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Letter to the Editor

Reversible splenial lesion in a patient with new-onset refractory status epilepticus (NORSE)

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ABSTRACT

New-onset refractory status epilepticus (NORSE) is a rare neurological emergency condition with poor prognosis. A 30-year-old male suddenly had tonic-clonic convulsions seven days after a preceding fever and diarrhea. MRI showed a reversible splenial lesion, and he developed refractory multifocal and generalized seizures in spite of anticonvulsant medication. He was diagnosed with NORSE and received a combination treatment with immunotherapy and targeted temperature management (TTM), which effectively decreased his seizures. This case suggests that even for patients with reversible splenial lesions, NORSE should be considered, and that treatment with immunotherapy and TTM may be effective.

Dear Editor,

Reversible splenial lesions of the corpus callosum have been reported in a variety of disease conditions. Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is the most common occurrence of reversible splenial lesions [1]. New-onset refractory status epilepticus (NORSE) is a rare neurological emergency condition, and manifests as antiepileptic drug-resistant refractory status epilepticus with poor prognosis [2]. Here, we report a case of NORSE that presented with a reversible splenial lesion on MRI at the disease onset and responded to targeted temperature management (TTM) and immunotherapy.

1. Case presentation

A 30-year-old man with no significant medical history visited a family doctor, complaining of 39 °C fever and diarrhea. Four days later, he was admitted to a general hospital with a severe headache. Three days after hospitalization, tonic-clonic convulsions suddenly occurred (Fig. 1A). T2 and fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) showed a high-intensity signal in the splenium of the corpus callosum (Fig. 1B). Cerebrospinal fluid (CSF) testing showed an increase in the number of cells (total 260/mm^3, neutrophils 204 vs lymphocytes 56) and the level of protein (65 mg/dl). Cultures of blood and stool were negative for any bacteria, and CSF were negative for human simplex virus in a polymerase chain reaction test. The patient was initially diagnosed with MERS and treatment with methylprednisolone pulse (1 g/day for 3 days) therapy as well as administration of anti-epileptic drugs were started. Despite the treatment, he developed status epilepticus and was transferred to our hospital on the 10th day since onset. All anti-nuclear antibodies and antibodies against Aquaporin 4 (AQP4), voltage-gated potassium channel (VGKC) and *N*-methyl-D-aspartate receptor (NMDAR) were negative. The electroencephalogram showed diffuse high-voltage slow-background activity and frequent bilateral multifocal spikes and sharp waves. Although, the splenial lesion on brain MRI had disappeared, symmetrical T2/FLAIR hyperintensities appeared in the hippocampus, amygdala, insula, claustrum, perisylvian operculum, and basal ganglia (Fig. 1C). Arterial spin labeling showed increased blood flow at the same site, which was considered to be caused by the persistent seizure activity (Fig. 1D). Multiple antiepileptic drugs were administered, but they were ineffective. Based on the patient's clinical course, we diagnosed him with NORSE.

Since treatment with intravenous immunoglobulin (0.4 mg/kg/day for 5 days) started on the day after admission did not improve the patient's condition, we started plasma exchange (PLEX). After a total of nine rounds of PLEX, his status epilepticus remarkably improved and, for a few hours, he could respond to simple instructions. Although PLEX seemed to be effective, his seizures had remitted and continued. Moreover, he had extremely high fever (> 42 °C). The patient entered a shock and disseminated intravascular coagulation state on day 29, and developed heart failure. We considered his condition an “autonomic storm”. From day 31, we used continuous hemodiafiltration, and the patient's fever decreased. We started TTM using the Arctic Sun 5000 system (Medivance, Inc., Louisville, CO, USA), with the target body temperature set at 37.0 °C. Using this temperature-control system, the patient's general condition was stabilized and convulsions were alleviated. After a total of 16 rounds of PLEX, his status epilepticus and disturbed consciousness improved. The patient was transferred to a rehabilitation hospital on day 124, and discharged home 1 1/2 months later.

2. Discussion

This case reveals two important clinical issues. First, NORSE can present with a reversible splenial lesion. Second, TTM and

Abbreviations: *, discontinued due to liver failure; **, discontinued due to granulocytopenia.; mPSL, methylprednisolone pulse; IVIg, intravenous immunoglobulin; PLEX, plasma exchange; LEV, levetiracetam; LCM, lacosamide; PMP, perampanel; KBr, potassium bromide; CBZ, carbamazepine; PB, phenobarbital; PHT, phenytoin; ZNS, zonisamide; DZP, diazepam; CHDF, continuous hemodiafiltration

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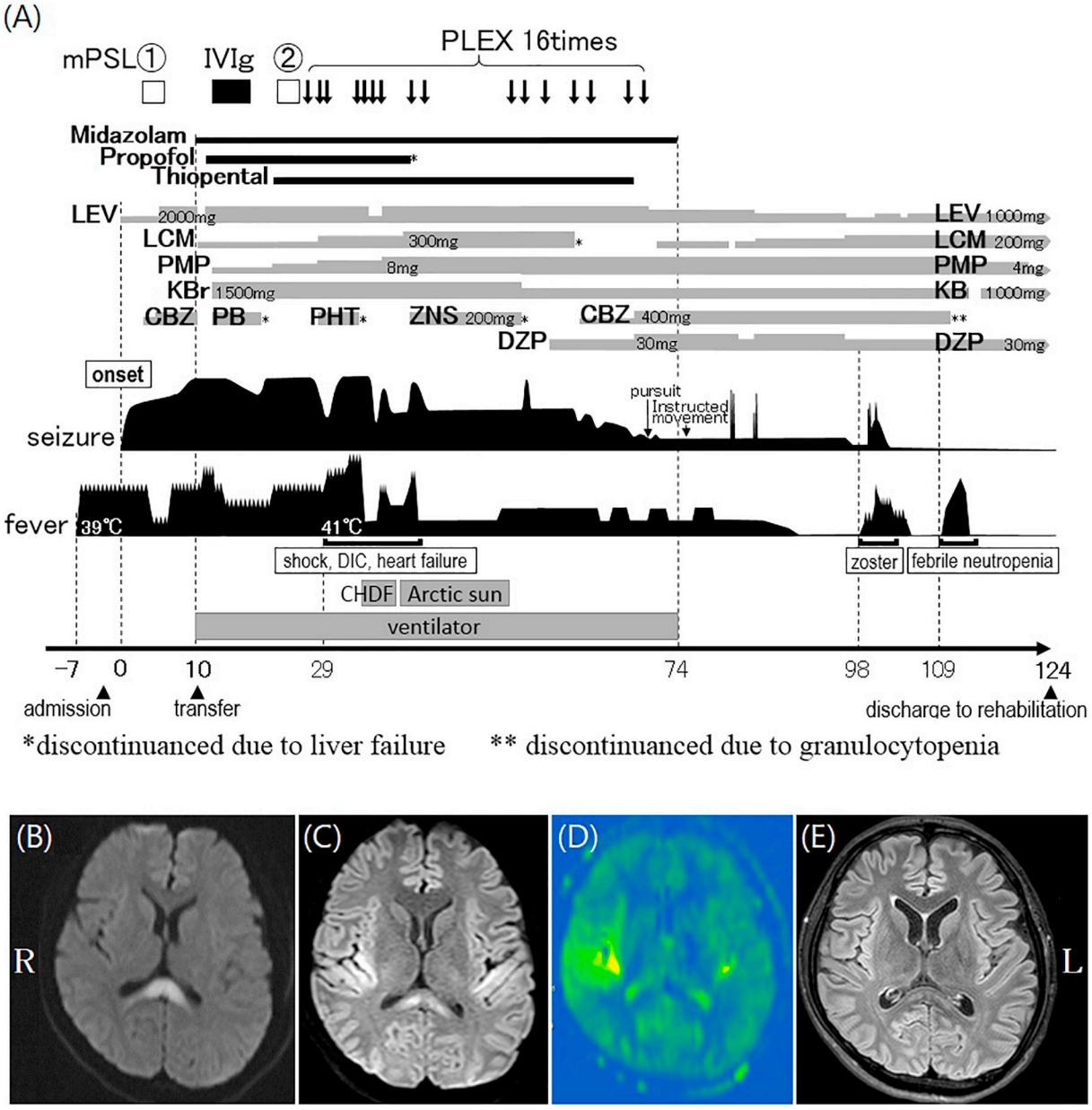

Fig. 1. (A) Timeline depicting patient admission, examination, and treatment. For further details, see main text. (B) The splenial lesion on MRI at onset. (C) Symmetric T2/FLAIR hyperintensities appeared in the hippocampus, amygdala, insula, claustrum, perisylvian operculum, and basal ganglia. (D) Arterial spin labeling showed increased blood flow at the same site, assumed to be due to the persistent seizure activity. (E) Three months after discharge, the symmetric T2/FLAIR hyperintensities disappeared.

immunotherapy are useful for the treatment of a patient with NORSE who has a high fever.

The MRI findings of a patient with NORSE can show a reversible splenial lesion. MERS is the most common cause of reversible splenial lesions [1]. Febrile infection-related epilepsy syndrome (FIRES), which is found mainly in children, is defined as a subgroup of NORSE [3]. Both NORSE and FIRES present with super-refractory status epilepticus, and have unfavorable outcomes [3]. There is one report of reversible splenial lesions in a child with FIRES [4], and there might be one case in NORSE [5]. It is unclear why splenial lesions occurred in these cases while they are not seen in many other cases of NORSE. In these cases, when the splenial lesions appeared, there were no metabolic abnormalities and no infections, and no medication had been administered.

TTM and immunotherapy may be useful for the treatment of NORSE. The etiology of NORSE is thought to be wide, and includes viral and autoimmune causes [6,7]. TTM has been reported to be useful for neuroprotection from various brain injuries [8,9]. Management of hypothermia is considered to inhibit all destructive processes at the brain injury site, such as excitotoxicity, neuroinflammation, apoptosis, and free radical production [10]. TTM has been reported as useful for children with acute encephalopathy [11]. Although the previous case reported by Mao et al. [5] showed good recovery without TTM, our case showed an obvious decrease in seizure episodes and clinical improvement of consciousness after the introduction of a combination therapy of TTM and immunotherapy.

To summarize, our case shows that a reversible splenial lesion on MRI does not always indicate mild encephalopathy, and that a TTM/immunotherapy combination might be useful for patients with high fever but no infection. Clinicians should therefore, in suspicious cases of NORSE, consider aggressive treatment including TTM and immunotherapy might.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

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