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Case Report

Reversible splenial lesion in new-onset refractory status epilepticus: A case report

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ABSTRACT

A 33-year-old man developed a generalized tonic-clonic seizure after a week of fever and fatigue. Diffusion weighted and fluid attenuated inversion recovery magnetic resonance imaging showed a hyperintense lesion in the splenium of the corpus callosum, and the lesion disappeared within a few days. The patient developed refractory status epilepticus despite treatment with multiple antiepileptic drugs. After concurrent administration of high-dose methylprednisolone, intravenous immunoglobulin, intravenous anesthetics and antiepileptic drugs, the patient achieved complete suppression of seizures. To the best of our knowledge, this is the first case of a new-onset refractory status epilepticus with a reversible splenial lesion.

1. Introduction

The term “new-onset refractory status epilepticus (NORSE)” has been used to describe previously healthy patients who develop refractory status epilepticus [1]. NORSE is currently considered a non-distinct entity and regarded as a syndrome. The causes of NORSE are not clear, but autoimmune encephalitis and viral encephalitis are considered as possible etiologies. Brain magnetic resonance imaging (MRI) in patients with NORSE often shows abnormal signal intensity in the cerebral cortex and limbic system but abnormalities in the splenium of the corpus callosum have not been reported. Here, we describe the case of a patient with NORSE presenting with a reversible splenial lesion (RSL) on brain MRI.

2. Case report

The patient was a 33-year-old man with no history of convulsions or epilepsy. He had high fever and fatigue for 1 week. He developed a generalized tonic-clonic seizure (GTCS) and was admitted to our hospital. The neurological examination revealed disturbance of consciousness and his Glasgow Coma Scale score was E1V1M5. He presented with miosis and the diameter of both papillae was 2 mm. He did not present with obvious motor paralysis. The deep tendon reflex was normal, and no pathological reflex was observed. Sensory systems were normal.

Laboratory studies showed no abnormalities except for increased white blood cell count and C-reactive protein level. Rapid antigen detection assay using a nasopharyngeal swab failed to detect the influenza virus. A lumbar puncture revealed pleocytosis of 13 cells/μL (mononuclear cells, 9; polymorphonuclear cells, 4), elevated protein level of 81 mg/dL, and normal glucose level. Anti-NMDAR antibody was not detected in the cerebrospinal fluid (CSF). Polymerase chain reaction of a CSF sample did not detect the DNA of the herpes simplex virus. No bacteria, fungi, or tubercle bacilli appeared in CSF and blood culture. Brain MRI obtained on admission day showed ovoid high-intensity signal in the splenium of the corpus callosum on diffusion weighted imaging and fluid attenuated inversion recovery imaging (Fig. 1A, B). An electroencephalogram (EEG) performed in the interictal period on the second day of admission showed background slowing, but epileptiform discharges were not observed (Fig. 2A).

After admission, the patient was administered high-dose methylprednisolone (1 g/day) for 3 days and intravenous levetiracetam to treat the seizures. Acyclovir was administered until it was confirmed that no herpes simplex virus DNA was present and that there were no pathogens in the patient’s CSF. The patient developed another GTCS on day 4, and the frequency of GTCSs gradually increased. Brain MRI performed on day 5 showed that the abnormal lesion on the splenium of the corpus callosum had disappeared (Fig. 1C, D). Despite

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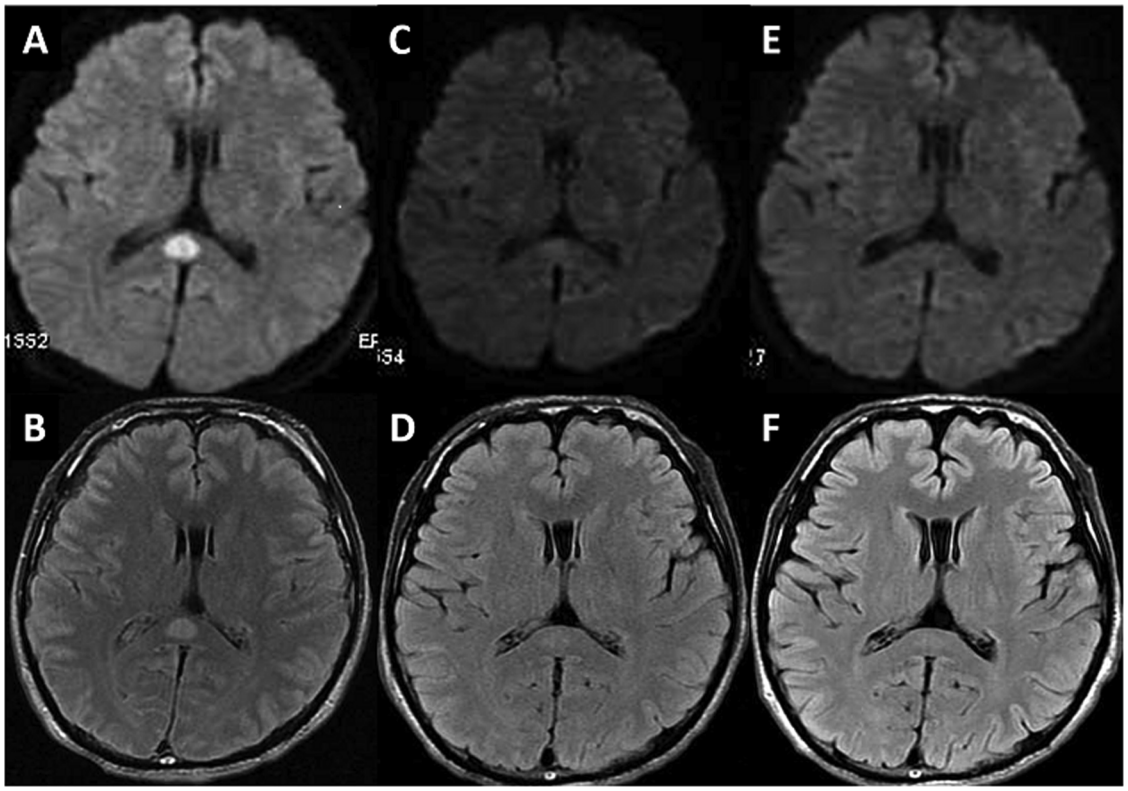

Fig. 1. Brain magnetic resonance images.
Axial diffusion weighted imaging (DWI) (A) and fluid-attenuated inversion recovery (FLAIR) imaging (B) show a hyperintense lesion in the splenium of the corpus callosum on admission day. The splenial lesion disappeared on both DWI (C) and FLAIR images (D) on day 5. Brain MRI performed on day 62 did not show any abnormal findings on both DWI and FLAIR images (Fig. 1E, F).

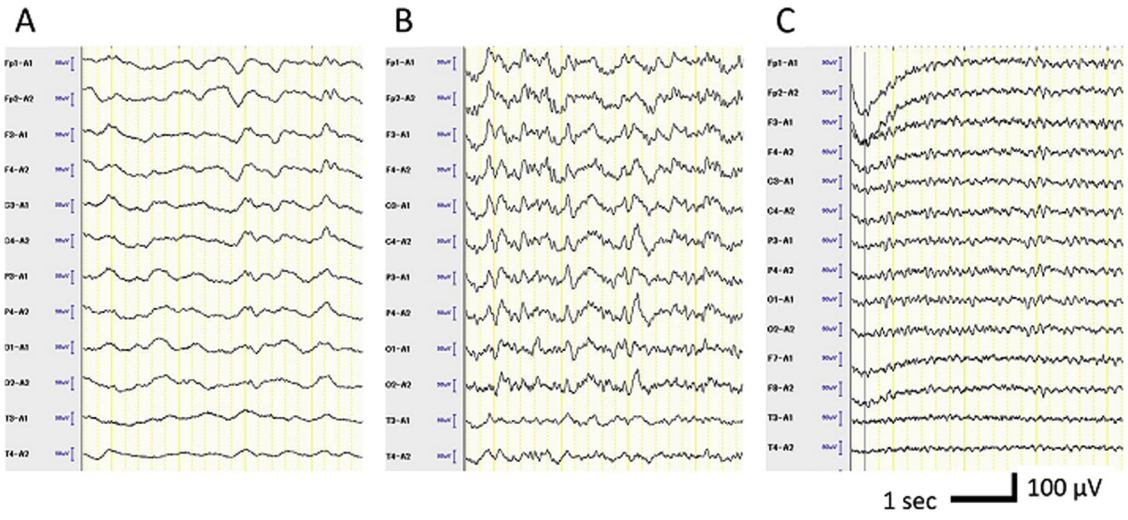

Fig. 2. Electroencephalography (EEG).
EEG performed on day 2 (A) showed slowed background activity. On EEG performed on day 17 (B), fast activity and slow activity coexisted irregularly. EEG performed 4 months after onset (C) showed normal background activity and no epileptiform discharges.

administering an adequate dose of diazepam, levetiracetam, and fosphenytoin, the patient developed status epilepticus and required intubation and respiratory support through mechanical ventilation on day 7. We initiated continuous infusion of propofol and a second course of high-dose methylprednisolone (days 7–9). On EEG performed on day 17, fast activity and slow activity coexisted irregularly (Fig. 2B). On day 19, we tried discontinuing the infusion of propofol; however, the GTCSs immediately relapsed. The patient was administered further antiepileptic drugs and intravenous immunoglobulin (IVIG, 400 mg/kg/day on days 20–24). With this regimen, the continuous propofol infusion could be withdrawn and discontinued on day 31. Respiratory support was weaned off on day 32. The patient achieved complete suppression of seizures with a combination of orally administered antiepileptic drugs (levetiracetam 3000 mg/day, phenytoin 240 mg/day, gabapentin 1200 mg/day, topiramate 200 mg/day, clonazepam 1 mg/day). After propofol infusion was discontinued, he was not able to walk without assistance because of prolonged immobilization, and he showed cognitive dysfunction especially in the memory of recent events. His motor

and cognitive functions gradually improved, and he was able to walk independently on day 47. His Mini Mental State Examination score was 17/30 on day 49 and improved to 23/30 on day 62. Brain MRI performed on day 62 did not show any abnormal findings (Fig. 1E, F). The patient was transferred to another hospital to continue rehabilitation. Though his memory disorder persisted at a moderate degree, he was able to perform his activities of daily living independently and was discharged from the hospital 3 months after the onset of the disease. On EEG performed 4 months after onset, background activity was normal and epileptiform discharge was not observed (Fig. 2C).

3. Discussion

The patient presented with acute encephalitis with disturbance of consciousness and GTCS a week after an episode of antecedent infection. The brain MRI showed an RSL. Because the results of the tests for infectious pathogens, autoantibodies, and malignancy were all negative, we could not reveal the cause of the encephalitis. Although the splenial lesion disappeared within a few days, he developed refractory status epilepticus resistant to multiple antiepileptic drugs and required intravenous anesthesia and respiratory support through mechanical ventilation. Based on the clinical course, we finally diagnosed the patient with NORSE.

RSLs may accompany viral infection and bacterial infections, metabolic disorders, and withdrawal of antiepileptic drugs, and are associated with encephalopathy/encephalitis [2]. The symptoms of encephalopathy/encephalitis with RSL include headache, vertigo, disturbance of consciousness, and convulsions, but usually the symptoms are minor and improve without neurological sequelae within a few months. A viral infection could have caused the RSL in our patient. However, he developed severe refractory status epilepticus and persistent memory disorder; his clinical course was dissimilar to that of patients with encephalopathy/encephalitis with reversible splenial lesion. An RSL was reported in a pediatric patient with febrile infection-related epilepsy syndrome, which is regarded as the same entity as NORSE [3]. However, an adult case of NORSE with RSL has not been previously reported. To the best of our knowledge, this is the first case report of a patient with NORSE with RSL. RSLs may present with more serious complications such as NORSE.

No treatment has been so far established for NORSE and is usually associated with a poor prognosis [1]. However, a few cases of NORSE treated with immunotherapy, such as steroids, IVIG or plasma exchange, achieved a favorable outcome [4,5]. Our patient achieved complete suppression of seizures and became able to perform his activities of daily living independently; thus, the outcome was relatively favorable compared to that of other cases of NORSE. The early initiation of immunotherapy may have been responsible for the favorable outcome in our patient.

4. Conclusion

We reported the case of a patient with NORSE with RSL. This report indicates that an RSL does not always indicate favorable prognosis and may result in NORSE.

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References

[1] N. Gaspard, B.P. Foreman, V. Alvarez, C. Cabrera Kang, J.C. Probasco, A.C. Jongeling, E. Meyers, A. Espinera, K.F. Haas, S.E. Schmitt, E.E. Gerard, T. Gofton, P.W. Kaplan, J.W. Lee, B. Legros, J.P. Szaflarski, B.M. Westover, S.M. LaRoche, L.J. Hirsch, Critical Care EEG Monitoring Research Consortium (CCEMRC), New-onset refractory status epilepticus: Etiology, clinical features, and outcome, Neurology 85 (2015) 1604–1613, https://doi.org/10.1212/WNL.0000000000001940.

[2] H. Tada, J. Takanashi, A.J. Barkovich, H. Oba, M. Maeda, H. Tsukahara, M. Suzuki, T. Yamamoto, T. Shimono, T. Ichiyama, T. Taoka, O. Sohma, H. Yoshikawa, Y. Kohno, Clinically mild encephalitis/encephalopathy with a reversible splenial lesion, Neurology 63 (2004) 1854–1858, https://doi.org/10.1212/01.WNL.0000144274.12174.CB.

[3] F. Nozaki, T. Kumada, T. Miyajima, T. Kusunoki, I. Hiejima, A. Hayashi, T. Fujii, Reversible splenic lesion in a patient with Febrile Infection-Related Epilepsy Syndrome (FIRES), Neuropediatrics 44 (2013) 291–294, https://doi.org/10.1055/s-0033-1348030.

[4] C.R. Gall, O. Jumma, R. Mohanraj, Five cases of new onset refractory status epilepticus (NORSE) syndrome: outcomes with early immunotherapy, Seizure 22 (2013) 217–220, https://doi.org/10.1016/j.seizure.2012.12.016.

[5] A.M. Khawaja, J.L. DeWolfe, D.W. Miller, J.P. Szaflarski, New-onset refractory status epilepticus (NORSE)–The potential role for immunotherapy, Epilepsy Behav. 47 (2015) 17–23, https://doi.org/10.1016/j.yebeh.2015.04.054.