Pediatric Neurology 57 (2016) 64–73

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Long-Term Neurocognitive, Psychosocial, and Magnetic Resonance Imaging Outcomes in Pediatric-Onset Acute Disseminated Encephalomyelitis

Cynthia Beatty MD [a], Rachael A. Bowler BA [b], Osman Farooq MD [a], Lindsay Dudeck MD [a], Deepa Ramasamy MD [c], E. Ann Yeh MD [d], Robert Zivadinov MD, PhD [c], Bianca Weinstock-Guttman MD [b], Joy B. Parrish PhD [b,*]

[a] *Division of Pediatric Neurology, Department of Neurology, University at Buffalo, Women & Children's Hospital of Buffalo, Buffalo, New York*
[b] *Department of Neurology, University at Buffalo, Buffalo, New York*
[c] *Department of Neurology, Buffalo Neuroimaging Analysis Center, Buffalo, New York*
[d] *Department of Neurology, Sick Kids Hospital, Toronto, Canada*

ABSTRACT

BACKGROUND: Acute disseminated encephalomyelitis (ADEM) is a demyelinating disorder that is usually self-limited. Recent studies have suggested ongoing neurological deficits and neurocognitive impairment in these patients. Little information on the correlation of clinical and neuroimaging markers in ADEM is available. We examined potential clinical factors (e.g., age of onset, acute symptom duration, magnetic resonance imaging [MRI] lesions) and their relation to neurocognitive and psychosocial outcomes. **METHODS:** This is a retrospective chart review of consecutive pediatric patients diagnosed with ADEM between 2006 and 2012. Patients were evaluated with standard neurological assessment, MRI of the brain, and neuropsychological evaluation. **RESULTS:** Twenty-three patients with ADEM with average age at neuropsychological assessment of 10.1 years (±3.50) were included. Five (22.7%) patients were impaired on three or more neurocognitive measures. Psychosocial problems were reported in 20%-40% of patients. Earlier age of onset was correlated with poorer sustained attention and psychosocial problems, whereas acute symptom duration and Expanded Disability Status Scale were not. MRI outcomes were correlated with psychosocial outcomes but not neuropsychological findings. **CONCLUSIONS:** Our findings suggest lingering cognitive and psychosocial deficits in children with a history of ADEM. Clinical features and MRI findings correlated more strongly with psychosocial outcomes than cognitive functioning. Further studies are needed to confirm relationships and other possible contributing factors to lingering deficits.

Keywords: demyelinating diseases, cognition, depression, fatigue, age of onset, seizure

Pediatr Neurol 2016; 57: 64-73

Introduction

Acute disseminated encephalomyelitis (ADEM) is a relatively rare demyelinating disorder affecting the central nervous system (CNS), which usually has a self-limited course.[1] It typically strikes young children with a slight predominance in males, and an annual incidence between 0.2 and 0.8 per 100,000.[2-9] The consensus definition for ADEM by the International Pediatric Multiple Sclerosis (MS) Study Group (IPMSSG, 2007, 2013) is that of a "first polyfocal, clinical CNS event with a presumed inflammatory demyelinating cause, and encephalopathy that cannot be explained by fever." Brain magnetic resonance imaging (MRI) abnormalities are typically characterized by diffuse, poorly defined, large lesions predominantly in cerebral white matter, although gray matter can also be involved[1,10] (see Fig 1).

Article History:
Received November 12, 2014; Accepted in final form January 1, 2016
* Communications should be addressed to: Dr. Parrish; Department of Neurology; University at Buffalo; Buffalo, NY 14203.
E-mail address: jparrish@buffalo.edu

0887-8994/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2016.01.003

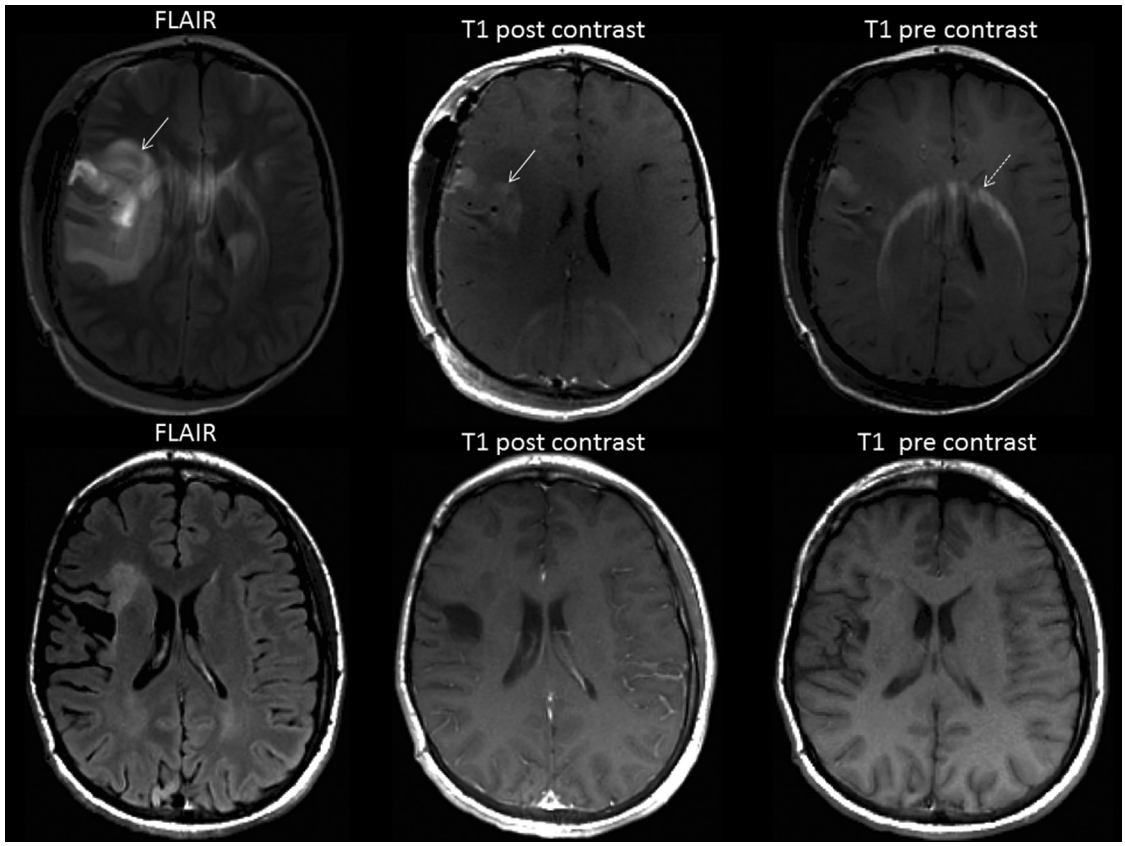

FIGURE 1.
Upper row represents baseline fluid-attenuated inversion recovery (FLAIR), T1 precontrast, and T1 postcontrast images with diffuse lesions of a 13-year-old diagnosed with acute disseminated encephalomyelitis. Lower row images represent recovery after six years follow-up. The gadolinium enhancement seen at baseline (white arrows) resolved at follow-up. Artifacts (dotted white line) seen at baseline are due to orthodontic braces. SE, spin echo.

The prognosis for ADEM is favorable, with more than half of patients showing complete resolution of clinical symptoms.[8,11-14] The majority of children diagnosed with ADEM are reported to have complete motor recovery.[2,8,12,15-19] However, these studies often lack detailed follow-up data and focus primarily on motor deficits.

Some studies have shown a variety of residual mild cognitive deficits in several cognitive domains (visuospatial processing, attention, executive function) as well as mood, behavior, and social deficits.[20-23] In one follow-up study, Dale et al.[16] found that within the ADEM and multiphasic disseminated encephalomyelitis group, 11% had cognitive deficits and 11% had residual behavioral problems. Outcomes were described as diminished intelligence quotient (IQ), aggression, and obsessive compulsive disorder.[16] Other studies have shown ongoing impairment in attention and executive function,[22,23] as well as specific cognitive and behavioral sequelae in patients with ADEM with cerebellar involvement.[21] Suppiej et al.[24] have recently described the long-term neuropsychological effects of ADEM and found that cognitive impairment in the early years following the clinical event subsequently improved with longer-term follow-up. Earlier age of onset and disease severity, but not MRI lesion load, have been correlated with cognitive performance.[20] Unfortunately, assessment of cognitive functioning has typically been limited to broad measures of intellectual functioning.[20]

Given the limited data on long-term neurocognitive and psychosocial status in patients with ADEM, we conducted a retrospective assessment of children with ADEM followed prospectively in our specialty pediatric demyelinating disorders clinic. We included a comprehensive evaluation of neurocognitive and psychosocial functioning, as well as quantitative MRI findings in analyzing correlations between lesion volume and outcomes. Our objective was to determine factors at presentation (age of onset, acute symptom duration), as well as MRI findings that may be associated with long-term neurocognitive and psychosocial functioning. We hypothesized that earlier age of onset and longer acute symptom duration would be correlated with poor outcome on neurocognitive and psychosocial measures. We also hypothesized that the residual MRI lesion volume would correlate with neurocognitive outcomes, such that larger volume would be associated with poorer performance.

Methods

This was a retrospective review of patients (age 2 to18 years) diagnosed with ADEM seen at a specialized pediatric demyelinating disorders clinic between 2006 and 2014. Approval for the study was granted