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Roles of neuroimage in toxic encephalopathy induced by 1, 2-Dichloroethane

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ABSTRACT

Objectives: Toxic encephalopathy induced by exposure to 1,2-dichloroethane(1,2-DCE) may result in central nervous system (CNS) abnormalities. The study was to describe the clinical and neuroimaging features in toxic encephalopathy induced by 1, 2-DCE.

Patients and Methods: The study evaluates six patients with clinical symptoms and neuroimaging who are exposed to 1, 2-DCE, including medical and neurologic examination, CT imaging, proton MR spectroscopy (MRS), Diffusion weighted MR (DW MR) and T1-and T2-weighted MR imaging. Results: All patients who had been exposed to DCE subsequently had seizures or symptoms of intracranial hypertension,including headache, nausea, and vomiting. CT findings: All lesions appeared as low density and bilateral symmetry. The lesions appeared in white matter of cerebral hemisphere diffusely, bilateral cerebellar dentate nuclei, thalamus and globus pallidus. MRI features: All lesions showed high signal intensity on T2WI. Cerebral sulci swelling and compressed or occluded ventricles were seen on CT and MRI. DW MR images obtained at b = 1000s/mm2 revealed symmetrical high signal intensity changes. The apparent diffusion coefficient (ADC) values of lesions were decreased. MR spectroscopic findings established the spectral patterns: increased choline-containing compounds and decreased N-acetylaspartate.

Conclusion: The clinical symptoms of intracranial hypertension and the features of CT and MR imagings are useful for early diagnosis and prompt treatment in toxic encephalopathy.

1. Introduction

The chemical compound 1,2- DCE, commonly known by its old name of ethylene dichloride, is a hydrocarbon. South China is one of the fastest developing regions, with many factories manufacturing products such as footwear, handicrafts and electronics including DCE. Human exposure to 1,2- DCE usually is through inhalation, skin contact or oral ingestion.Acute toxicity is frequently caused by industry accidents [1] [8]. Subacute toxicity is common than that of acute toxicity. Misdiagnoses of the subacute toxicity often occur due to the obscurity onset and the various clinical appearances. The features of CT and MR imaging patterns can be of great value in guiding the diagnostic process. In this article, CT and MR imaging findings for 7 patients of subacute toxic encephalopathy are described and analyzed in details. All of the patients were workers exposure to 1,2- DCE.

2. Materials and methods

All 7 patients were workers with experiences of occupational exposing to DCE for about 14 days to 7 years. Physical symptoms included headache and fatigue(7/7, 100%), nausea(6/7, 85.7%), vomiting (6/7, 85.7%), speech disorder(4/7, 57.1%), apathy(4/7, 57.1%), staggering (3/7, 42.9%), sleepiness(2/7, 28.6%), fuzzy vision(2/7, 28.6%), memory loss(1/7, 14.3%), weakness (1/7, 14.3%), and twitch (1/7, 14.3%). One patient with sudden coma died in E.R. 5 days after CT and MR examination. The clinical symptoms of another patient aggravated comparatively slower. However, the patient died even after receiving symptomatic treatment. The other five patients are still living with neurologic sequels.

All neurological symptoms reported were attributable to the toxic encephalopathy. The 6 female patients were examined between 5 days to 1 month after the onset of symptoms. The average age of the 6 patients was 33 (SD5.9, range 29–42) years. 5 cases were conducted with

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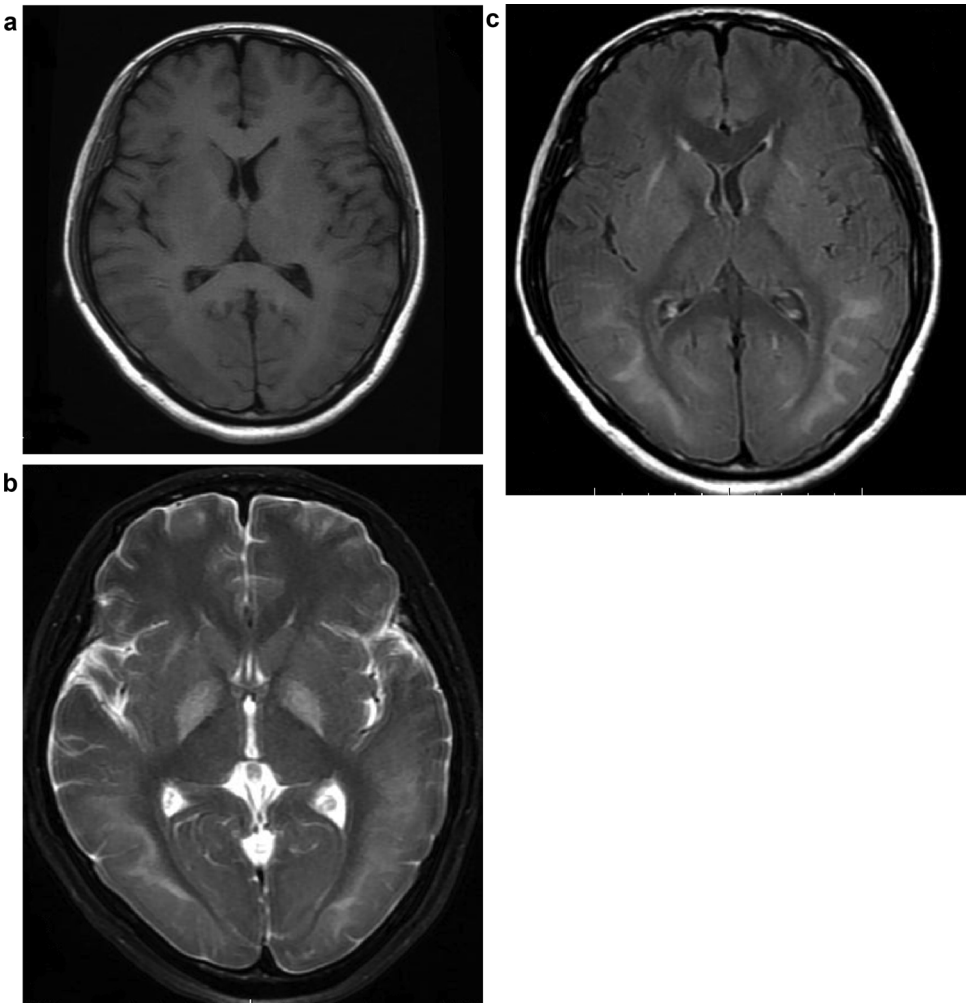

Fig. 1. A 39-year-old women with toxic encephalopathy induced by 1, 2-DCE. T1-weighted image (Aa) showed swelling gyrus and shallow sulcus in bilateral occipital lobes. T2-weighted image (Ab) showed bilaterally symmetrical hyperintensities in the globus pallidus and the posterior deep white matter. Fluid-attenuated inversion recovery (FLAIR) image (Ac) showed high signal intensity lesions in the same area. No abnormal enhancement of the lesions has found on the enhanced T1-weighted MR images (Ad).

CT examination, while 5 cases had MRI tests (explicitly, 4 cases with DW MR imaging, and 1 case with MRS). The CT and MRI features of all cases were retrospectively analyzed.

Brain CT images were obtained in the transverse plane parallel to the orbitomeatal line in 5-mm thicknesses for all sections with gapless scanning. The helical conventional method was used with a tube voltage of 120–140 kV and a tube current of 150–250 mA.

Localized proton MR spectroscopy and MR imaging were performed on a 1.5-T system. MR images were obtained using a head coil, multiplanar classic spin-echo pulse sequences, and a field of view of 21–24 cm. Axial, sagittal, and coronal T1 weighted spin echo (SE) (T1 flair, TR 2293 ms, TE 9 ms) images were obtained as well. (Fig. 1, Fig. 4a).

Axial DW MR imaging was performed (TR 4200, TE 77) on MRI axial multi-slices, which were acquired in T2 weighted SE (FRFSE, TR 4500, TE 97) with 5 mm section thickness, 2.5-mm section gap and a 256 × 192 acquisition matrix. And also, heavily diffusion weighted ($b = 1000s/mm^2$) images and automatically generated ADC maps were studied. ADC values were calculated using electronic readings from the ADC maps by variably sized circular region-of-interest evaluations (Fig. 2).

MR spectroscopy was performed by selecting a $2 \times 2 \times 2cm^3$ volume of interest area in the parietooccipital deep white matter from preliminary axial images (Fig. 3).

ointresolved spectroscopy (PRESS) and multi-voxel were used. Metabolic resonance peaks were integrated and metabolic ratios were calculated for NAA/Cho, Cho/Cre, and NAA/Cre. Then, axial and coronal enhanced T1 weighted SE images were obtained after 0.2 mmol/kg intravenous gadopentetate dimeglumine (Gd-DTPA; scans at 2–3 minutes after Gd administration) (Fig. 3b).

3. Results

3.1. CT imaging

CT showed low-density abnormalities of bilateral cerebral hemisphere in all patients including 5 with abnormalities in deep white matter, 3 with abnormalities in thalamus, 4 with abnormalities in globus pallidus, 4 with abnormalities in cerebellar dentate nucleus (Table1). All of the patients had gyrus swelling, sulcus shallowing and compression of ventricles.

3.2. MR imaging

All patients had bilateral lesions, among which the most common one was white matter, including: extensive bilateral white matter (n = 4), bilateral thalamus (n = 3), and globus pallidus (n = 4), bilateral cerebellar dentate nucleus (N = 4) (Table1). Both the

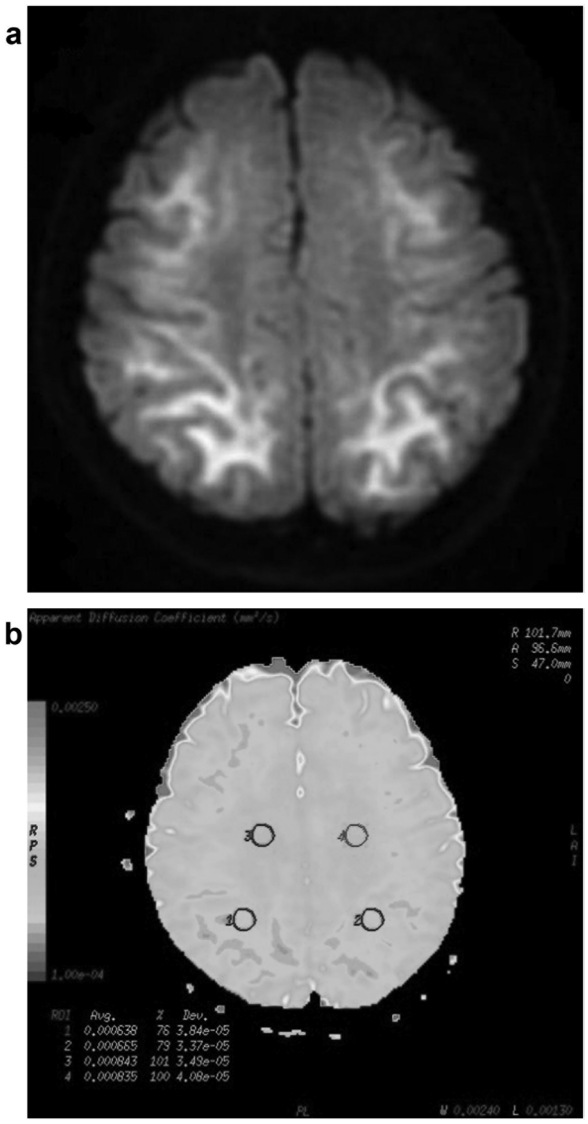

Fig. 2. Diffusion-weighted images (Ba) demonstrated bilateral symmetric lesions in the subcortical white matters. Images were obtained at b value of 1000sec/mm, consistent with restricted diffusion. The corresponding ADC images (Bb) showed lesions in the bilateral subcortical white matters.

subcortical and the deep white matter were involved. The lesions were shown with prolonged T1 and T2 relaxation times on MR images with fuzzy boundary. Consistent with CT findings, all of the patients had gyrus swelling, sulcus shallowing. Some of them also had compression of ventricles. The contrast-based axial T1-weighted MR images showed no abnormal enhancement in all lesions. (Fig. 1, Fig. 4)

3.3. DW MRI findings

DW MR images were obtained at b = 1000s/mm^2. Widespread symmetrical hyperintense changes, consistent with restricted diffusion, were evident and involved globus pallidus, the subcortical and the deep white matter in both cerebral hemispheres (Fig. 2). ADC maps revealed low ADC values ranging from 0.574 to 0.653 $\times 10^{-3}$ s/mm^2. ADC values from lesions were lower than those from the unaffected area (0.743-0.843 $\times 10^{-3}$ s/mm^2), and the surrounding cortices were normal. (Fig. 2, Fig. 4d).

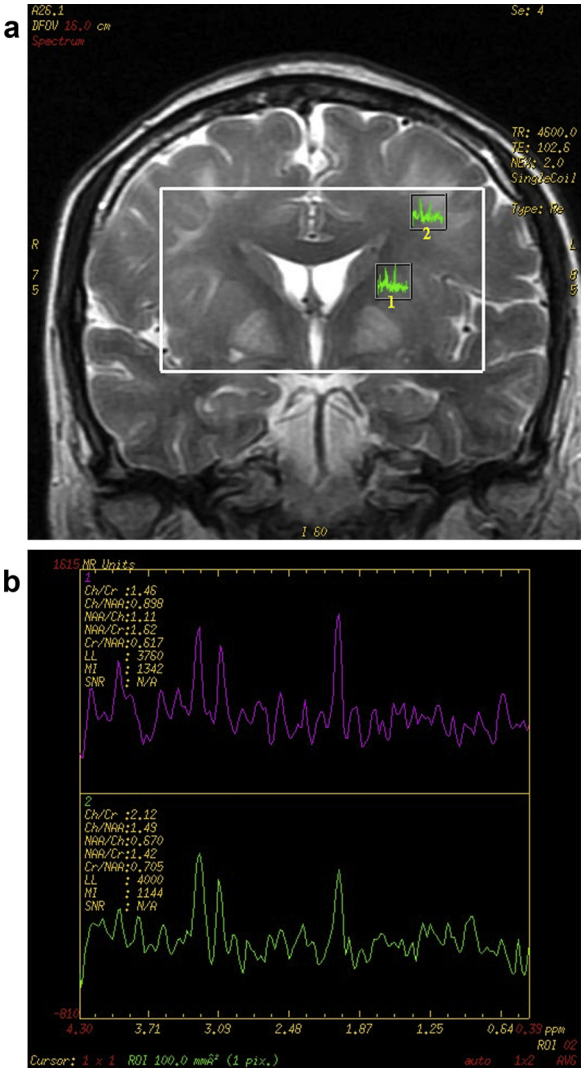

Fig. 3. MRS images (Ca) revealed increased signal intensity in lesions. Relative to the normal area(1), spectra from the lesions (2) showed slightly decreased NAA/Cr (1.42) ratios, and dramatically increased Cho/Cr ratio (2.12) (Cb).

3.4. MRS findings

The NAA/Cre and NAA/Cho ratios of lesions significantly decreased in lesions of toxic encephalopathy in comparison with normal area. Furthermore, most of the lesions were characterized by higher Cho/Cre ratios than normal area (Fig. 3).

4. Discussion

About 80% of 1,2-DCE in the world is mainly used to produce hydrogen chloride monomer (VCM, vinyl chloride) with hydrogen chloride as a by-product. It is the main component of industrial glue water and a commonly used industrial solvent. As a result, there is a high potential incidence of toxic encephalopathy for workers in these factories experiencing occupational exposure to DCE. 1, 2-DCE is toxic, especially by inhalation due to its high vapour pressure. For our patients, neurological symptoms appeared between 1 month and 7 year after exposing to DCE. One patient didn't put on a respirator when she was working while the rest five patients worked in a small factory where draught fans were not equipped.

After the incident, industrial hygiene measurements were taken in this factory and 1, 2-DCE concentration in the air was much higher than the currently adopted permissible concentration standard. With the

Table 1
Clinical characteristics and CT, MR Imaging Findings of patients with toxicated encephalopathy induced by exposure to 1, 2-DCE.

Patient	Age (yr)	Time of espousing to DCE	onset time	Symptoms	CT Imaging Findings	MR Imaging Findings	clinical outcome
1	36	7 years	15 days	Headache, fatigue, memory loss, weakness		1 lesions with prolonged T1 and T2 relaxation times and fuzzy boundary involved bilateral subcortical white matters and bilateral globus pallidus 2 gyrus slight swelling, sulcus shallowing 3 DW MR images obtained at b =1000 s/mm^2 revealed symmetrical high signal intensity changes 4 4. MRS: the lesions were characterized by decreased NAA/Cho ratios and increased Cho/Cre ratios	living with neurologic sequels
2	42	2 months	10 days	Headache, fatigue, nausea, staggering, speech disorder, apathy, sleepiness	1 low-density abnormalities in bilateral subcortical white matters, bilateral globus pallidus and cerebellar dentate nucleus 2 2. gyrus slight swelling, sulcus shallowing	1 lesions with prolonged T1 and T2 relaxation times and fuzzy boundary involved bilateral subcortical white matters, bilateral globus pallidus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing 3 DW MR images obtained at b =1000 s/mm^2 revealed symmetrical high signal intensity changes	living with neurologic sequels
3	29	3 months	1 month	Headache, fatigue, nausea, vomiting, staggering, twitch, apathy, sleepiness, fuzzy vision	1 1.low-density abnormalities in bilateral subcortical white matters, thalamus, globus pallidus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing	1 lesions with prolonged T1 and T2 relaxation times and fuzzy boundary involved bilateral subcortical white matters, thalamus, globus pallidus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing 3 DW MR images obtained at b =1000 s/mm^2 revealed symmetrical high signal intensity changes	Died
4	30	50 days	20 days	Headache, fatigue, nausea, vomiting, speech disorder, apathy	low-density abnormalities in bilateral subcortical white matters and cerebellar dentate nucleus		living with neurologic sequels
5	36	3 months	15 days	Headache, fatigue, nausea, staggering, speech disorder	1 low-density abnormalities in bilateral subcortical white matters, thalamus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing	1 lesions with prolonged T1 and T2 relaxation times and fuzzy boundary involved bilateral subcortical white matters, thalamus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing	living with neurologic sequels
6	41	45 days	5 days	Headache, fatigue, nausea, vomiting, speech disorder, apathy, fuzzy vision	1 low-density abnormalities in bilateral subcortical white matters, globus pallidus and cerebellar dentate nucleus 2 gyrus slight swelling, sulcus shallowing		Died
7	39	14days	3days	Headache, fatigue, nausea, vomiting		1 lesions with prolonged T1 and T2 relaxation times and fuzzy boundary involved bilateral subcortical white matters, thalamus, globus pallidus and cerebellar dentate nucleus. 2 gyrus slight swelling, sulcus shallowing 3 Despite the distortion of DW MR images caused by artifacts, bilateral symmetrical hyperintense lesions in the same area as T2WI could be clearly seen.	living with neurologic sequels

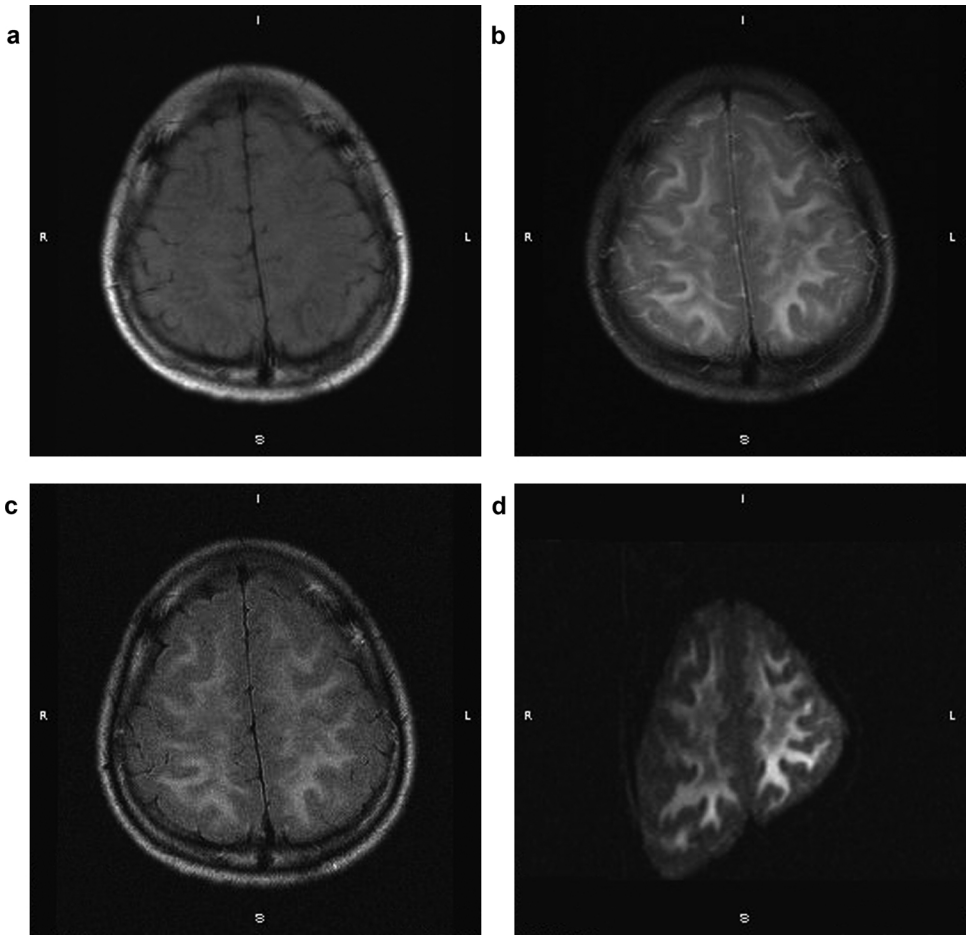

Fig. 4. A 42-year-old female worker worked in a poorly ventilated factory for two weeks. Three days later, she was hospitalized for headache, nausea and frequent vomiting. Combined with the investigation of the working environment, the final diagnosis was toxic encephalopathy induced by 1, 2-DCE. T1-weighted images (Fig. 4a) showed low signal intensity lesions with fuzzy boundary involved bilateral subcortical white matters, while on T2-weighted images (Fig. 4b) and Fluid-attenuated inversion recovery (FLAIR) image (Fig. 4c), bilateral symmetrical swelling could be seen in bilateral frontal and parietal cortex, and bilateral symmetrical high signal intensity could also be seen. Despite the distortion of diffusion-weighted images (Fig. 4d) caused by artifacts, bilateral symmetrical hyperintense lesions in the frontal and parietal lobes could be clearly seen. History combined with characteristic imaging findings was helpful for clinical diagnosis.

development of industry, 1,2-DCE resulting in a toxic encephalopathy with serious brain edema was not infrequently observed in small- and medium-sized factories in south China [12,13]. Just like many other developing countries, training in occupational health and industrial medicine is not keeping pace with the changing industrial growth and technologies in China. Poor occupational protection leads to high incidence of occupational diseases. Exposure to DCE causes CNS depression nausea, vomiting, weakness, tremor, and vertigo in our patients.

In the literature, there are several case reports of DCE toxic encephalopathy [20,6]. However, the features of CT and MR in DCE toxic encephalopathy have seldom been reported though it is important for early diagonosis of DCE toxic encephalopathy. In our study, extensive brain lesions were present in all patients as revealed by CT and MR imaging. (Table 1 and Figs. 2,3). As shown above, most of the lesions presented as low-density abnormalities with fuzzy edge on CT images. We could only confirm the lesion range according to these images, while it is difficult to have a positive diagnose. In neurology, MR imaging is considered as the “golden standard” for detecting and delineating intracranial and spinal lesions [6]. There is a report showing that examination by T2-weighted MR images appears to be superior to routine light microscopic examination in delineating the lesions induced by toxic encephalopathies in the rat brain [9]. In MR T2-weighted imaging, the verge of lesions was much clearer than that in CT imaging. The combination of T2-weighted, diffusion-weighted imaging and ADC mapping was ideal for depicting brain lesions in the early period of toxic encephalopathy in our study. The assessment of self-diffusion of molecules by DW MR techniques can provide information about microscopic tissue compartments and structural anisotropy [11,17]. Chien D et al. reported that DW MRI and ADC mapping can differentiate types of brain edema [5,22].

In our study, increased signals on DWI were observed in all the examined patients and decreased ADC values occurred in only one patient, reflecting cytotoxic oedema. Cytotoxic edema is characterized by an abnormal uptake of water by the cellular elements of the brain.The failure of Na^+/K^+-ATPase, excessive release of excitatory amino acids, and increased membrane permeability are the proposed mechanisms of cytotoxic oedema. [25,16].

Our results on 1H-MRS studies in one patient with toxic encephalopathy showed dynamic metabolic changes in brain lesions. Although the role of NAA in CNS is not well established, most researchers agree that this amino acid, located exclusively in neurons and their processes, may be a marker of neuronal viability [23]. The NAA/Cr ratio is often used as an internal standard in vivo evaluation of relative concentrations of metabolites [14,18]. It was reported that Cr is assumed to be a relatively stable brain metabolite both in normal and pathological conditions. In our study, we observed the NAA/Cre and NAA/Cho ratios of lesions significantly decreased in lesions of toxic encephalopathy in comparison with normal area. The reduction in the NAA/Cr ratio depends on a selective reduction of NAA. NAA is a neurochemical marker for mature neurons and axons, and reduced NAA is generally interpreted as indicating neuronal damage, such as stroke and dementia [7,19], or axonal injury, such as multiple sclerosis [15,24]. Furthermore, most of the lesions were characterized by higher Cho/Cre ratios than normal area in our study. Elevated Cho, which is an important constituent of membranes, is frequently observed with cerebral infarct, demyelination, and inflammation [2,3].

Though the presence of contrast enhancement might indicate more severe brain damage [26], in our study, contrast enhancement did not contribute to the detection of brain abnormalities. In our hospital, we routinely used contrast-enhanced imaging in patient who took MR

imaging with brain lesions on CT images. But we did not find any abnormal enhanced lesions. Based on our study results, we believe that contrast-enhanced imaging had no value to the early diagnosis of toxic encephalopathy induced by 1,2-DCE. (Fig. 1d)

5. Conclusion

Patients with toxic encephalopathy induced by exposure to 1, 2-DCE frequently have CT and MR imaging with abnormalities and neurologic disorders, consistent with toxic damage. Our results indicate that the combination of T2-weighted and DW MR imaging is useful for delineation the pattern of brain damage from 1, 2-DCE poisoning. A neurometabolic pattern characterized by increased Cho/Cr and deceased NAA/Cr occurs in the patient who underwent MRS examination, which could be able to detect early neuroaxonal changes providing a potential prognostic indication of clinical outcome. Detailed studies of more cases will be needed to determine the pattern of MRS in toxic encephalopathy induced by 1, 2-DCE.

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