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Diffusion MR findings in cyclosporin-A induced encephalopathy

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Abstract Cyclosporin encephalopathy is a well-known entity, which is clinically characterized by altered mental status, vision problems, focal neurological deficits and seizures. The exact pathophysiology of the cyclosporin encephalopathy has not yet been defined. We report the diffusion-weighted MR imaging and proton MR spectroscopy findings in a case of cyclosporin encephalopathy. The white-matter lesions with reversible restricted diffusion supported the hypothesis of reversible vasospasm induced by the cyclosporin.

Keywords Cyclosporin · Encephalopathy · Magnetic resonance · Diffusion · Spectroscopy

Introduction

The encephalopathy induced by cyclosporin is clinically characterized by altered mental status, vision problems, focal neurological deficits and seizures. The exact pathophysiology of cyclosporin-induced encephalopathy (CIE) is not yet defined, although it has been hypothesized to be multifactorial [1, 2].

We report the unusual cranial-diffusion MR imaging and spectroscopy findings of a patient with CIE.

Case report

A 34-year-old male patient had been followed with a diagnosis of hemophagocytic syndrome. Cyclosporin-A therapy had been started. Five days later, he had aphasia and weakness in the right side of his body. He had two grand mal seizures in the following 48 h. The neurological examination revealed decreased muscle strength (grade 3 on a scale of 1–5) in the right upper and lower extremities. The blood pressure was within normal

limits. The hemoglobin level was 6.1 g/dl. The blood cyclosporin level was below the therapeutic window. The cyclosporin treatment was discontinued.

Cranial MR and MR-angiography studies were performed to investigate the neurological symptoms. T2-weighted MR images revealed the patchy, hyperintense signal-intensity changes in both corona radiata. The areas which had hyperintense signal-intensity change on T2-weighted images were hyperintense on diffusion-weighted images and hypointense on the apparent diffusion coefficient (ADC) maps (Fig. 1). The calculated ADC values in these regions ranged between 57×10^{-3} and $68 \times 10^{-3} \text{ mm}^2/\text{s}$ (the normal values on the contralateral side ranged between 87×10^{-3} and $93 \times 10^{-3} \text{ mm}^2/\text{s}$). Post-contrast T1-weighted images revealed no pathological parenchymal or leptomeningeal enhancement. The calibers of the intracranial arteries were normal on MR-angiography images. Proton MR spectroscopy examination was performed to evaluate the neurometabolite levels in the lesions located in the corona radiata (STEAM; TR/TE 1500/30 ms) (Fig. 2). The integrals of metabolite peaks and then the ratios of metabolite integrals to that of creatine were calculated. The metabolite ratios were N-acetylaspartate/creatinine = 2.39, choline/creatinine = 0.71, myo-inositol/creatinine = 0.19. There was no apparent difference between the spectra and metabolite ratios of the patient and those of an age-matched control subject.

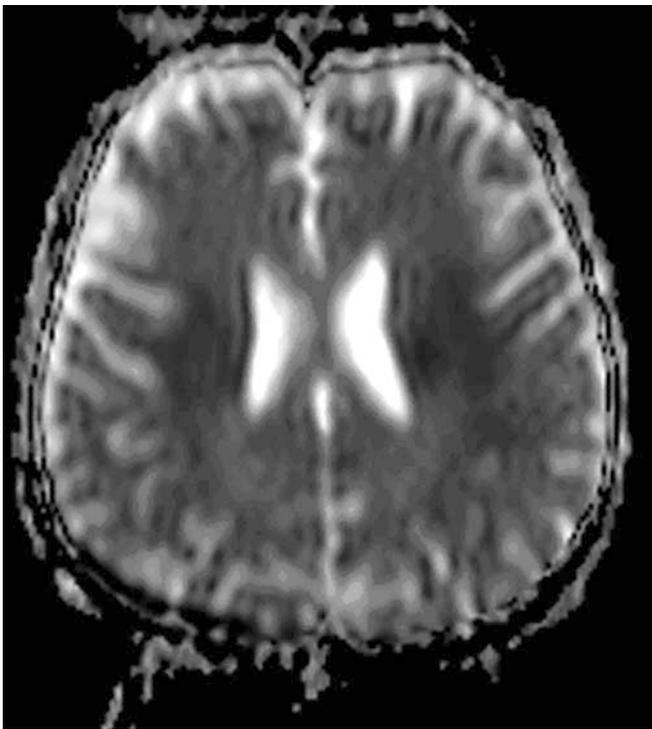


Fig. 1 ADC map image reveals the symmetrical lesions restricted diffusion in the corona radiata

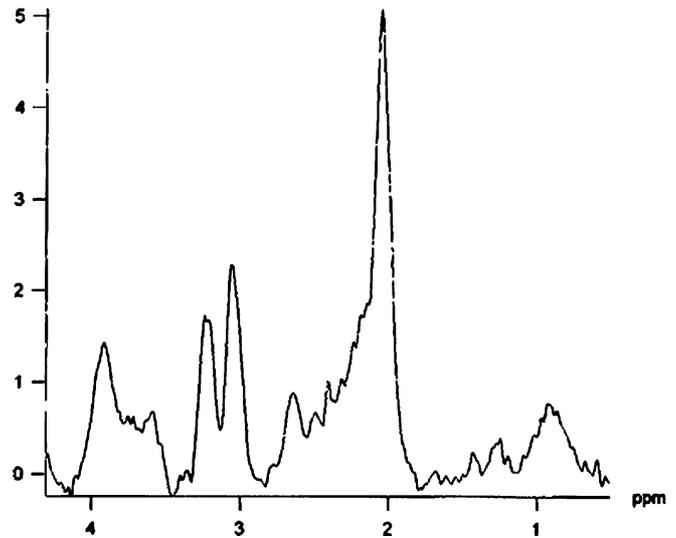


Fig. 2 Proton MR spectroscopy performed in the lesion located in the right corona radiata reveals normal spectral pattern

The neurological symptoms gradually regressed and totally resolved within 2 weeks after the cessation of cyclosporin treatment. The follow-up MR examination was performed 3 weeks after the start of cyclosporin treatment. The hypointensity of the lesions on the initial ADC maps disappeared on the follow-up images (Fig. 3). The ADC values in the corona radiata ranged between 89×10^{-3} and $94 \times 10^{-3} \text{ mm}^2/\text{s}$.

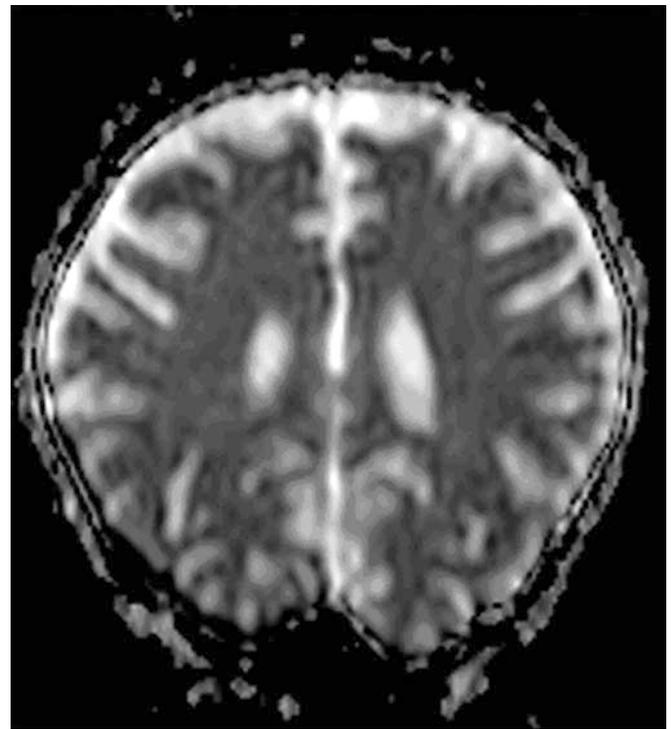


Fig. 3 The follow-up ADC map image shows the complete regression of the lesions

Discussion

The exact pathophysiology of CIE has not yet been defined, although hypertension, direct neurotoxicity, thrombotic microangiopathy, metabolic disturbances, or a combination of these factors have been proposed [2]. In two recent studies, the vasospasm of intracranial arteries was demonstrated in the patients with CIE and was suggested to have contributed to the mechanism of encephalopathy [2, 3]. Bartynski et al. reported the narrowing and irregularity due to vasospasms in the posterior cerebral arteries and T2W hyperintense lesions localized in the cortex–subcortical white matter of the occipital lobes [2]. The autopsy findings of this case showed vasogenic edema and ischemic neuronal necrosis in the watershed regions of the occipital lobes. In the other case, Lim et al. reported vasospasms in the multiple intracranial arteries and a lesion in the parietooccipital cortex–subcortical white matter which had decreased diffusion due to cytotoxic edema [3]. Although the lesions with restricted diffusion in the literature were located in the cerebral cortex and watershed regions, the lesions in our case were located in the deep periventric-

ular white matter. There was no vasospasm on the MR-angiography images of our case. The restricted diffusion in corona radiata might have been caused by the microangiopathy and vasospasm of the smaller arteries feeding white matter. There was no apparent difference in the metabolite ratios between the patient and control subject. The lack of lactate peak in the proton spectra demonstrated that ischemic necrosis did not develop in the regions with restricted diffusion. However, the lack of lactate peak could not exclude the vasospasm in our case. In a study conducted by Domingo et al., it was demonstrated that reversible vasospasm led to the production of lactate—which was apparent in the proton spectroscopy—and restricted diffusion in the brain tissue [4]. The follow-up spectroscopy and diffusion MR examinations showed that although lactate peak disappeared shortly after the cessation of vasospasm, the restricted diffusion recovered more slowly.

In conclusion, we report a reversible restriction of diffusion in an unusual location, which might be produced by reversible vasospasm induced by cyclosporin-A.

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