2 brainstem lesion
Callen et al,[11] 2009	MR imaging criteria to distinguish a first attack of MS from monophasic ADEM Two of the following: 1. Absence of a diffuse bilateral T2 lesion pattern 2. Presence of black holes 3. $\geq$2 T2 periventricular lesions
Verhey et al,[9] 2011	MR imaging parameters that predict MS in children with acute demyelination Two of the following: 1. $\geq$1 T2 periventricular lesion 2. $\geq$1 T1-hypointense lesion