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Case report

Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion Accompanied by Takotsubo Cardiomyopathy

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ABSTRACT

Background: Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is characterized by biphasic seizures and impaired consciousness. Takotsubo cardiomyopathy (TKC), which is typically triggered by psychological or physical stress, is characterized by transient myocardial dysfunction affecting the left ventricular apex. Recent reports have suggested that seizures can also trigger TKC. However, no cases of TKC accompanied by AESD have been reported.

Patient: A previously healthy 4-year-old girl was brought to a hospital with first-time febrile generalized tonic-clonic convulsions, which lasted approximately 40 min. After the seizure resolved, she was intubated due to respiratory deterioration. On the next day, her cardiac function deteriorated and echocardiography revealed systolic apical ballooning of the left ventricle accompanied by hyperkinesis of the basal wall, which are typical in patients with TKC. Her condition gradually improved, and catecholamine support was tapered. However, 6 days after admission, she experienced a cluster of brief convulsions. Ten days after admission, head MRI revealed lesions with reduced diffusion throughout the cortex, except in the occipital lobe, as well as perirolandic sparing. Follow-up MRI 35 days after onset revealed whole-brain atrophy, following which she developed severe cognitive dysfunction.

Conclusions: Our patient developed TKC accompanied by features of AESD. Our findings may thus provide insight into the development of TKC and prompt further studies regarding the relationship between prolonged seizures and TKC.

Key words: catecholamine; creatine kinase; status epilepticus; takotsubo syndrome; troponin-T; N-terminal pro-brain natriuretic peptide; stress

INTRODUCTION

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is characterized by biphasic seizures and impaired consciousness. After several days, secondary seizures are followed by reduced diffusion in the cortical and subcortical white matter on magnetic resonance imaging (MRI) [1-3]. Although viral infection represents the primary etiology of AESD [1], several cases associated with bacterial infection have also been reported [2,3].

Takotsubo cardiomyopathy (TKC), which is typically triggered by psychological or physical stress, is characterized by transient myocardial dysfunction affecting the left ventricular apex [4,5]. Symptoms of TKC usually resolve within a few weeks in most cases. Creatine kinase (CK), troponin, and N-terminal pro-brain natriuretic peptide (NTproBNP) levels may be elevated in patients with TKC. Furthermore, initial ST elevation can be observed via electrocardiography (ECG) in patients with TKC, dramatically shifting to negative T-waves as the condition progresses [4]. However, there are no definitive diagnostic criteria for TKC in children, likely due to the rarity of the condition and coronary heart disease in general among children.

While several recent reports have suggested that TKC can be triggered by seizures [4-6], no cases of AESD accompanied by TKC have been reported. Here, we discuss a rare case in which a 4-year-old girl developed TKC accompanied by features of AESD.

CASE REPORT

A previously healthy 4-year-old girl was brought to a previous hospital with first-time febrile generalized tonic-clonic convulsions, which lasted approximately 40 min. Initial examination revealed hemoptysis originating from the nose and mouth, while venous blood gas analysis revealed severe acidosis (pH: 6.726, pCO_2: 204.0 mmHg, lactate: 26 mg/dL). Although the seizure resolved following the administration of intravenous midazolam and thiopental, she was intubated due to respiratory deterioration. Following intravenous administration of fosphenytoin (22.5 mg/kg), she was admitted to the intensive care unit, where she received a continuous infusion of midazolam and remained on mechanical ventilation. Head computed tomography (CT) revealed slight brain edema. On the next day, she developed hemodynamic instability, and her cardiac function deteriorated (ejection fraction (EF): 34% as determined via echocardiography). As myocarditis was suspected, she was transferred to our hospital under catecholamine support (dopamine: 3 μg/kg/min, dobutamine: 3 μg/kg/min, adrenaline: 0.15 μg/kg/min).

Upon admission, she exhibited tachycardia (heart rate: 172) without abnormal

blood pressure or dilation of the pupils. Echocardiography revealed a left ventricular EF of 47%, which was accompanied by apical ballooning and hypercontractility of the basal portion (EF: 60.7%) (Fig.1). Laboratory testing revealed abnormal cardiac enzymes (CK: 428 U/L, normal range: 46-230 U/L; troponin-I: 4.59 ng/mL, normal range: ≤0.04 ng/mL; and NTproBNP: 8,669 pg/mL, normal range: ≤125 pg/mL). Therefore, she was diagnosed with TKC.

Catecholamine support was continued (adrenaline: 0.05 μg/kg/min, milrinone: 0.5 μg/kg/min), and mechanical ventilation with high positive end-expiratory pressure was required due to pulmonary edema. As we could not perform a lumbar puncture due to hemodynamic instability, vancomycin (60 mg/kg/day) and acyclovir (30 mg/kg/day) were administered in addition to cefotaxime (300 mg/kg/day). Continuous electroencephalogram (EEG) monitoring was performed, and the patient was started on levetiracetam (60 mg/kg/day), which was gradually tapered. Fortunately, her hemodynamic status gradually improved, and catecholamine support was discontinued the next day. Echocardiography revealed an improvement in cardiac function (Fig. 1). However, 6 days after admission, she experienced a cluster of brief convulsions, during which continuous EEG monitoring revealed diffuse, rhythmic, high-voltage slow activity. Intravenous midazolam was administered for seizure control. A single-dose of phenobarbital (10 mg/kg) was also administered, following which no seizures occurred. As blood cultures obtained at the previous hospital were negative, cefotaxime and vancomycin were discontinued 7 days after admission. Laboratory data revealed a dramatic improvement in cardiac enzymes (CK: 60 U/L, troponin-I: 0.05 ng/mL, and NTproBNP: 1,118 pg/mL) on the same day. Eight days after admission, she was extubated. Ten days after admission (11 days after onset), head MRI revealed lesions with reduced diffusion throughout the cortex, except in the occipital lobe, as well as perirolandic sparing (Fig. 2). Based on her clinical course, the patient was ultimately diagnosed with AESD accompanied by TKC. Acyclovir was discontinued on the same day. Seventeen days after admission, she was transferred to the previous hospital for rehabilitation. At this point, she was alert, could walk smoothly, and could eat using a spoon or fork without assistance. However, she exhibited cognitive dysfunction and could speak in single words only. Follow-up MRI 35 days after admission revealed whole-brain atrophy (Fig. 2). Although she exhibited no motor impairments and could speak in single words, she developed severe cognitive dysfunction and communication difficulties.

DISCUSSION

In the present report, we discussed a rare case of TKC followed by symptoms of AESD in a 4-year-old patient. To the best of our knowledge, the present case is the first to document a case of AESD accompanied by TKC.

Recent studies have increasingly reported an association between seizures and TKC [4-6]. In a review of 59 reports, Finsterer et al. identified 74 adult patients (age range: 18 to 82 years) with seizure-triggered TKC, most of whom were female (86%). Triggering events included generalized tonic-clonic seizures, generalized status epilepticus, and complex partial seizures in 60%, 32%, and 6.4% of cases, respectively. Outcomes were relatively good, and full recovery was reported in 97% of cases [5].

Although the underlying cause of TKC in the present case remains unclear, there are several possible explanations. First, previous studies have suggested that catecholamine excess represents the main mechanism underlying the development of TKC. Upon initial assessment, our patient exhibited hemoptysis as well as severe acidosis. Therefore, the intense physical stress caused by febrile status epilepticus itself may have triggered a catecholaminergic storm, which may have in turn resulted in myocardial apical hypokinesia. Catecholamine support was less likely to have induced TKC because the patient's cardiac condition deteriorated prior to the initiation of catecholamine support at the previous hospital.

Second, recent studies have indicated that focal epileptic activity in the temporal lobe may cause cardiac damage [7]. The temporal lobe has been associated with the regulation of autonomic function, while the insular cortex adjacent to the temporal cortex plays an important role in autonomic control of cardiac activity [6]. In our case, head MRI revealed lesions with reduced diffusion in the cortex of the temporal lobe. Thus, prolonged seizures may have damaged this region, thereby inducing cardiac damage.

Previous reports have also documented cases of transient dysautonomia or paroxysmal sympathetic hyperactivity (PSH) in patients with encephalitis or encephalopathy [8,9]. PSH is a severe dysautonomic condition that has been associated with acquired brain injuries, resulting in over-activation of the sympathetic nervous system [9]. The "disconnection" theory argues that dysautonomia of excitatory centers is due to abnormalities in higher-order control centers, while the "excitatory/inhibitory ratio (EIR) model" suggests that damage to regulatory centers in the brainstem or diencephalon releases excitatory neurotransmitters that influence spinal cord processes [10]. In the present case, we observed broad lesions throughout the cerebral cortex but not within the brainstem or lower brain levels, potentially supporting the former

hypothesis. However, no previous studies have reported an association between TKC and transient dysautonomia or PSH. Therefore, further studies are required to elucidate the relationship between TKC and PSH.

In conclusion, we described a very rare case of TKC accompanied by features of AESD. Despite our findings, further studies are required to determine the precise relationship between TKC and acute encephalopathy.

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Declaration of Conflict of Interests

The authors declare no potential conflicts of interest and received no financial support.

References

[1] Takanashi J. Two newly proposed infectious encephalitis/encephalopathy syndromes. Brain Dev 2009; 31: 521-8.

[2] Yamaguchi H, Tanaka T, Maruyama A, Nagase H. Septic Encephalopathy characterized by acute encephalopathy with biphasic seizures and late reduced diffusion and early nonconvulsive status epilepticus. Case Rep Neurol Med 2016; 2016: 7528238.

[3] Yamaguchi H, Nagase H, Ito Y, Matsunoshita N, Mizutani M, Matsushige T, et al. Acute focal bacterial nephritis characterized by acute encephalopathy with biphasic seizures and late reduced diffusion. J Infect Chemother, 2018, in press. doi: 10.1016/j.jiac.2018.04.007.

[4] Finsterer J, Wahbi K. CNS disease triggering Takotsubo stress cardiomyopathy. Int J Cardiol 2014; 177: 322-9. Review.

[5] Finsterer J, Bersano A. Seizure-triggered Takotsubo syndrome rarely causes SUDEP. Seizure 2015; 31: 84-7.

[6] Oppenheimer SM, Gelb A, Girvin JP, Hachinski VC. Cardiovascular effects of human insular cortex stimulation. Neurology 1992; 42: 1727-32.

[7] Naganuma M, Isoda K, Ishizaki M, Ito K, Hirano T, Uchino M. Epilepsy and takotsubo cardiomyopathy: a case report. Intern Med 2011; 50: 2397-9.

[8] Ichimiya Y, Kaku N, Sakai Y, Yamashita F, Matsuoka W, Muraoka M, et al.

Transient dysautonomia in an acute phase of encephalopathy with biphasic seizures and late reduced diffusion. Brain Dev 2017; 39: 621-4.
[9] Farias-Moeller R, Carpenter JL, Dean N, Wells EM. Paroxysmal sympathetic hyperactivity in critically ill children with encephalitis and meningoencephalitis. Neurocrit Care 2015; 23: 380-5.
[10] Baguley IJ, Heriseanu RE, Cameron ID, Nott MT, Slewa-Younan S. A critical review of the pathophysiology of dysautonomia following traumatic brain injury. Neurocrit Care 2008; 8: 293-300.

Figure 1.

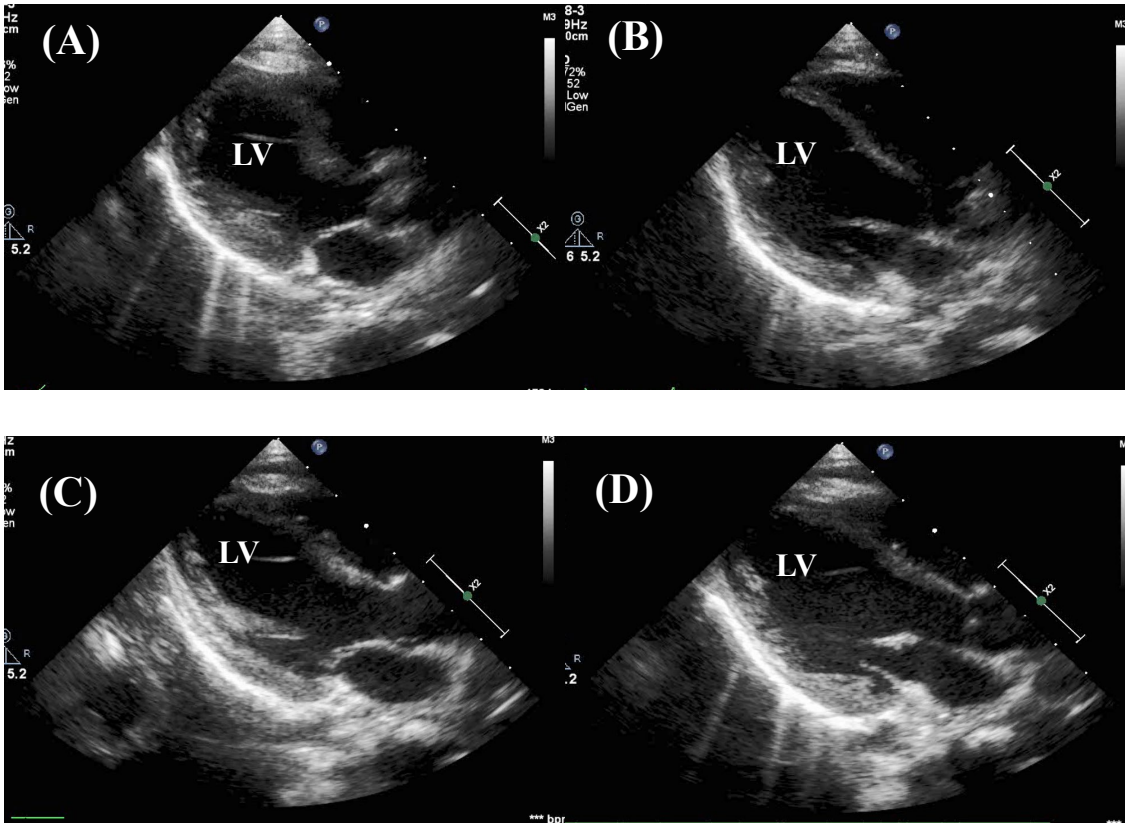

Figure 2.

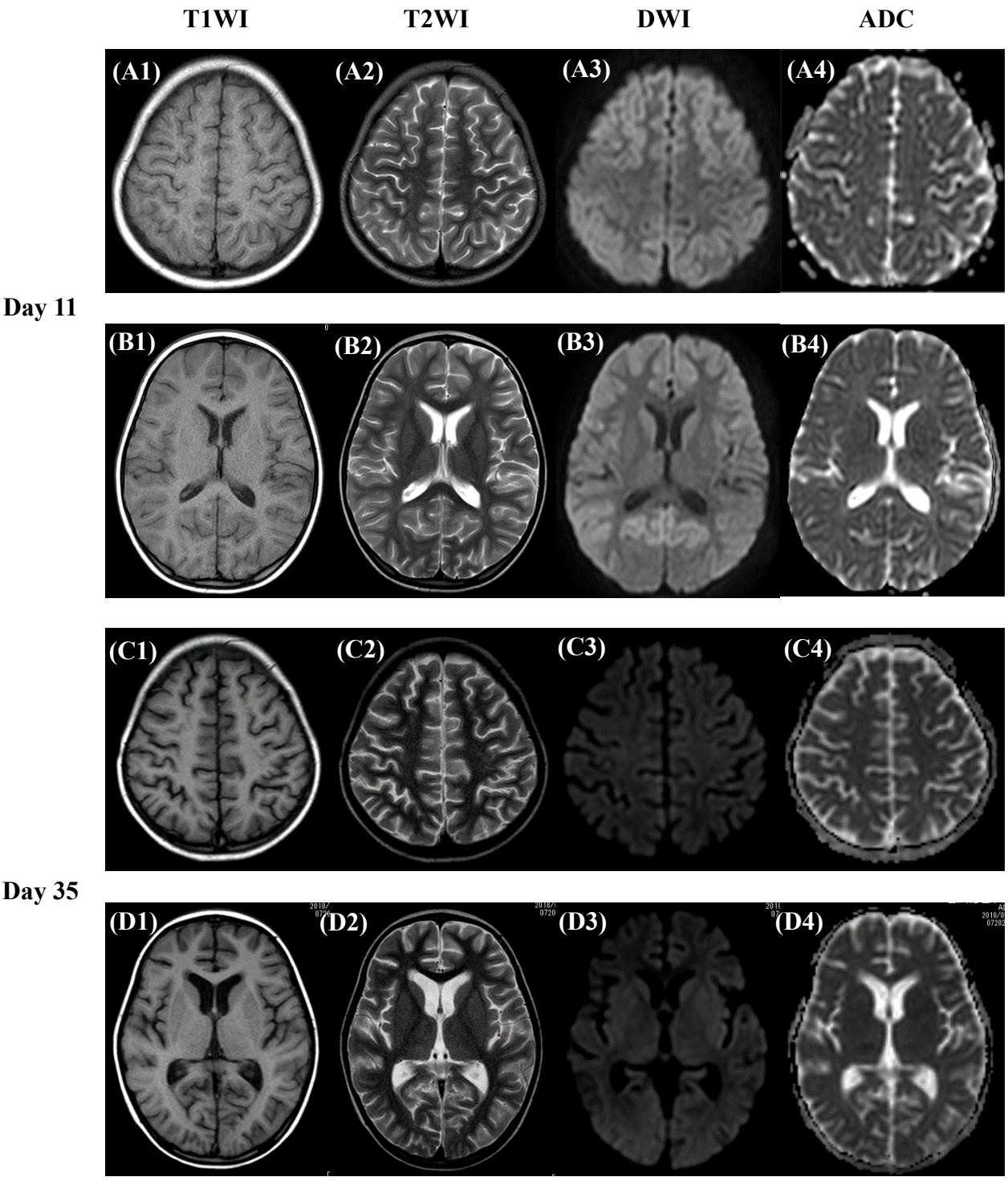
T1WI
T2WI
DWI
ADC
(A1)
(A2)
(A3)
(A4)
Day 11
(B1)
(B2)
(B3)
(B4)
(C1)
(C2)
(C3)
(C4)
Day 35
(D1)
(D2)
(D3)
(D4)

Figure legends

Figure 1. Echocardiography results during systole (A) and diastole (B). Substernal long-axis views show systolic apical ballooning of the left ventricle (LV) accompanied by hyperkinesis of the basal wall, relative to diastole. Improvements in basal hyperkinesis and apical ballooning were observed the next day (systole (C) and diastole (D)).

Figure 2. Serial cranial MRI findings (A1-B4) on admission. From left to right: T1-weighted images (T1WI), T2-weighted images (T2WI), diffusion-weighted images (DWI), and apparent diffusion coefficient (ADC) map at the parietal level (A1-A4 and C1-C4) and basal ganglia-thalamus level (B1-B4 and D1-D4). Images were obtained on day 11 and day 35. DWIs on day 11 revealed lesions with reduced diffusion throughout the cortex, except in the occipital lobe, as well as perirolandic sparing (A3 and B3). Diffuse brain atrophy was observed on day 35 (C1-D4).