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The assessment of mild encephalopathy with a reversible splenial lesion (MERS) using high b-value DWI

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Abstract

Introduction: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) was shown to have a transient reduction in diffusion. Such changes would be used as an early detection to reduce excessive treatments and promote recovery without sequelae. The current research evaluated the high b-value (b = 3000 s/mm^2) diffusion-weighted imaging (DWI) assessment in MERS.

Methods: Sixteen pediatric patients showed MERS used DWI (b = 1000 and 3000 s/mm^2). To record number of lesions, the signal intensities, signal-to-noise ratios (SNRs), contrast-to-noise ratios (CNRs), contrast ratios (CRs), the apparent diffusion coefficients (ADCs) were measured in the normal parenchyma and lesions.

Results: Lesions were more apparent with high b-value. The ADC values and CNR in the lesions and surrounding normal brain parenchyma were relatively low at a high compared to standard b-value DWI (SNR: 144.67 ± 33.03, 85.72 ± 31.50; CNR: 20.82 ± 17.64, 49.62 ± 33.06; for b = 1000 and 3000 s/mm^2). The CR was significantly higher at a high compared to low b-value DWI (CR: 0.06 ± 0.07 versus 0.40 ± 0.14).

Conclusion: High b-value DWI could detect more lesions and could obviously improve the detection of lesions in pediatric patients with MERS.

Abbreviations: ADC = apparent diffusion coefficient, CNR = contrast to noise ratio, CR = contrast ratio, DWI = diffusion-weighted imaging, FOV = field of view, MERS = mild encephalopathy with a reversible splenial lesion, MRI = magnetic weighted imaging, SI = signal intensity, SNR = signal to noise ratio, TE = echo time, TR = repettiion time.

Keywords: diffusion-weighted imaging, high b-value, mild encephalopathy with a reversible splenial lesion, standard b-value

1. Introduction

Mild encephalopathy with reversible splenial lesion (MERS) is a clinicoradiological syndrome. Patients with these lesions in the splenium of the corpus callosum showed transiently reduced diffusion on magnetic resonance imaging (MRI). A few studies examined clinically mild encephalitis/encephalopathy by MRI.[1–3] Various neurological symptoms in these patients include altered consciousness, behavioral changes, and seizures, which symptoms can be resolved over days with complete neurological recovery in the absence of treatment. Follow-up MRIs were normal with neither cerebral atrophy nor neurological sequelae. Notably, early detection to reduce excessive treatments is clinically crucial. Although there is no guideline for treatment, Chinese children with MERS may have a favorable prognosis.[4] Thus, clinical symptoms should be considered in treatment planning.[5]

MRI excels in evaluating the early functional and mechanical changes in brain lesions. Most if not all lesions were reversible with transiently reduced diffusion laterally extended from the splenium into the subcortical white matter nearby the central sulcus and anteriorly extended to the entire corpus callosum.[3,6]

Diffusion-weighted imaging (DWI) measures water molecule diffusion and is superior to conventional MRI for visualizing abnormal lesions, such as brain infarct,[7] gliomas grading,[8] and primary central nervous system lymphoma in adults.[9] DWI also favored the diagnosis and assessment of neurological disorders during childhood such as hypoxic–ischemic encephalopathy,[10]

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Informed consent was obtained from all individual participants included in the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This was a retrospective study and was approved by the local Ethics Committee of t (KYZ-2014-010).

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acute encephalopathy with biphasic seizure and late reduced diffusion,[11] and MERS.[1–3] MR scanners with a static magnetic field of up to 1.5 T have typically been used in a clinical setting. This has limited b-values in the range of 1000 to 1500 s/mm^2 in brain applications to maintain reasonable image quality. High field (3T) MRI allows high b-value DW for better diagnostic outcomes. Studies have suggested better diagnosis for acute stroke and the better differentiation of lesions and normal tissue. Particularly in neurodegenerative disease, it is easier to detect small lesions with high DWI, as shown in our previous studies.[9] However, limited studies investigated pediatric neurological disorders with high b-value DWI. To the best of our knowledge, few reports have investigated the assessment of MERS with high b-value DWI. The present study used a 3T MR system to compare regular and high b-value DWI in children with MERS to evaluate diagnosis and assess performance.

2. Material and methods

2.1. Patients

This was a retrospective study and was approved by the local Ethics Committee of t (KYZ-2014-010). Written informed consent was obtained. According to the diagnostic criteria of Takanashi et al,[3] pediatric MERS patients were identified by reviewing the inpatient database of the local hospital. The MRI with DWI was acquired from MERS patients during August 2014 and March 2017. Sixteen patients (5 males and 11 females; mean age 8 years' old) were admitted to the hospital with fever (n = 8), vomiting (n = 4), cough (n = 5), abdominal pain (n = 3), headache (n = 1), and diarrhea (n = 4). The MRI was performed within 3 days. Patient presentations are shown in Table 1.

2.2. MRI

A 3T MRI system (Magnetom Verio Tim, Siemens, Erlangen, Germany) was used for all data collection. Head coil with 8-channel phased-array, single-shot echo-planar and DWI with b-values = 1000 and 3000 s/mm^2 were acquired, similar to previous studies.[9,12] Other imaging parameters are as follows: repetition time (TR) /echo time (TE) = 8200 ms/91 ms (b = 1000 s/mm^2) and 8200 ms/100 ms (b = 3000 s/mm^2); field of view (FOV) = 22 × 22 cm^2; matrix = 128 × 128; slice thickness = 6 mm; average = 2. T1-weighted images (TR/TE = 250 ms/2.48 ms; FOV = 22 × 22 cm^2; matrix = 320 × 256; slice thickness = 6 mm; average = 1), T2-weighted images (TR/TE = 6000 ms/96 ms; FOV = 22 × 22 cm^2; matrix = 320 × 320; slice thickness = 6 mm; average = 1), fluid-attenuated inversion imaging (TR/TE = 4000 ms/94 ms; inversion recovery time = 1530 ms; FOV = 22 × 22 cm^2; matrix = 256 × 320; slice thickness = 6 mm; average = 1) were also acquired.

Table 1

General information of the patients with reversible splenial lesion syndrome.

Patient	Sex	Age	Etiological agent	Initial MRI scan
1	M	1 y 6 mo	Rotavirus infection	<2 days
2	M	5 y	Pneumonia	<1 day
3	F	6 y	Diarrhea	<3 days
4	F	4 y	Influenza virus	<2 days
5	F	2 y	Influenza virus	<3 days
6	F	10 y	Bacterial infection	<1 day
7	M	8 mo	Pneumonia	<1 day
8	M	1 y 3 mo	Diarrhea	<1 day
9	M	4 y	Influenza virus	<3 days
10	F	12 y	Fever and vomiting	<2 days
11	F	3 y	Influenza virus	<3 days
12	F	1 y 7 mo	Rotavirus infection	<2 days
13	F	2 y	Unknown	<2 days
14	F	5 y	Influenza virus	<1 day
15	F	3 y	Rotavirus infection	<3 days
16	F	2 y	Unknown	<3 days

MRI = magnetic resonance imaging.

2.3. Image analyses

The 2 neuroradiologists evaluated the DWI, apparent diffusion coefficient (ADC) maps, and other MRIs without referring to patient history or information to determine the extent of restricted diffusion. All images of the patients were presented in a set, yet the sets were presented in a random manner. If there was any disagreement between neuroradiologists, consensus was reached through examination by a third neuroradiologist. The number of lesions in both b-values were counted. Parenchymal lesions in comparison with adjacent normal brain parenchyma were used as a reference.

2.4. Quantitative analyses

ADC maps for each b-value were computed with a nondiffusion weight image (b = 0 s/mm^2). Manually defined regions of interest were placed in the located lesions at b = 1000 s/mm^2 ADC maps; they were also placed as similarly as possible on b = 3000 s/mm^2 ADC maps (Fig. 1). Mean and standard deviation (SD) values for signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), contrast ratio (CR) are shown in Table 2; ADC_{mean}, ADC_{min}, and ADC_{max} are summarized in Table 3. The SNR, CNR, and CR were computed as follows[13]:

$$SNR = S_{lesion}/\sigma_{noise},$$

$$CNR = |S_{lesion} - S_{brain}|/\sigma_{noise},$$

$$CR = |S_{lesion} - S_{brain}|/|S_{lesion} + S_{brain}|;$$

Where S_{brain} is the average signal intensity (SI) of the normal brain tissue in the contralateral hemisphere, S_{lesion} is the average SI of the lesion, and σ_{noise} is the SD of background noise.

2.5. Statistic analysis

Statistical analyses were carried out using SPSS 16.0 for Windows (SPSS Inc, Chicago, IL) and MedCalc (version 9.3; MedCalc Software, Mariakerke, Belgium). The mean of the SNR, CNR, CR, and ADC values (b = 1000 and 3000 s/mm^2) were compared by Student t test. P values <0.05 were considered statistically significant.

3. Results

Twenty-eight lesions were identified in 16 patients, and 21 lesions were hyperintense in DWI (Fig. 1). High b-value DWI revealed 7 additional lesions (Fig. 2), indicating that a high b-value was more likely to detect lesions than a standard b-value. SNRs were higher on DWI using b = 1000 than a high b value DWI, and CNR and CR

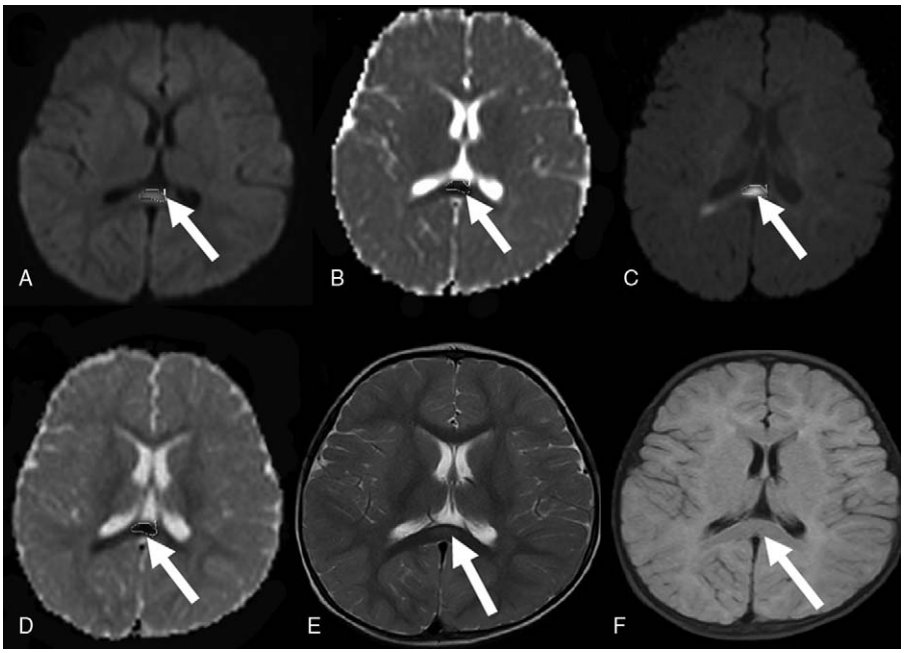

Figure 1. (A) Axial diffusion-weighted imaging (DWI) (b = 1000 s/mm^2) magnetic resonance (MR) image shows hyperintensity incorporis callosi splenium, (c) axial DWI (b = 3000 s/mm^2), (E) axial T2-weighted imaging, and (F) axial T2- fluid-attenuated inversion MR image shows in corporis callosi splenium. Also, low apparent diffusion coefficient values calculated from (B) b = 1000 s/mm^2 and (D) b = 3000 s/mm^2 were found.

(Table 2, Fig. 2A–C) were higher for b = 3000 s/mm^2 DWI. ADCmean, ADCmin, and ADCmax values were all significantly lower at high b-values (Table 3, Fig. 2D).

On b = 3000 s/mm^2 images, the SNR was not decreased (144.67 ± 33.03 and 85.72 ± 31.50; b = 1000 and 3000 s/mm^2 images, respectively; Table 2). The CNR was decreased (20.82 ± 17.64 and 49.62 ± 33.06; b = 1000 and 3000 s/mm^2 images, respectively; Table 2). The CR was significantly greater in the b = 3000 s/mm^2 images compared to the b = 1000 s/mm2 ($P < .0001$; 0.06 ± 0.07, 0.40 ± 0.14; b = 1000 and 3000 s/mm^2 images, respectively, Table 2). The ADC_{mean}, ADC_{min}, and ADC_{max} values in b = 3000 s/mm^2 were inferior to the b = 1000 s/mm^2 images (Table 3).

4. Discussion

All of the patients with MERS underwent MRI over 3 days. DWI of high b-value was found to be more sensitive than standard b-value DWI in detecting lesions. No lesions were found in T1-weighted imaging, T2-weighted imaging, or b-value (b = 1000 s/mm^2) DWI for some cases without specific symptoms. All of the patients recovered within 2 weeks with no residual neurological deficits upon follow-up, as reported.[14]

DW MRI applies phase gradients to measure water diffusion in biological systems. The b-value of a DWI depends on the duration, strength, time interval between gradients. The b-value of routine DW examination was 1000 s/mm^2. Image contrast or diffusion sensitivity can be altered with the b-value. Regarding the development of the MRI gradient, a long gradient duration was not needed to obtain high b-values up to 3000 s/mm.[2,13] DWI showed reduced diffusion in MERS lesions (Fig. 1). Spatial delineation of the restricted diffusion lesion was less defined for standard b-value DWI compared to high b-value DWI. There were additional lesions revealed in the white matter, which is consistent with a previous study[3] (Fig. 2). These provide extra information to clinicians and reduce unnecessary diagnosis. To our knowledge, there have been no reports on high b-values in MERS. The ADC_{min}, ADC_{max}, and ADC_{mean} values obtained with a high b-value were consistently lower in the present study, which is consistent with a previous study on lymphoma.[9] For b-values >1000 s/mm^2, ADC values decrease with b-values. This reflects the nature of a biexponential diffusion signal decay and slow diffusion measured with high b-values. Furthermore, a previous report also suggested that higher sensitivity of lesions detection and signal contrast between lesions and normal tissue could be obtained in higher b-value imaging.[9]

Table 2

SNR, CNR and CR measurements in b = 1000 and 3000 s/mm^2 DWI.

	b = 1000	b = 3000	*P*
SNR	144.67 ± 33.03	85.72 ± 31.5	<.05
CNR	20.82 ± 17.64	49.62 ± 33.06	<.05
CR	0.06 ± 0.07	0.40 ± 0.14	<.05

CR = contrast ratio, CNR = contrast-to-noise ratio, SNR = signal-to-noise ratio. SNR, CNR, and CR measurements in b = 1000 and 3000 s/mm^2 diffusion-weighted imaging.

Table 3

ADC values calculated from b = 1000 and 3000 s/mm^2 DWI.

	b = 1000	b = 3000	*P*
ADC_{mean}	0.60 ± 0.16	0.35 ± 0.94	<.05
ADC_{min}	0.39 ± 0.20	0.21 ± 0.12	<.05
ADC_{max}	0.94 ± 0.19	0.58 ± 0.84	<.05

ADC = apparent diffusion coefficient. ADC values computed from b = 1000 and 3000 s/mm^2 Diffusion-weighted imaging.

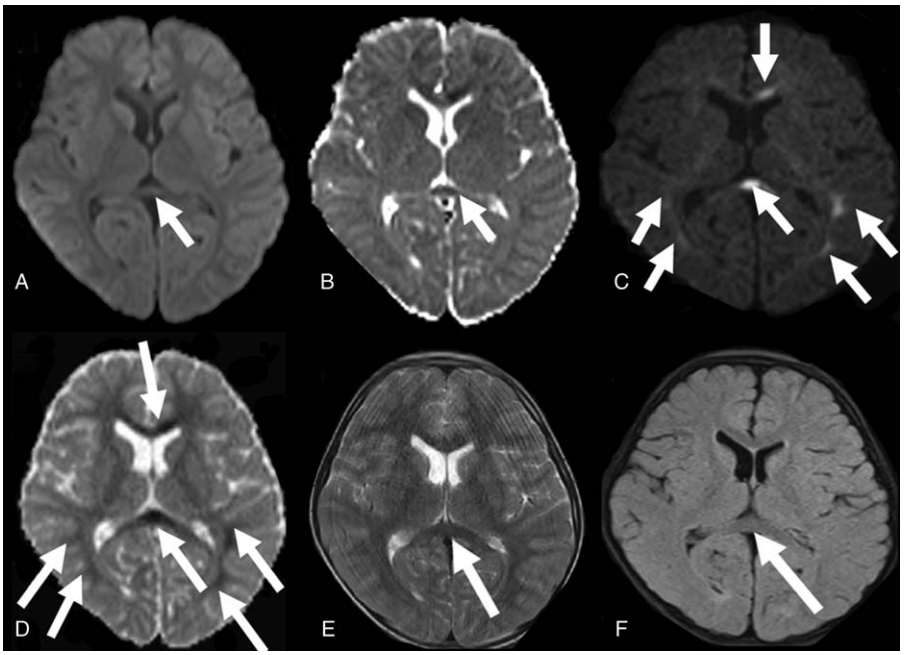

Figure 2. (A) Axial diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) maps calculated from (B) b = 1000 s/mm^2, magnetic resonance (MR) image shows no apparent abnormalities were found; (D) b = 3000 s/mm^2, (E) T2-weighted imaging, and (F) T2-fluid-attenuated inversion. MR image shows ADC map shown for the corporis callosi splenium. However, the hyperintensity signal on DWI and low ADC value were found in different areas, including the genu of corpus callosum and bilateral and symmetrical temporal occipital lobe (C and D, white arrow).

MERS has various prodromal syndromes consisting of fever, cough, vomiting, or diarrhea and followed by encephalopathy 7 days later. Fever is the most common prodrome.[1,15,16] A wide range of infectious agents showed to associate with MERS in children, as reported, and the viruses were most frequent.[17] Other reasons could be fluid imbalance,[18] dysregulation,[19] and other diseases including SLE.[20] Transiently reduced diffusion detected by DWI could be attributed to intramyelinic edema, interstitial edema in tightly packed fibers, or transient inflammatory infiltrate.[1,2] It is occasionally accompanied with hyponatremia.[21] Rotavirus infection or influenza and Kawasaki disease have also been associated with transient splenial lesion.[21,22] Many patients with clinical symptoms also showed encephalitis.

The pathogenesis of MERS remains unclear thus far. Previous studies showed that inflammatory markers in MERS, including white cell count, C-reactive protein, lactate dehydrogenase, CK-MB in serum, are elevated, and in majority of cases cerebrospinal fluid examinations are normal; this evidence supports the hypothesis that MERS is an infection-associated encephalopathy disease rather than an encephalitis.[5] Although neurologic sequelae are typically not observed in MERS patients, they are often observed in acute encephalopathy with biphasic seizures, delayed restricted diffusion, and acute necrotizing encephalopathy patients. Acute disseminated encephalomyelitis (ADEM) should be considered as a differential diagnosis. Although the clinical presentations of these 2 conditions were similar, with white matter lesions, MRI findings are distinct. In ADEM, MRI typically shows lesions with asymmetrical T2-weighted hyperintensity without diffusion restriction, which can be observed upon gadolinium enhancement. In contrast, symmetrical lesions in the corpus callosum were commonly found in MERS, particularly for extensive involvement. Diffusion was restricted without contrast enhancement.[15] Cerebral infarction should be distinguished from MERS. Follow-up MR showed softening in cerebral infarction without lesions in MERS. Infection-associated acute encephalopathy (AE) is characterized by convulsions, prolonged impairment of consciousness, as well as pyrexia. Infants and young children were more vulnerable to AE, which often results in sever neurological sequelae or even to death. Distinct pathophysiology was found in MERS compared to AE, which involved hyponatremia. In addition, the rate of complete recovery in AE is low.[15,23] MERS in children has a wide spectrum of clinic-radiological manifestations that may improve diagnosis. Irrespective of treatment strategies, most MERS provide a favorable prognosis. Follow-up MR scan with no signal abnormalities was found in both b = 1000 s/mm^2 and b = 3000 s/mm^2 (Fig. 3). An 18-month-old male pediatric patient, owing to vomiting and fever for 2 days and diarrhea for 1 day, MR showed with the lesion of corpus callosum, who was considered to have viral encephalitis, so lumbar puncture was inevitably performed, and the results indicated that the cerebrospinal fluid was normal. The early diagnosis of pediatric MERS favors treatment outcomes and avoids unnecessary treatments.[5]

This study showed that a high b-value DWI is a robust technique for early lesion detection. The lack of confirmation of pathological results and the relatively small number of cases are the defects of this study, and further research is needed in the future.

5. Conclusions

DWI with b = 1000 and 3000 s/mm^2 was available in all 3T MR scanners, and the technique is very simple and rapid. High

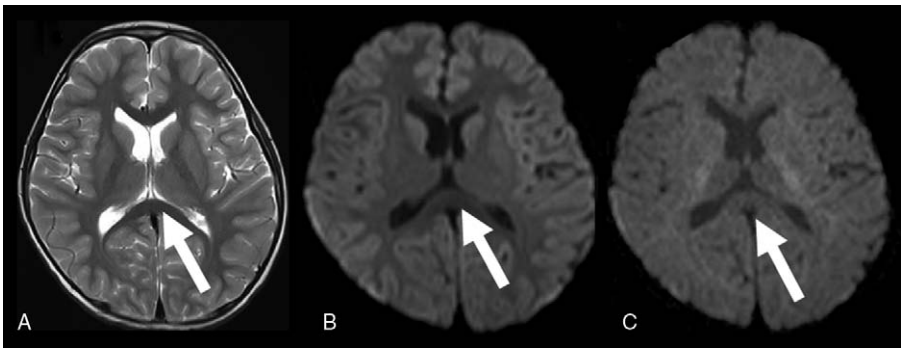

Figure 3. Same case of Figure 2. (A) Axial T1-weighted imaging, (B) axial diffusion-weighted imaging (DWI) (b = 1000s/mm^2), and (c) axial DWI (b = 3000s/mm^2) shows no signal abnormalities.

b-value DWI provides more sensitive detection of lesions in MERS. This technique improves diagnosis and avoids unnecessary tests or excessive treatments in MERS for better clinical management of MERS.

Author contributions

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Validation: Bimei Zhuang, Haiwei Han.
Writing – original draft: Bimei Zhuang.
Writing – review & editing: Bimei Zhuang.

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