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ORIGINAL ARTICLE

Delayed appearance of transient hyperintensity foci on T1-weighted magnetic resonance imaging in acute disseminated encephalomyelitis

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Abstract

Purpose To evaluate the frequency, characteristics, and clinical significance of transient hyperintensity foci on T1-weighted images (T1WI) in acute disseminated encephalomyelitis (ADEM).

Materials and methods Patients diagnosed with ADEM underwent MR studies at the time of disease onset and every 3 months or more often thereafter. The frequency and appearance timing of abnormal signals including T1WI and their morphological characteristics were evaluated. Relations between patient symptoms and abnormal signals on MRI were also evaluated.

Results Five ADEM patients were included in this study. Linear ($n=2$) or nodular ($n=1$) T1-hyperintensity foci appeared in 3 patients (60%, 3/5). Locations of T1-hyperintensity foci were both cortical/subcortical region and basal ganglia ($n=1$), subcortical region alone ($n=1$), and internal capsule ($n=1$). Those T1-hyperintensity foci were located within the T2-weighted image (T2WI) and fluid-attenuated inversion recovery (FLAIR) hyperintensity foci on initial MRI. Some T1-hyperintensity foci also showed hyperintensity on diffusion-weighted image (DWI) and contrast enhancement. T1-hyperintensity appeared at 14–43 days (median, 28 days), and disappeared in 2 patients at 91 days and 627 days after disease onset. There were no neurological sequelae remained in any patients.

Conclusion T1-hyperintensity foci is not a rare finding (60%) and it can be observed after improvement in symptoms in ADEM.

Keywords Acute disseminated encephalomyelitis · hyperintensity lesions · T1-weighted images · magnetic resonance imaging

Introduction

Acute disseminated encephalomyelitis (ADEM), an inflammatory demyelinating disorder of the central nervous system, is usually triggered by viral infections and vaccinations [1, 2]. It is characterized by the acute or subacute onset of multifocal neurologic disturbance. The clinical curse of ADEM is usually monophasic and good prognosis [1, 2].

Diagnosis of ADEM is usually made based on clinical symptoms and radiological findings [3, 4]. Brain MR imaging plays an important role in the diagnosis and evaluation of treatment response for ADEM [5]. Typical MR findings of ADEM are an appearance of multifocal hyperintensity foci on T2-weighted images (T2WI) and fluid-attenuated inversion recovery (FLAIR) imaging, which are located in the white matter as well as gray matter including the basal ganglia and thalamus [5–7]. Usually, such multifocal hyperintensity foci on T2WI and FLAIR images present at the time of disease onset. On the other hand, abnormal findings on diffusion-weighted images (DWI) are not always observed [8]. Restricted diffusion can be sometimes observed within the first 7 days after disease onset, which subsequently changes to the pattern of increased diffusion thereafter [8]. Contrast-enhanced foci with various shape can be observed in 30–100% of patients with ADEM in their acute phase [8].

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Abnormal intensity on T1WI can also be observed in patients with ADEM. Indeed, there are some cases those presenting the T1-hyperintensity foci during their clinical course. However, the frequency, characteristics, and clinical significance of T1-hyperintensity foci have not been well investigated. To evaluate the frequency, characteristics, and clinical significance of T1-hyperintensity foci, we retrospectively evaluated the MR imaging findings of patients those were clinically diagnosed as ADEM.

Materials and methods

Patients

This retrospective study was approved by our institutional review board. Written informed consent to participate in this study was waived because of the retrospective nature of this study.

All patients diagnosed with ADEM who presented between November 2007 and December 2017 at our hospital were included in this study. Diagnosis of ADEM was made based on the definition of the International Pediatric MS Study Group (Table 1) [3, 9]. Details of their clinical events were collected, including the date of disease onset, clinical symptoms, possible cause of ADEM, clinical course after diagnosis, and treatment.

Imaging techniques and schedule

Brain MR imaging was acquired using either a 3-T (Achieva; Philips, Best, NL) or a 1.5-T (Intera; Philips, Best, NL) MR unit with the use of a head coil. The following six sequences were obtained for each patient: (a) an axial unenhanced T1-weighted fast spin-echo (FSE) sequence (TR/TE, 450–521/10 ms; flip angle, 80–90°), (b) an axial T2-weighted FSE sequence (TR/TE, 3000–4518/80–100 ms; flip angle, 90°; Turbo spin echo factor 13–15), (c) an axial T2-weighted FLAIR sequence (TR/TE, 6000–11000/99–125 ms; inversion time, 2700–2800 ms; flip angle, 90°; Turbo spin echo factor, 15–27; sense factor, 1.0–1.9), (d) an axial echo-planar imaging (EPI) diffusion-weighted image (DWI) sequence (TR/TE, 2300–3000/68–71 ms; flip angle, 90°; $b = 1000$ s/mm^2), (e) an axial T2*-weighted gradient-recalled echo (GRE) sequence (TR/TE, 591/18 ms; flip angle, 18°) or susceptibility-weighted imaging (SWI) sequence (TR/TE, 26/37 ms; flip angle, 10°), and (f) an axial contrast-enhanced T1-weighted FSE sequence (TR/TE, 450–521/10 ms; flip angle, 80–90°). Gadopentetate dimeglumine (Magnevist®; Bayer Yakuhin, Ltd., Osaka, Japan) of 0.1 mmol Gd/kg was injected intravenously to obtain contrast-enhanced T1-weighted images (T1WI).

Initial brain MR images were acquired 2–35 days (median: 16) after onset of the disease. Then, they were scheduled to be obtained every 3 months or more often thereafter. Follow-up by MR images were continued until 91–1013 days (median: 756 days) after disease onset.

Assessments

Brain MR images were interpreted by the consensus of two neuroradiologists with experience of 26 (KA) and 5 (YK) years, respectively. If any abnormal signal was observed on each brain MR study, then their timing of appearance, duration, location, and morphology was recorded. Patient symptoms were reviewed using their medical records. Relations between patient symptoms and abnormal signals shown on MR imaging were also evaluated.

Results

Patient demographics

Between November 2007 and December 2017, 5 patients (2 females, 3 males) with median age of 6.2 years (range, 2.7–22 years) were clinically diagnosed as ADEM and included in this study (Table 2). Their possible causes of ADEM were regarded as viral infection in 4 patients (Cases 2–5; 80%, 4/5) and vaccination (Case 1; 20%, 1/5). Clinical symptoms were altered consciousness in 3 patients (Cases 1, 2, 5; 60%, 3/5), cranial nerve palsy in 2 patients (Cases 3, 4; 40%, 2/5), and visual field defect in a patient (Case 6; 20%, 1/5). All those symptoms were resolved in 4–20 days (median, 7 days) by the use of high-dose corticosteroid treatment.

Table 1 The criteria of monophasic pediatric ADEM (all are required) [9]

*A first polyfocal clinical CNS event with presumed inflammatory cause
*Encephalopathy that cannot be explained by fever
*MRI typically shows diffuse, poorly, demarcated, large, > 1–2 cm lesions involving predominantly the cerebral white matter
*T1 hypointense white matter lesions are rare
*Deep gray matter lesions (such as thalamus or basal ganglia) can be present
*No new symptoms, signs or MRI after 3 months of the incident ADEM

ADEM acute disseminated enchepharomyelitis, *CNS* clinical central nervous system

Table 2 Clinical symptoms and MRI findings

Case	Age (years)	Gender	Possible cause of ADEM	Clinical symptoms	Hyperintense foci on T1W1	
					Region	Shape
1	2.7	Male	Vaccination	Consciousness alteration	Cortex subcortical white matter Basal ganglia	Nodular
2	5.4	Male	Infection	Consciousness alteration	Subcortical white matter	Linear
3	22	Female	Infection	Paralysis cranial nerve palsy	Internal capsule	Linear
4	6.2	Female	Infection	Consciousness alteration	(–)	(–)
5	10	Male	Infection	Visual field defect	(–)	(–)

ADEM acute disseminated enchepharomyelitis, *T1WI* T1-weighted imaging

MR imaging

The timing of the appearance and the duration of abnormal intensity on each MR sequences in each patient are summarized in Figure 1. Hyperintensity foci on T2WI and FLAIR images were observed at 2–35 days (median: 16) after disease onset in all patients (100%, 5/5) (Figs 2a, 3a, 4a). The signal differences between the hyperintensity foci on T2WI/FLAIR images and the surrounding normal signals became smaller during their clinical course (median, 756 days; range, 70–1013 days) (Fig 2c).

Abnormal enhancements on contrast-enhanced MR imaging were observed at the T2WI/FLAIR hyperintensity foci in two patients (40%, 2/5; Case 1 and 3) in their initial MR studies. Those enhancements disappeared in the following MR imaging at 21 days (case 1) and 36 days (case 3) after disease onset. Contrast-enhanced studies were not always performed in every MR studies. Contrast-enhanced MR studies were performed 3 times in case 1, 1 time in case 2, and no time in case 3 before the appearance of hyperintensity foci on T1WI.

Hyperintensities on DWI were also observed at the T2WI/FLAIR hyperintensity foci in three patients (Case 1, 2, and 3; 60%, 3/5) in their initial MR studies, and those signals disappeared at 42 days (case 1), 96 days (case 2), and 43 days (case 3) after disease onset (Fig 3b).

Linear (case 2 and 3; 40%, 2/5) or nodular (case 1; 20%, 1/5) hyperintensity foci on T1WI appeared at 14–43 days (median, 28 days) after disease onset (Fig 2d, 3c, 4b), although those signals were not observed in their initial MR studies (Fig 1, 2b). Those T1-hyperintensity foci were observed in both cortical/subcortical region and basal ganglia (case 1), subcortical region alone (case 2), and internal capsule (case 3). There was no patient showing T1-hyperintensity in the dentate nucleus. Locations of those T1-hyperintensity foci were within the hyperintensity regions on initial T2WI/FLAIR images in all cases. Moreover, some T1-hyperintensity foci were also showed hyperintensity on DWI and contrast enhancement. T1-hyperintensity foci disappeared at 627 days (case 2) and 91 days (case 3) after disease onset. Slight T1-hyperintensity foci remained until the last follow-up (756 days after disease onset) in a patient (case 1).

There were not abnormal low-intensity areas on T2*WI or SWI during the clinical course (Fig. 2e).

T1-hyperintensity foci and clinical symptoms

All T1-hyperintensity foci appeared during (case 1) or after (cases 2 and 3) the improvement of their clinical symptoms (Fig. 1). There were no neurological sequelae remained in any patients. However, those T1-hyperintensity foci

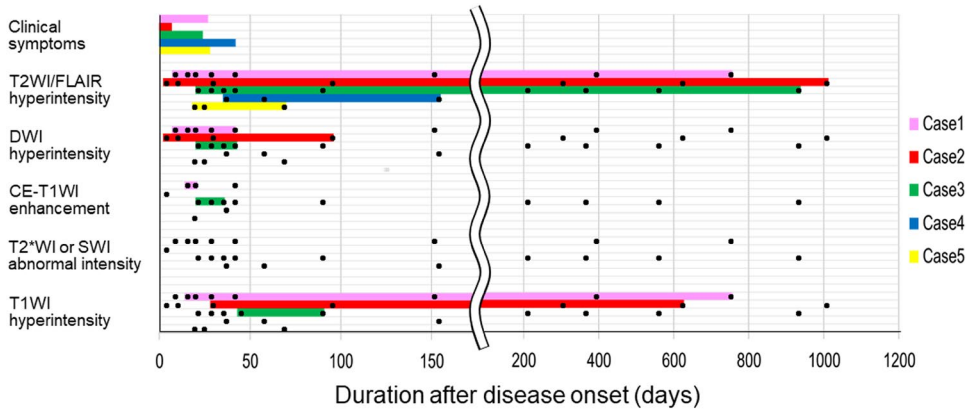

Fig. 1 Duration of clinical symptoms and abnormal intensity on MR imaging. The timings of each MR exams were marked by black circle. *WI* weighted image, *FLAIR* fluid-attenuated inversion recovery, *DWI* diffusion-weighted image, *CE* contrast enhancement, *SWI* susceptibility-weighted imaging

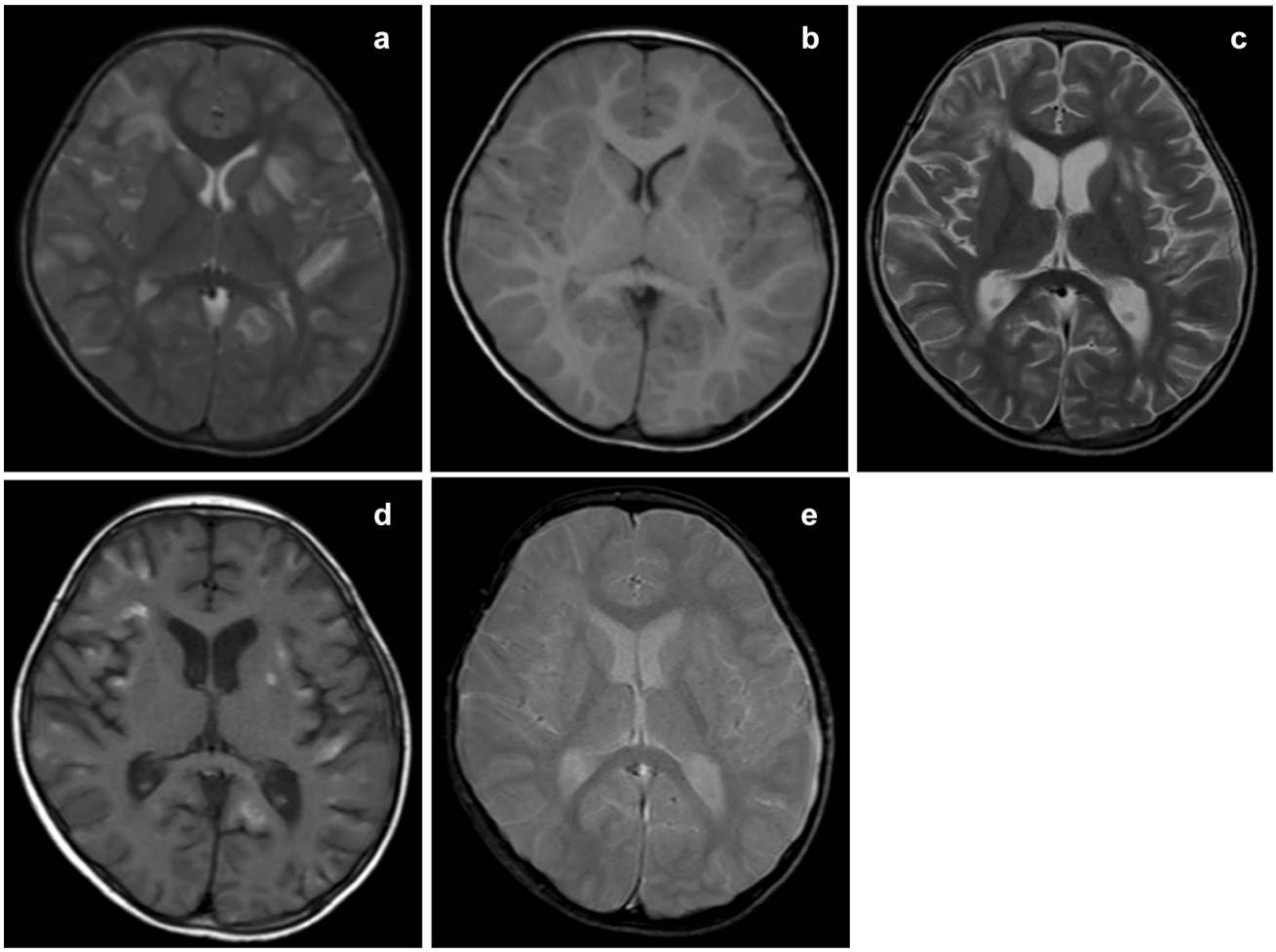

Fig. 2 Two-year-old boy with ADEM (Case 1). **a** T2-weighted image (T2WI) on admission (7 days after onset) demonstrated multifocal, hyperintense, bilateral, asymmetric lesions in the white matter. **b** T1-weighted image (T1WI) showed slightly low intensity. **c** Lesions with hyperintensity on T2WI were reduced on MRI of 27 days after onset. **d** Nodular hyperintense lesions on T1WI increased on MRI of 27 days after onset. **e** No abnormal low signal was found on T2*WI

remained even after the complete disappearance of their clinical symptoms.

Discussion

Results of this study demonstrated that appearance of T1-hyperintensity foci is not a rare finding in patients with ADEM. It was transiently observed from 14–43 days to 91–756 days after disease onset in 3 out of 5 (60%) patients.

Appearance of T1-hyperintensity foci has been known in patients with demyelinating disease such as multiple sclerosis (MS) and progressive multifocal leukoencephalopathy (PML)[10, 11]. T1-hyperintensity foci in MS is reported to reflect macrophage containing myelin and their degeneration products [12]. Similarly, T1-hyperintencity foci in in PML is reported to reflect macrophage infiltration and demyelination in addition to reactive astrocytes [11]. Therefore, T1-hyperintensity foci observed in our ADEM cases may reflect the similar pathological changes as MS and PML. In histopathological examination, macrophage infiltration and demyelination are also reported to be observed in ADEM patients [13]. Given that T1-hyperintensity foci appeared after improvement in symptoms in our study, T1-hyperintensity foci might reflect macrophage infiltration and reactive astrocytes after subsidence of inflammation-causing symptoms.

Recent studies have been suggesting that T1-hyperintensity foci can be observed at the dentate nucleus and globus pallidus in patients who received repeat contrast-enhanced MR studies using gadolinium-based contrast agents [14]. Therefore, such intracranial gadolinium deposition can be a potential cause of T1-hyperintensity foci observed in this study. However, contrast-enhanced MR studies were performed 3 times in case 1, 1 time in case 2, and no time in case 3 before the appearance of

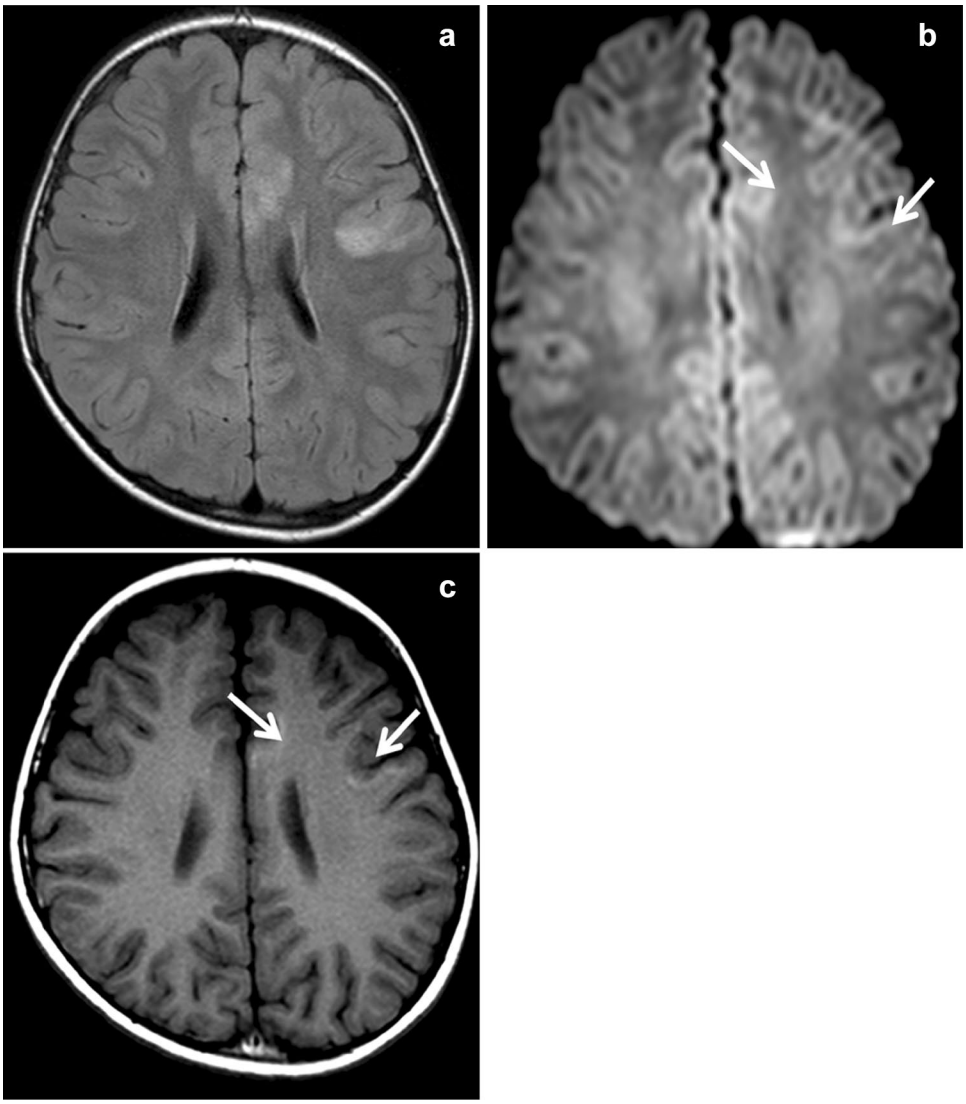

Fig. 3 Five year old boy with ADEM (Case 2). **a** Fluid-attenuated inversion recovery (FLAIR) on admission (9 days after onset) demonstrated hyperintense lesions in the cortex/subcortical white matter of left frontal lobe. **b** Diffusion-weighted image (DWI) showed hyperintensity in subcortical white matter lesion (arrow). **c** T1-hyperintensity foci appeared in subcortical matter on follow-up MRI (28 days after onset). These lesions showed linear shape (arrow)

T1-hyperintensity foci. Moreover, there was no patient showing T1-hyperintensity in the dentate nucleus in this study. Therefore, the effect of the deposition of gadolinium can be negligible in our series.

The frequencies in the appearance of T1-hyperintensity foci have been reported to be 78% and 61% in MS and PML, respectively [10, 11]. Therefore, T1-hyperintensity foci is not rare finding in MS, PML, and ADEM. As for lesion shape and location, various lesion shapes such as nodular, linear, and ring-shaped T1-hyperintensity foci can be observed in perivascular region, subcortical region, and deep white matter in MS [10]. Linear T1-hyperintensity foci are reported to be observed adjacent to subcortical region in PML [11]. In our ADEM series, nodular and linear T1-hyperintensity foci were observed in cortical/subcortical region, basal ganglia, and internal capsule. Therefore, it is important to know that T1-hyperintensity foci similar to those in MS or PML can also be observed in ADEM patients.

The retrospective nature of this study and the small patient number are fundamental limitations. Lack of histological proof is another limitation of this study, although pathological findings are unlikely to be obtained because ADEM is a clinically benign disease.

Conclusion

Transient appearance of T1-hyperintensity foci is not a rare finding (60%) and it can be observed after improvement in symptoms in ADEM.

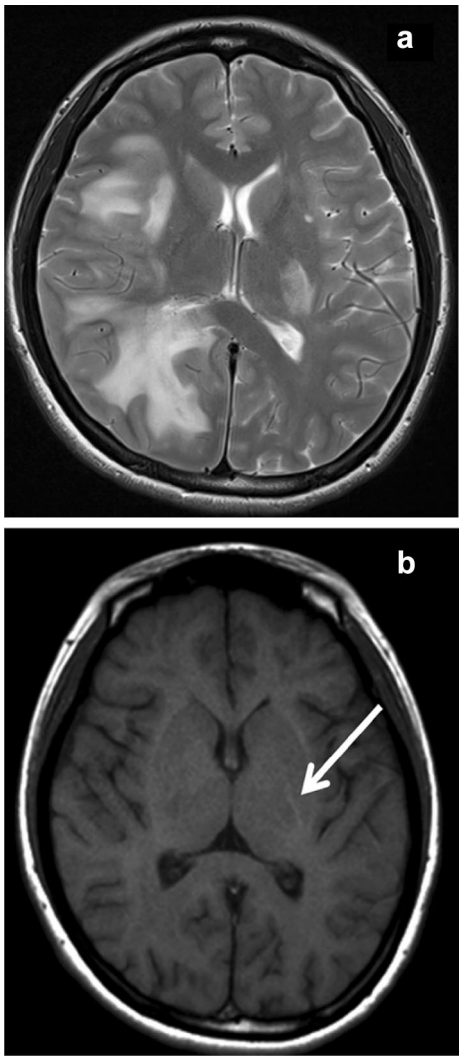

Fig. 4 Twenty-two-year-old female with ADEM (Case 3). **a** T2-weighted image (T2WI) on admission (20 days after onset) demonstrated hyperintense lesions in right hemisphere and left internal capsule or thalamus. **b** T1-hyperintensity foci appeared in internal capsule on 43 days after onset. This lesion showed linear shape (arrow)

Compliance with ethical standards

Conflict of interest No author has any conflict of interest to declare.

Ethical standards All procedures performed in this study 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.

Ethical approval This retrospective study was approved by our institutional review board.

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