Pediatric Neurology 52 (2015) 36–41

Contents lists available at ScienceDirect

Pediatric Neurology

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

Original Article

Susceptibility-Weighted Imaging Helps to Discriminate Pediatric Multiple Sclerosis From Acute Disseminated Encephalomyelitis

James E. Kelly MD [a,*], Soe Mar MD [b], Gina D'Angelo PhD [c], Gongfu Zhou PhD [c], Dhanashree Rajderkar MD [e], Tammie L.S. Benzinger MD, PhD [a,d]

[a] *Department of Radiology, Washington University School of Medicine, St. Louis, Missouri*
[b] *Department of Pediatrics, Washington University School of Medicine, St. Louis, Missouri*
[c] *Department of Biostatistics, Washington University School of Medicine, St. Louis, Missouri*
[d] *Department of Neurological Surgery, Washington University School of Medicine, St. Louis, Missouri*
[e] *Department of Pediatric Radiology, University of Florida College of Medicine, Gainesville, Florida*

ABSTRACT

BACKGROUND: Susceptibility-weighted imaging is a relatively new magnetic resonance imaging sequence that can identify lesions of multiple sclerosis in adults. This study was designed to determine if susceptibility-weighted imaging is a useful discriminator between children who develop multiple sclerosis and children with monophasic acute disseminated encephalomyelitis. **METHODS:** Eighteen children who presented with acute central nervous system demyelination and had a brain magnetic resonance imaging study including susceptibility-weighted imaging within 6 months of the first clinical attack were studied. Final diagnosis was based on international consensus definitions. Brain lesions detected on the fluid-attenuated inversion recovery sequence were assessed for abnormal signal on susceptibility-weighted imaging. The burden of susceptibility abnormalities was then analyzed for differences between the multiple sclerosis and acute disseminated encephalomyelitis groups. **RESULTS:** Eight patients had a final diagnosis of acute disseminated encephalomyelitis and ten had multiple sclerosis. Twenty-two percent of fluid-attenuated inversion recovery lesions were identified on susceptibility-weighted imaging. The percentage of fluid-attenuated inversion recovery lesions identified on susceptibility-weighted imaging differed between the multiple sclerosis and acute disseminated encephalomyelitis groups ($P = 0.04$). The median percentage (minimum-maximum) of lesions identified on susceptibility-weighted imaging in the multiple sclerosis group was 0.22 (0-0.68) and in the acute disseminated encephalomyelitis group was 0.0 (0-0.17). **CONCLUSION:** Susceptibility-weighted imaging may be a useful technique in differentiating acute disseminated encephalomyelitis from multiple sclerosis at initial presentation.

Keywords: multiple sclerosis, acute disseminated encephalomyelitis, ADEM, susceptibility-weighted imaging, pediatric demyelination

Pediatr Neurol 2015; 52: 36-41

Introduction

Pediatric demyelinating diseases are rare, with an overall incidence of 1.66 per 100,000 person-years.[1] A single acute central nervous system inflammatory demyelinating episode may represent acute disseminated encephalomyelitis (ADEM), clinically isolated syndrome, or neuromyelitis optica depending on the clinical presentation. Patients may be diagnosed later with multiple sclerosis if they have relapses and fulfill International Pediatric Multiple Sclerosis Study Group criteria.[2] The risk of conversion to multiple sclerosis from ADEM is low (0%-17%), but from clinically isolated syndrome is high (46-72%).[3-5] Although multiple sclerosis and ADEM each have a classic clinical presentation, there is substantial overlap. No clinical features, magnetic resonance imaging (MRI), cerebrospinal fluid, or serum biomarkers can absolutely distinguish ADEM from multiple sclerosis. However, it is desirable to predict

Article History:
Received September 18, 2013; Accepted in final form October 9, 2014
* Communications should be addressed to: Dr. Kelly; Department of Radiology; Washington University School of Medicine; Barnes-Jewish St. Peters Hospital; 70 Jungermann Circle, Suite 100; St Peters, MO 63376.
E-mail address: kellyj@mir.wustl.edu

0887-8994/$ - see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2014.10.014

TABLE.
Individual Subject Characteristics and Results

Patient	Final Diagnosis	Age at First Clinical Presentation, years	MRI Time From Presentation	Months Follow-up	Total Lesions	SWI (+) Lesions	Fraction SWI (+)
1	ADEM	10	1 day	40	6	1	0.17
2	ADEM	9	1 day	32	4	0	0
3	ADEM	6	5 days	25	32	0	0
4	ADEM	5	0 days	20	19	2	0.11
5	ADEM	4	0 days	40	62	10	0.16
6	ADEM	0	1 day	30	4	0	0
7	ADEM	8	1 day	17	34	0	0
8	ADEM	3	37 days	17	10	0	0
9	MS	13	0 days	29	24	6	0.26
10	MS	15	6 mo	41	90	22	0.24
11	MS	15	1 mo	34	5	1	0.2
12	MS	16	0 days	30	15	6	0.4
13	MS	15	6 mo	28	9	0	0
14	MS	15	5 days	53	20	0	0
15	MS	17	1 day	46	100	68	0.68
16	MS	15	20 days	26	160	16	0.1
17	MS	18	0 days	13	25	8	0.32
18	MS	15	0 days	10	26	2	0.08

Abbreviations:
ADEM = Acute disseminated encephalomyelitis
MRI = Magnetic resonance imaging
MS = Multiple sclerosis
SWI = Susceptibility-weighted imaging

the conversion to multiple sclerosis at the time of the first demyelinating episode to assess the risk of relapse and disability, initiate the appropriate immunomodulatory therapy, and potentially spare anxiety.

Much work has been done examining the MRI features of multiple sclerosis and ADEM using standard clinical sequences. MRI criteria have been proposed to diagnose multiple sclerosis in the pediatric population and also to separate children with a first episode of demyelination into those with ADEM and those who have likely experienced a first episode of multiple sclerosis. These criteria are based on T_2/fluid-attenuated inversion recovery (FLAIR) and T1 characteristics, and they include the total number of T_2/FLAIR hyperintense white matter lesions, the location of these lesions (i.e., periventricular, brainstem), whether there is a diffuse and bilateral distribution of the lesions, orientation of the lesions (i.e., perpendicular to the long axis of the corpus callosum), whether the lesions are well-defined, and whether the lesions are hypointense on T_1-weighted imaging ("black holes"). MRI parameters used by a Canadian cohort study and the Callen pediatric multiple sclerosis-ADEM criteria have demonstrated the best predictability of multiple sclerosis, with sensitivity of 81%-84% and specificity of 93%-95%.[6,7]

Susceptibility-weighted imaging (SWI) is a relatively new, gradient-echo sequence that provides information about local tissue susceptibility.[8] Recently, researchers have investigated the role of SWI as it relates to multiple sclerosis in the adult population. SWI has been demonstrated to identify the demyelinating lesions of multiple sclerosis as having hypointense signal in a number of different patterns, and it has been proposed that the SWI images provide a measure of iron deposition within the lesions.[8,9] The goal of this study was to investigate whether SWI can help discriminate children with a first episode of multiple sclerosis from those with ADEM.

Methods

Patients

Approval for the study was obtained from the institutional review board. The subjects in this study were identified from a dataset of 109 patients prospectively enrolled in an ongoing examination of MRI findings in pediatric demyelinating disease. Entry criteria included a final diagnosis of ADEM or multiple sclerosis, an MRI including SWI obtained within 6 months of diagnosis, and clinical follow-up of $\geq$12 months. Detailed serial histories and neurological examinations were performed by a pediatric neurologist (S.M.). The final diagnosis was based on the International Pediatric Multiple Sclerosis Study Group criteria[2] on review of the complete medical records. Eighteen total patients met these criteria, including eight patients with ADEM and 10 patients with multiple sclerosis. The mean length of follow-up for the children in this study was 27.6 months (range, 17-40 months) for ADEM and 31.0 months (range, 10-53 months) for multiple sclerosis.

MRI protocol and analysis

Patients underwent brain MRI on a 3-T Siemens TIM Trio (3T Trio, Siemens, Erlanger, Germany) during the acute period (within 6 months of clinical episode). This consisted of a standard clinical protocol, including T_1-weighted imaging pre- and post-gadolinium contrast, FLAIR, T_2, diffusion, and SWI. For each MRI, the FLAIR and T_1 postcontrast sequences were assessed for the presence, size, location, and enhancement of FLAIR hyperintense lesions. Using a semiautomated technique with standard clinical viewing software, FLAIR images were coregistered with the SWI images, and each lesion was assessed for its SWI characteristics.

Two separate criteria (the "Callen" criteria and the "Verhey" criteria) for separating ADEM patients from multiple sclerosis patients using conventional magnetic resonance were applied to the patients in this study.[6,7] In the Callen study, the following criteria were used to distinguish multiple sclerosis from ADEM: any two of (1) absence of a diffuse bilateral lesion pattern; (2) presence of black holes; and (3) presence of two or more periventricular lesions. In the Verhey study, the criteria for multiple sclerosis included either one or more T_1-weighted hypointense lesions or one or more periventricular lesions. The Callen and Verhey criteria were applied separately by a board-certified neuroradiologist