Archives of Epilepsy

Case Report

A Case of LGI1 Encephalitis Presenting with NORSE

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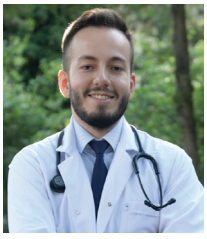

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Cite this article as: Metin G, Kamışlı Ö. A Case of LGI1 Encephalitis Presenting with NORSE. *Arch Epilepsy.* 2024;30(1):36-38

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Received: 07.08.2023 **Accepted:** 25.09.2023 **Publication Date:** 13.03.2024
DOI: 10.4274/ArchEpilepsy.2023.23093

Abstract

New-onset refractory status epilepticus (NORSE) is a rare, life-threatening clinical presentation in patients without a known history of epileptic seizures. Autoimmune encephalitis is the most common cause identified in adults; however, in up to 50% of cases, no cause can be found. We present a case of a previously healthy 26-year-old male admitted to the intensive care medicine with NORSE, whose condition improved with the initiation of immunotherapy. Later, he was diagnosed with anti-leucine-rich glioma-inactivated 1 (anti-LGI1) antibody encephalitis. Despite prompt initiation of immunotherapy, cognitive function deterioration and resistant seizures persisted. NORSE is a critical condition that requires urgent treatment. In patients with a negative initial work-up, a preliminary diagnosis of autoimmune encephalitis should be considered. It is critical to begin immunotherapy before the autoimmune encephalitis panel results, as early treatment improves outcomes and long-term prognosis.

Keywords: Antibody, autoimmune, encephalitis, leucine-rich glioma-inactivated 1, LGI1, neuroimmunology, neurology, norse, status epilepticus

INTRODUCTION

New-onset refractory status epilepticus (NORSE) is a rare but life-threatening condition. NORSE is defined as refractory status epilepticus (SE) that occurs without a known history of epilepsy and without a structural, toxic, or metabolic cause.[1]

NORSE has been reported at all ages, although it is more common in healthy young adults.[2] Although its incidence is not fully known, it is believed to constitute approximately 20% of refractory SE cases.[3] In approximately half of adult NORSE cases, the underlying cause in the etiology has not been identified, and sporadic or paraneoplastic/autoimmune encephalitis constitutes most identified causes.[2,3] In addition, rarer infectious encephalitis, genetic disorders, and toxic causes have also been reported.[4] N-methyl-D-aspartate (NMDA) receptor antibodies and voltage-gated potassium channel (VGKC) antibodies have been detected most frequently among patients with autoimmune encephalitis.[2] In this article, we present the case of a patient without a history of seizure before, who applied to our hospital with NORSE and was diagnosed with leucine-rich glioma-inactivated 1 (LGI1) encephalitis and then followed up with refractory epilepsy.

CASE PRESENTATIONS

A 26-year-old male patient with no pre-existing disease was admitted to the emergency department with a generalized tonic-clonic (GTC) seizure. Because he had a 4 GTC seizure on the same day that he did not regain consciousness, he was accepted as SE and admitted to the intensive care unit (ICU) of a different center. He had no known disease in his history; however, he had a history of upper respiratory tract infection a week ago. No smoking, alcohol, or substance use. No abnormality was found in routine blood tests, except for a slight elevated creatine kinase level. The biochemistry of the cerebrospinal fluid (CSF) of the patient was normal. No cells were observed by CSF microscopy. CSF brucella, ARB, herpes simplex virus, mycoplasma, Epstein-Barr virus, cytomegalovirus, toxoplasma, and rubella IgM tests were negative. Severe acute respiratory syndrome coronavirus 2 was also negative. When the seizures could not be controlled despite valproic acid and phenytoin loading, midazolam infusion was initiated. In addition, acyclovir was started with the preliminary diagnosis of viral encephalitis. In brain magnetic resonance imaging (MRI), T2 hyperintensity with edematous signal intensity was detected in both parahippocampal areas (predominantly in right temporal lobe); these lesions showed contrast enhancement in T1-post gadolinium MRI (Figure 1). The patient, whose seizures continued despite antiviral and anti-seizure treatments and anesthetic agents, was referred to our hospital for further examination and treatment. Immunotherapy was planned for the patient by considering possible autoimmune encephalitis. He was admitted to the ICU of our hospital, and an autoimmune encephalitis panel was sent. Pentothal infusion and intravenous immunoglobulin (IVIG) treatment at 2 g/kg for 5 days were administered. After the completion of IVIG treatment, seizures lasted, and the patient was extubate after 2 days. Generalized slow wave activity (5-6 Hz) was observed in the EEG (Figure 2). Anti-LGI1 antibody was positive because of the autoimmune encephalitis panel. He was taking levetiracetam 3000 mg/day and valproate 2000 mg/day as

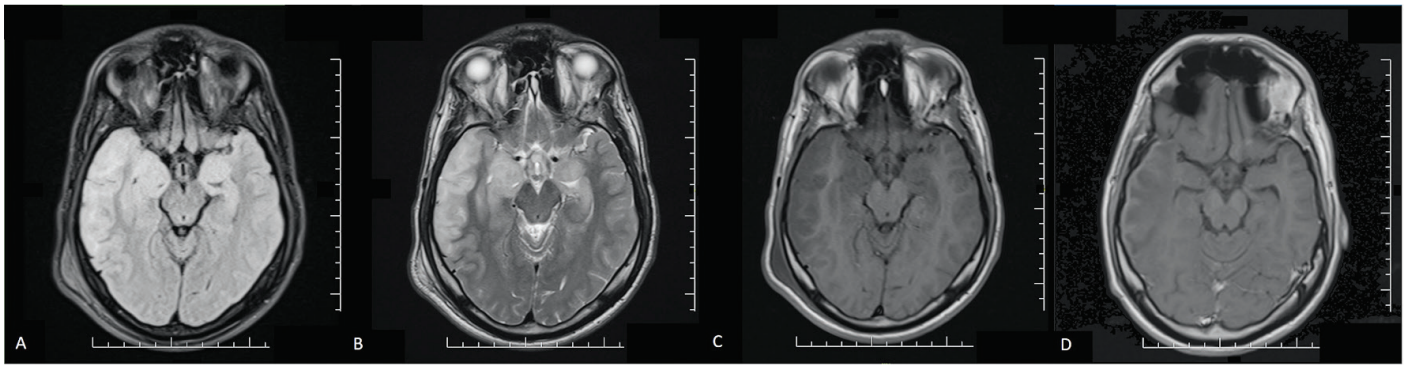

Figure 1. A-D) MRI findings of patient
MRI: Magnetic resonance imaging

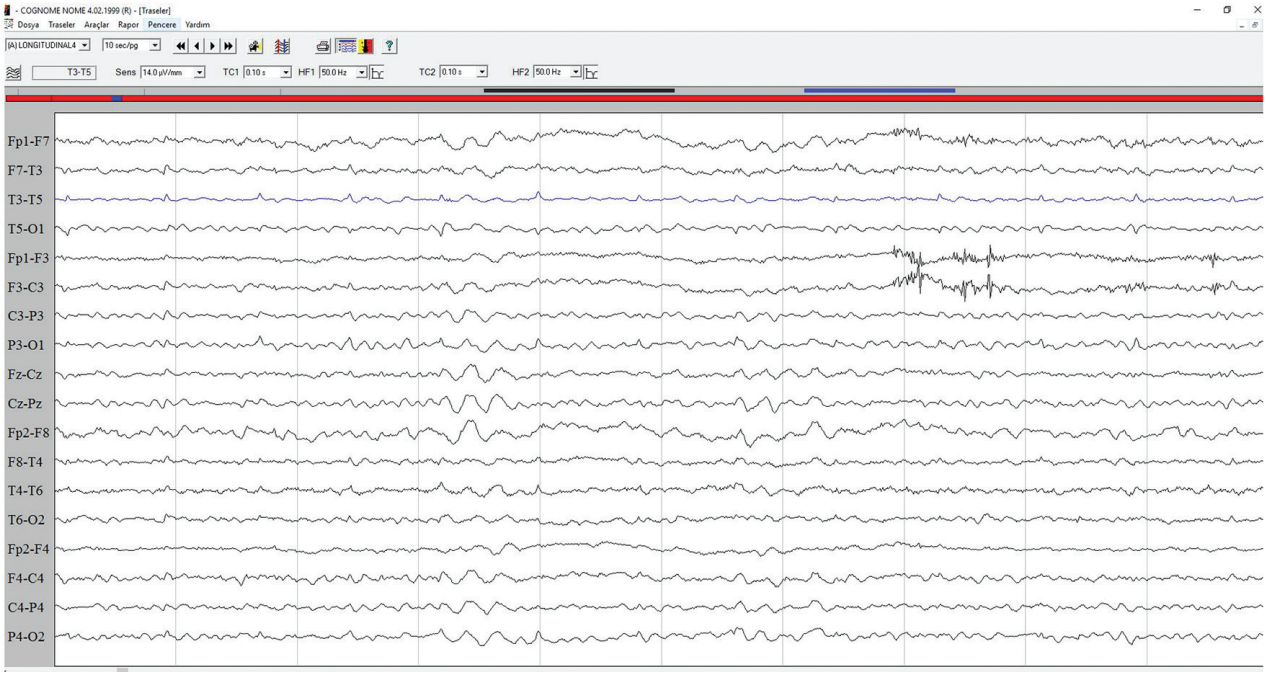

Figure 2. EEG of patient
EEG: Electroencephalography

anti-seizure medication. The patient had cognitive impairment and retrograde amnesia. The Montreal Cognitive Assessment (MoCA) test, which was conducted to evaluate cognitive functions, resulted as 18/30. The patient was also administered 1000 mg IV methylprednisolone treatment for 7 days and then continued with oral maintenance therapy. Malignancy screening was performed in terms of paraneoplastic etiology, and no malignancy was detected. The patient was discharged with a monthly single dose (0.4 g/kg) IVIG, oral steroids, and anti-seizure medications. The MoCA test, which was repeated at the 3-month follow-up, was found to be 27/30, but retrograde amnesia was ongoing. Because of the increase in the frequency of seizures and impaired cognition, rituximab treatment was initiated as second-line immunotherapy. Our patient is still being followed up with rituximab treatment, and his cognitive impairment and resistant seizures remain sequelae.

MAIN POINTS

- It's important to suspect an autoimmune aetiology in patients with refractory seizures and a negative initial work-up.
- Immune causes of seizures often respond to immunotherapy. However, they are usually resistant to antiseizure medication.
- Treatment shouldn't be delayed in patients with a suspected autoimmune cause, as early treatment can reduce disability.

DISCUSSION

NORSE is a life-threatening clinical condition defined by a new onset of refractory SE without a known cause or pre-existing neurological disorder. After extensive work-up, if no cause is found to explain the NORSE clinic, cryptogenic NORSE is mentioned and the underlying cause is not found in approximately half of the cases.[1] In the remaining half, autoimmune or paraneoplastic encephalitis is the leading underlying cause. NMDA and VGKC receptor encephalitis (LGI1 and Contactin-associated protein-like 2) are the most common autoimmune encephalitis etiologies.[1,3]

Most patients with LGI1 present with limbic encephalitis. The clinic is characterized by subacute memory, behavioral changes,

and epileptic seizures.[5] The semiological features of seizures seen in LGI1 encephalitis are well defined. Fasciobracial dystonic seizures are typical for LGI1, and they are in the form of numerous (up to hundreds) involuntary contractions lasting 1-2 s per day on the arm and face.[5,6] Early notice of these seizures, early diagnosis, and early initiation of treatment are important in terms of long-term prognosis.[5,7] In our patient, no faciobrachial dystonic seizures were observed; all seizures were GTCS. The highest frequency of SE was reported in NMDA generalized tonic-clonic seizures. encephalitis (27%) in a study investigating the semiology of seizures in autoimmune encephalitis, and in the same study, it was found to be only 6% in LGI1 encephalitis.[8] However, to the best of our knowledge, LGI1 autoimmune encephalitis with NORSE has not been reported in the literature. Hyponatremia, which is frequently reported in cases of anti-LGI1 encephalitis, was not observed in our patient.

The most affected areas in NORSE are unilateral or bilateral limbic and/or neocortical regions, basal ganglia, and periinsular areas.[2] Therefore, when these areas are affected, encephalitis and autoimmune etiology should definitely be considered. In our patient, although it was more prominent on the right side, bilateral temporal lobes and limbic structures were affected, and the preliminary diagnosis was viral encephalitis.

NORSE treatment is an important and urgent condition; treatment of seizures within the first 48 h is the same as acute treatment of refractory SE, and there is a consensus on this issue.[9] There is no specific treatment for NORSE; anti-seizure medications, anesthetics, immunotherapy, and ketogenic diet combinations can be used[4,9], and cases with early or late vagus nerve stimulation implantation have also been reported in resistant cases.[10]

The most important difference in treatment from refractory SE is that corticosteroids, IVIG, and plasma exchange are performed in first-line immunotherapy in NORSE, and it should be started in the first 72 h after the onset of SE.[1,5] If infectious causes are excluded, it is recommended to start immediately in the first 48 h.[5,9] If seizures continue despite first-line immunotherapies, it is necessary to switch to second-line immunotherapies quickly within 1 week after the onset of SE. If infectious causes are excluded, rituximab treatment is also the most commonly used second-line immunotherapy.[5]

Even if the patient recovers in the long-term prognosis, severe memory defects and resistant seizures may remain sequelae.[10,11] Therefore, treatment in the early stage is essential. In our patient, treatment was started in the ICU for 15 days with the diagnosis of refractory SE; however, after immunotherapy, deterioration in cognitive functions and resistant seizures remained sequelae.

CONCLUSION

In conclusion, autoimmune encephalitis should be considered admitted to the NORSE clinic in patients who present with NORSE, and considering the long-term results, it is important to start immunotherapy before the autoimmune encephalitis panel results. The importance of early treatment in terms of long-term effects should not be ignored.

Ethics

Informed Consent: Written informed consent was obtained from the patient for the case report.

Authorship Contributions

Surgical and Medical Practices: G.M., Ö.K., Concept: G.M., Design: G.M., Data Collection or Processing: G.M., Analysis or Interpretation: Ö.K., Literature Search: Ö.K., Writing: G.M., Ö.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

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