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Letter to the Editor

Anti-LGI1 Encephalitis Presented With Prominent Psychosis Without Loss of Consciousness

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Dear Editor,

Anti-leucine-rich glioma-inactivated protein 1 (LGI1) encephalitis is a disease having an autoimmune pathology associated with voltage-gated potassium channel (VGKC) networks.[1-3] VGKC related limbic encephalitis such as anti-LGI1 encephalitis responds well to an immunotherapy.[1,4] Faciobrachial dystonic seizures (FBDS), cognitive decline, behavioral and personality changes, and hyponatremia are main symptoms of anti-LGI1 encephalitis.[1,2,6] In brain magnetic resonance imaging (MRI), T2 hyperintensity of limbic system is usually observed.[1,6] However, early diagnosis is difficult when patients complain of psychosis that is not typical of anti-LGI1 encephalitis. Herein, we report two cases of patients with anti-LGI1 encephalitis who presented salient psychosis without focal seizures and showed marked improvement after anti-immunotherapy.

Case 1: A 65-year-old man who complained psychosis and cognitive decline occurring four months ago came to our outpatient clinic. The patient's symptoms included aggression, visual hallucinations, and delusions such as thinking that his deceased older brother was still alive and at home. In neurological examination, there were disorientations of time and place with psychotic features. In his initial Mini-Mental State Examination (MMSE), he scored 20. There was cognitive decline in orientation, frontal lobe function, and memory with impairment of activities of daily living (ADL) in Seoul Neuropsychological Screening Battery (SNSB) (**Fig. 1A**). In brain MRI, T2-fluid attenuated inversion recovery image (FLAIR) revealed diffuse hyperintensity lesions in the bilateral medial temporal lobe (**Fig. 1B**). In electroencephalography (EEG), there were intermittent generalized theta-delta activities. Laboratory tests revealed mild hyponatremia with a serum sodium level of 129 mmol/L. Tumor marker and paraneoplastic antibody tests were all negative. In cerebrospinal fluid (CSF) study, there were no significant findings except elevation of protein (white blood cell [WBC]: 3 mm^3, protein: 92 mg/dL, glucose: 81 mg/dL, virus/bacteria polymerase chain reaction [PCR]: all negative). Tests for anti-LGI1 antibody in CSF and blood tests were positive. Thus, anti-LGI1 encephalitis was diagnosed. A steroid pulse therapy for 5 days was done initially. Right after steroid pulse therapy, intravenous immunoglobulin therapy for 5 days was done. At 11 days after treatment with steroid pulse and intravenous immunoglobulin therapies, the patient's cognitive and psychiatric symptoms returned to his previous levels. In MMSE, he scored 30. No SNSB test was performed after treatment because neither the patient nor caregivers complained of any symptoms.

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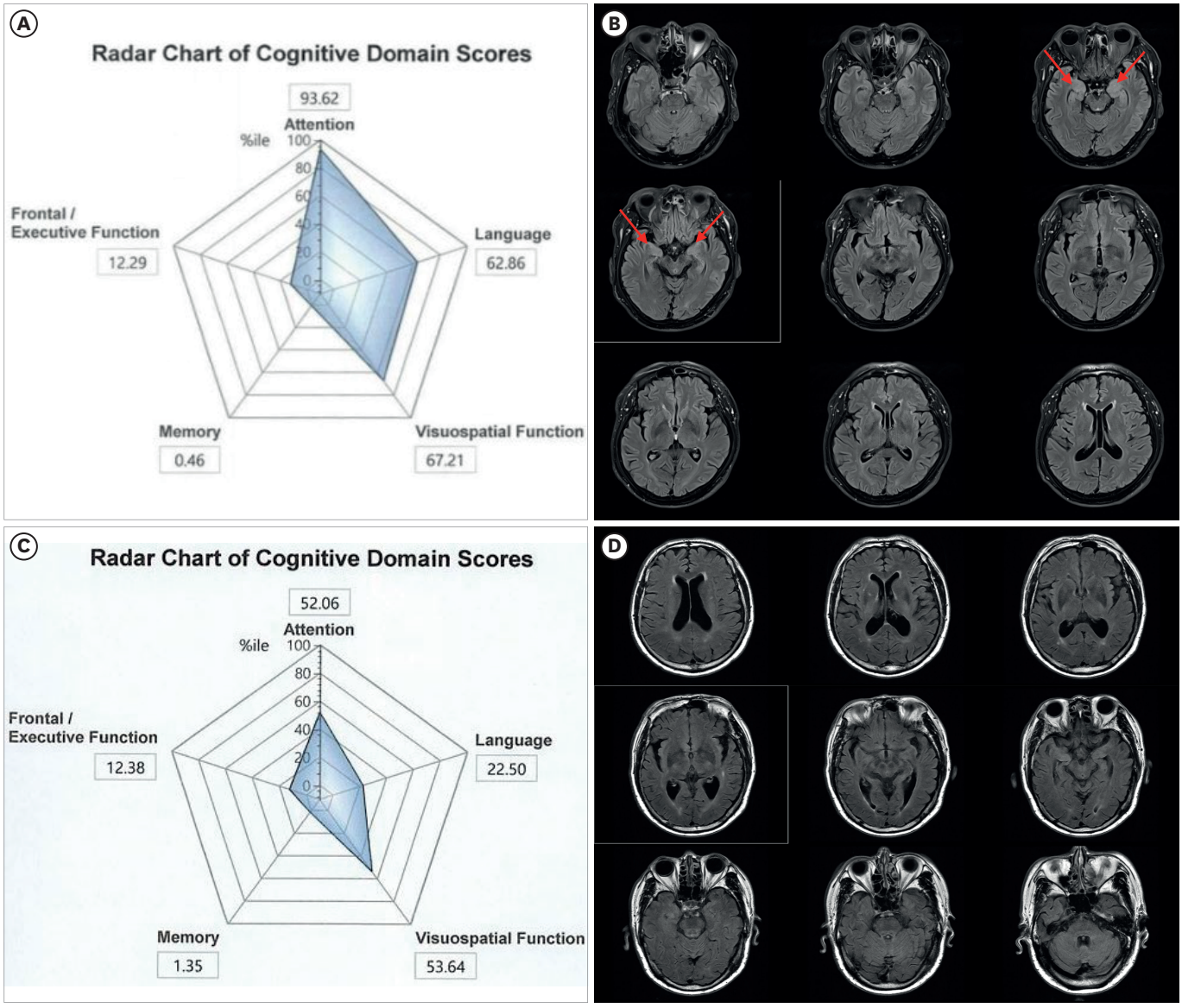

Fig. 1. SNSB and brain MRI in both cases. (A) In SNSB of Case 1, there were disorientation in MMSE (time and place), frontal lobe dysfunction in Korean-Color Word Stroop Test, and alternating hand movement test and memory impairment in Seoul Verbal Learning Test and Rey Complex Figure Test. (B) In brain MRI for Case 1, T2 FLAIR revealed diffuse hyperintensity lesions in the bilateral medial temporal lobe. (C) In SNSB of Case 2, there were disorientation in MMSE (time and place), frontal lobe dysfunction in Motor impersistence, Fist-Edge-Palm, alternating hand movement test, Controlled Oral Word Association Test and Korean-Color Word Stroop Test, memory impairment in Seoul Verbal Learning Test and Rey Complex Figure Test and naming problems in Boston Naming Test. (D) Brain MRI for Case 2 revealing no abnormalities.
SNSB: Seoul Neuropsychological Screening Battery, MRI: magnetic resonance imaging, MMSE: Mini-Mental State Examination, FLAIR: fluid attenuated inversion recovery image.

Case 2: A 75-year-old man who complained psychosis occurring four months ago visited the outpatient clinic. Symptoms of the patient were disorientation, aggression, and delusion. He thought that the reason he visited the hospital was not because he had an illness, but because of applying for a job. In neurological examination, there were disorientations of time, place, and person with psychosis. In his initial MMSE, he scored 21. In SNSB, his cognitive functions in naming, orientation, executive function, and memory decreased with impairment of ADL (**Fig. 1C**). Brain MRI revealed no abnormalities (**Fig. 1D**). In EEG, there were diffuse theta activities. Laboratory tests revealed mild hyponatremia with a

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serum sodium level of 134 mmol/L. Tumor marker and paraneoplastic antibody tests were all negative. Before visiting our outpatient clinic, he had no symptoms at all. He mainly complained of psychosis rather than memory impairment. Therefore, it was considered that rapid progressive dementia including encephalitis should be discriminated. Thus, CSF study was conducted. In CSF study, there were no significant findings except mild elevation of protein (WBC: 1 mm^3, protein: 48 mg/dL, glucose: 82 mg/dL, virus/bacteria PCR: all negative). In CSF and blood tests, anti-LGI1 antibody was positive. Thus, the patient was diagnosed as anti-LGI1 encephalitis. After steroid pulse therapy for 5 days, intravenous immunoglobulin therapy for 5 days, and rituximab therapy as first administration for 1 day, the patient showed improvement in psychotic features along with cognitive functions. In MMSE, he scored 25. Due to follow up loss, SNSB could not be implemented after treatment.

Symptoms of limbic encephalitis are mainly memory impairment, seizure, behavioral change, and personality change.[1,2,6] Among them, VGKC related limbic encephalitis is usually a reversible disease that responds well to immunotherapy.[1,4] Anti-LGI1 antibody encephalitis is the most common cause of VGKC related limbic encephalitis.[1,5] LGI1 protein is a protein in the VGKC network between presynaptic and postsynaptic terminal. It is involved in the inhibitory pathway. LGI1 protein is mainly distributed in the temporal cortex and hippocampus of the brain.[6] This is the reason why main symptoms of anti-LGI1 encephalitis are memory impairment and psychosis. Some symptoms of anti-LGI1 encephalitis, such as memory loss and behavioral changes, can be mistaken for disease states such as behavioral and psychological symptoms of Alzheimer's dementia or other types of dementia. In our cases, their psychotic features were more pronounced than typical symptoms such as seizures of FBDS and anti-LGI1 encephalitis. Psychosis and aggressive behavior can easily suggest mental disorders or behavioral and psychological symptoms of dementia. In particular, in elderly patients suffering from neurodegenerative diseases, it is necessary to differentiate psychosis from other diseases such as anti-LGI1 encephalitis. Therefore, it is essential for clinicians to perform careful history taking and appropriate diagnostic evaluation.

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