The Magnetic Resonance Imaging Appearance of Monophasic Acute Disseminated Encephalomyelitis

An Update Post Application of the 2007 Consensus Criteria

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KEYWORDS

• Acute disseminated encephalomyelitis • Consensus guidelines • Molecular mimicry
• Inflammatory cascade

KEY POINTS

- Acute disseminated encephalomyelitis (ADEM) typically occurs after a viral infection or recent vaccination.
- ADEM can represent a diagnostic challenge for clinicians, as many disorders (inflammatory and noninflammatory) have a similar clinical and radiologic presentation.
- The differential diagnosis for multifocal hyperintense lesions on neuroimaging includes an exhaustive list of potential mimickers, namely infectious, inflammatory, rheumatologic, metabolic, nutritional, and degenerative entities.

INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is an immunologically mediated inflammatory disease of the central nervous system (CNS) resulting in multifocal demyelinating lesions affecting the gray and white matter of the brain and spinal cord. ADEM is characteristically a monophasic illness that is commonly associated with an antigenic challenge (febrile illness or vaccination), which is believed to function as a trigger to the inflammatory response underlying the disease. It is most commonly seen in the pediatric population, but can occur at any age.[1–6] Symptoms are highly dependent on the area of the CNS affected, but are polyfocal in nature. Common symptoms include hemiparesis, cranial nerve palsy, seizures, cerebellar ataxia, and hypotonia.[3,7–9] The diagnosis of ADEM depends on the history, physical examination, and supplemental neuroimaging.

Despite the long-standing recognition of ADEM as a specific entity, no consensus definition of ADEM had been reached until recently. Historically, different definitions of ADEM have been used in

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published cases of pediatric and adult patients, which varied as to whether events required (1) monofocal or multifocal clinical features, (2) a change in mental status, and (3) a documentation of previous infection or immunization.[3,8–17] To avoid further misdiagnosis and to develop a uniform classification, the International Pediatric Multiple Sclerosis (MS) Study Group[18] proposed a consensus definition for ADEM for application in both research and clinical settings (**Box 1**). One of the most significant changes proposed by this definition was the mandatory inclusion of encephalopathy as a clinical symptom in patients presenting with ADEM. Before the development of the consensus definition, although encephalopathy was included in the clinical description it was not considered an essential criterion for the diagnosis. Thus, many of the previous studies investigating the clinical and radiologic features of pediatric ADEM were performed on patients who may no longer meet the consensus criteria, and may have led to the classification of other neurologic disorders as ADEM (**Table 1**). It may be that there is an inherent difference in the patients who present with multifocal symptoms and encephalopathy as opposed to those without encephalopathy; therefore, this distinction is imperative. Because of the lack of uniform description and clear clinical and neuroimaging diagnostic criteria in ADEM, caution must be exercised when applying previous clinical and radiologic descriptions of patients with this disorder.

This review is intended to give an overview of ADEM in the pediatric population, focusing on differences that have emerged since the consensus definition was established. Although the focus is on neuroimaging in these patients, a synopsis of the clinical features, immunopathogenesis, treatment, and prognosis of ADEM is provided.

Box 1
International MS Study Group monophasic ADEM criteria

- No history of prior demyelinating event
- First clinical event with presumed inflammatory or demyelinating cause
- Acute or subacute onset
- Affects multifocal areas of central nervous system
- Must be polysymptomatic
- Must include encephalopathy (ie, behavioral change or altered level of consciousness)
- Neuroimaging shows focal/multifocal lesion(s) predominantly affecting white matter
- No neuroimaging evidence of previous destructive white matter changes
- Event should be followed by clinical/radiologic improvements (although may be residual deficits)
- No other etiology can explain the event
- New or fluctuating symptoms, signs, or magnetic resonance imaging findings occurring within 3 months are considered part of the acute event

Data from Krupp LB, Banwell B, Tenembaum S. Consensus definitions proposed for pediatric multiple sclerosis and related disorders. Neurology 2007;68:S7–12.

EPIDEMIOLOGY AND CLINICAL PRESENTATION

Considering that the diagnostic criteria for ADEM were not elucidated before 2007, the annual incidence rate and prevalence within the population is not precisely known. In addition, no analyses of worldwide distribution of ADEM have been completed; therefore, the reported prevalence and incidence taken within a single area may not be generalizable to the population as a whole. Before 2007, the prevalence of ADEM within the pediatric population was estimated at 0.8 to 1.1 per 100,000 in those younger than 10 years.[6,7] A study by Leake and colleagues[11] evaluated the incidence of ADEM in San Diego County, USA. The investigators estimated this to be 0.4 per 100,000 per year in those younger than 20 years. More recent studies completed after the definition of ADEM had been established have suggested that these rates may actually be higher. Visudtibhan and colleagues[26] reported the prevalence of children with definite ADEM in Bangkok, Thailand to be 4.1 per 100,000. Another study from Fukuoka Prefecture, Japan reported the annual incidence to be 0.64 per 100,000.[27] The overall frequency of ADEM in Canadian children with acquired demyelinating disorders had been estimated at 22%.[28]

Although ADEM may present at any age, it is most frequently described in the pediatric population. The mean age of onset in the pediatric population is reported to be 7.4 $\pm$ 1.3 years of age and the median age of onset is 8 years, according to a recent meta-analysis.[7] However, 12 of the 13 studies included in the analysis were performed before the revised ADEM definition.[3,7–9,11–14,16,17,29–31] More recent studies using the new criteria for ADEM have shown a similar mean age of onset,