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Encephalitis with Anti-SOX1 Antibodies Presenting with New-Onset Refractory Status Epilepticus

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Dear Editor,

New-onset refractory status epilepticus (NORSE) is a rare but critical neurologic condition characterized by the occurrence of a prolonged period of refractory seizures without a clear acute or active structural, toxic, or metabolic cause.[1] Identifying the underlying etiology is crucial for effectively managing and predicting the prognosis of NORSE. However, the cause of NORSE in approximately half of affected patients remains uncertain despite extensive investigations.[2] Herein we report the first case of encephalitis with anti-SOX1 antibodies presenting with NORSE that responded favorably to immunosuppressive therapy.

A 76-year-old man presented in an acute confusional state that had been developed several hours prior to seeking treatment. He had a history of stage IIIB squamous-cell lung cancer, which was being treated with chemotherapy (two cycles of paclitaxel/carboplatin) in combination with radiation therapy. He had no history of recent medication that might affect the mental status. On examination he had no fever, his arterial blood pressure was normal, and he was alert but disoriented. Routine blood tests and brain magnetic resonance imaging revealed no significant abnormalities. Analysis of cerebrospinal fluid (CSF) showed pleocytosis with 22 white blood cells per cubic millimeter (comprising 70% neutrophils and 30% lymphocytes) and protein and glucose levels at 199 mg/dL and 116 mg/dL, respectively, giving a CSF-to-serum glucose ratio of about 0.6. No malignant cells were identified in CSF cytology. Electroencephalography (EEG) revealed periodic and rhythmic alpha activity originating from the right medial temporal area suggestive of nonconvulsive status epilepticus (Supplementary Fig. 1 in the online-only Data Supplement) that was detected three or four times hourly.

Due to the possibility of viral encephalitis being present, he was started on intravenous (IV) acyclovir (10 mg/kg every 8 hours). IV lorazepam (0.1 mg/kg) followed by IV fosphenytoin (30 mg/kg loading dose) was additionally administered, but the condition of the patient did not improve. His clinical and electrographic seizures persisted even after further adding levetiracetam (2,000 mg/day) and pregabalin (300 mg/day), although the seizure frequency decreased to once or twice hourly. Anti-SOX1 antibodies were detected in his serum on day 7, but the findings were negative in tests for other paraneoplastic antibodies including anti-Hu, anti-Yo, anti-Ri, anti-amphiphysin, anti-CV2, anti-Ma2, anti-recoverin, and anti-titin as well as in laboratory tests for infectious agents. Computed tomography of the chest showed that his lung cancer was unchanged from the previous study. He received IV immunoglobulin (400 mg/kg/day) for five consecutive days, during which his symptoms gradually improved. Follow-up EEG after the completion of the immunotherapy did not reveal any epileptiform discharges. The patient was discharged on day 15 after his symptoms had resolved completely.

The clinical course of our patient was compatible with the recent proposed consensus definition for NORSE (Fig. 1). NORSE is defined as new-onset status epilepticus that is re-

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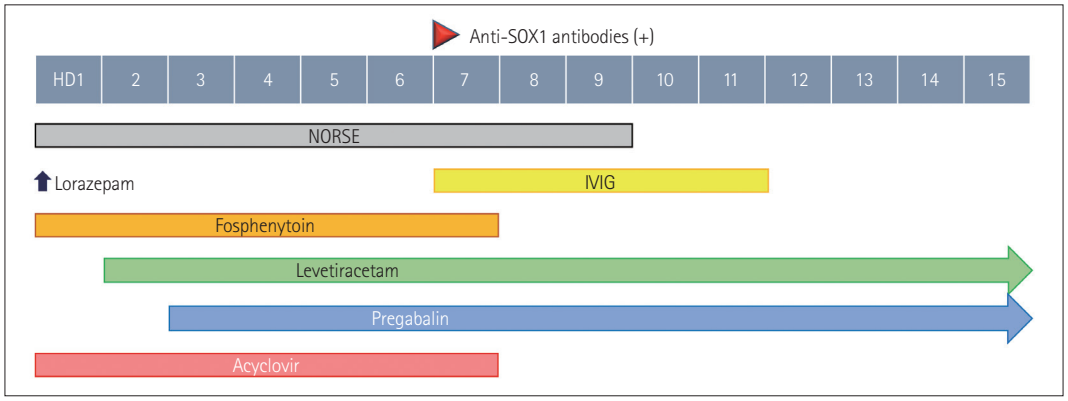

Fig. 1. Treatment timeline of the patient with encephalitis with anti-SOX1 antibodies who presented with NORSE. HD: hospital day, IVIG: intravenous immunoglobulin, NORSE: new-onset refractory status epilepticus.

fractory to appropriate doses of two or more types of antiepileptic drugs without a clear structural, toxic, or metabolic cause in patients without active epilepsy or a pre-existing relevant neurological disorder.[3] A nonparaneoplastic autoimmune or paraneoplastic etiology is the most common finding in NORSE. A large case series of 130 NORSE patients found that this condition was associated with various autoantibodies, especially anti-N-methyl-D-aspartate receptor (NMDA) and anti-voltage-gated potassium channel (VGKC)-complex antibodies.[2] However, some cases of cryptogenic NORSE showed a favorable response to immunosuppressive therapy, suggesting that there are unknown autoantibodies in NORSE.[4]

To the best of our knowledge NORSE has not been reported previously in a patient with encephalitis with anti-SOX1 antibodies, and so the present findings are the first to suggest that anti-SOX1 antibodies can be considered an associated factor of NORSE. Antibodies against SOX1 have been reported to occur in paraneoplastic neuropathy and Lambert-Eaton myasthenic syndrome.[5,6] In rare cases anti-SOX1 antibodies are related to paraneoplastic limbic encephalitis,[5] which is supported by the EEG findings of our patient. The most common type of cancer associated with anti-SOX1 antibodies is small-cell lung cancer, but other types of lung cancer have also been reported.[5,6] The titers of anti-SOX1 antibodies and anti-NMDA and anti-VGKC-complex antibodies were not tested in our patient, which may be a limitation of this study. We therefore cannot exclude the possibility that anti-SOX1 antibodies are simply a bystander. However, given that the association between non-small-cell lung cancer and anti-NMDA and anti-VGKC-complex antibodies remains unclear,[7] bias from misdiagnosis due to the presence of these antibodies is not likely to be significant.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2019.15.4.564.

Author Contributions

Conceptualization: Ryul Kim, Jin-Sun Jun. Investigation: Hee-Jin Cho, Jin-Sun Jun. Visualization: Hee-Jin Cho, Jin-Sun Jun. Writing—original draft: Hee-Jin Cho, Ryul Kim. Writing—review & editing: Ho-Won Lee, Jin-Sun Jun.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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