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CASE REPORT

Anti-LGI1 encephalitis preceded by psychiatric symptoms: A case report

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Abstract

Background: To date, only a few reports of anti-LGI1 encephalitis with isolated psychiatric symptoms in the initial phase have been reported. We present a relatively rare case of antileucine-rich glioma-inactivated 1 (LGI1) encephalitis that developed only psychiatric symptoms at the onset.

Case Presentation: The patient was a male in his 40s who developed anxiety and panic symptoms and was started on antidepressants after being diagnosed with panic disorder by a psychiatrist. He visited our hospital 2 months later presenting with hallucinations, delusions, mild cognitive decline, and faciobrachial dystonic seizures in the left upper extremity and face. Fluid-attenuated inversion recovery magnetic resonance imaging revealed swelling and hyperintensities in the right caudate nucleus and putamen. Cerebrospinal fluid analysis did not show increased protein levels or cell counts and revealed positive oligoclonal bands. Subsequently, positive results for anti-LGI1 antibodies were observed in the cerebrospinal fluid. Therefore, the patient was diagnosed with anti-LGI1 encephalitis.

Conclusion: This case highlights the need to consider anti-LGI1 encephalitis therapy in patients with acute-onset psychiatric symptoms.

KEYWORDS

antileucine-rich glioma-inactivated 1 encephalitis, anti-*N*-methyl-D-aspartate receptor encephalitis, autoimmune encephalitis, psychosis, seizures

BACKGROUND

Leucine-rich glioma-inactivated 1 (LGI1) is a protein specifically expressed in neurons that forms a complex with voltage-gated potassium channels.[1] Anti-LGI1 encephalitis is the second most common autoimmune encephalitis after anti-*N*-methyl-D-aspartate (NMDA) receptor encephalitis and is characterized by faciobrachial dystonic seizures (FBDSs), epileptic seizures, cognitive impairment, and hyponatremia.[1] Approximately 30%–70% of patients with anti-LGI1 encephalitis present with psychiatric symptoms, such as anxiety and psychosis.[1–3]

Approximately 70% of patients with anti-NMDA receptor encephalitis present with psychiatric symptoms, such as agitation and psychosis, at the time of initial diagnosis,[4] and approximately 4% of patients reportedly develop isolated psychiatric symptoms in the initial phase.[5] With regard to anti-LGI1 encephalitis, there are only a few reports of isolated psychiatric symptoms in the initial phase.[6–8]

Here, we report a case of anti-LGI1 encephalitis that developed with anxiety and panic symptoms, and subsequently presented with psychosis, leading to a psychiatric visit.

CASE PRESENTATION

The patient was a male office worker in his 40s. He had 14 years of education, an unremarkable clinical history, and no drug use that might have caused hallucinations or delusions. The patient visited the emergency department in December X − 1 year with chest heaviness, anxiety, and panic. Various examinations revealed no apparent physical abnormalities. There was no history of recent infection or inflammatory disease. In January X year, he visited a psychiatric clinic and was started on sertraline 25 mg/day for panic disorder. Subsequently, he developed hallucinations and delusion of observation and said, "I see a window in the air. Someone is watching us from that window." His hallucinations and delusions continued after discontinuing sertraline due to suspected drug-induced psychosis, and the patient visited our hospital in February X year. In addition to visual hallucinations and delusions of observation, he complained of "[his] body moving on its own, and being moved," reminiscent of delusions of control. Computed tomography showed no brain abnormalities, and blood tests revealed hyponatremia (131 mEq/L) with no other apparent abnormalities.

The patient's Mini-Mental State Examination (MMSE) score was 27, indicating mild amnesia due to attention deficits. Neurological examination revealed FBDSs involving the left upper extremity and face that occurred once every 3–5 min. An acute psychotic disorder or organic mental disorder, including autoimmune encephalitis, was suspected, and the patient was admitted to our hospital.

Fluid-attenuated inversion recovery magnetic resonance imaging (MRI) revealed swelling and hyperintensity in the right caudate nucleus and putamen (Figure 1a). Cerebrospinal fluid (CSF) analysis did not show increased protein levels or pleocytosis and revealed positive oligoclonal bands. Electroencephalography (EEG) did not show ictal changes, although motion artifacts were observed during seizures on the left side of the upper limb (Figure 2). Using the diagnostic criteria proposed by Graus et al.,[4] the patient was diagnosed with possible autoimmune encephalitis based on progressive psychiatric symptoms, seizures, and abnormal MRI findings. From the 6th hospital day, the patient received three courses of methylprednisolone pulse therapy at a dose of 1000 mg/day for 3 days in the neurology department, followed by oral methylprednisolone 60 mg/day, and the dose was reduced to 30 mg/day. Subsequently, CSF analysis using a commercially available fixed cell-based assay showed positivity for anti-LGI1 antibodies and negativity for anti-NMDA receptor antibodies and anti-contactin-associated protein 2 antibodies, while blood tests revealed negativity for other autoantibodies. Therefore, the patient was diagnosed with anti-LGI1 encephalitis presenting with characteristic symptoms, such as FBDSs, amnesia, and hyponatremia.[1]

After methylprednisolone pulse therapy, the abnormal MRI findings, psychosis, and seizures resolved (Figure 1b). The patient's MMSE score improved slightly to 28. In addition, the frequency of FBDSs reduced to once per day. The patient was discharged after 31 days of hospitalization without psychosis or FBDSs. Approximately 1 month after discharge, his FBDSs recurred and he was readmitted to the hospital, but no psychotic symptoms or cognitive impairment were observed. Following two courses of methylprednisolone pulse therapy at a dose of 1000 mg/day for 3 days, the FBDSs resolved,

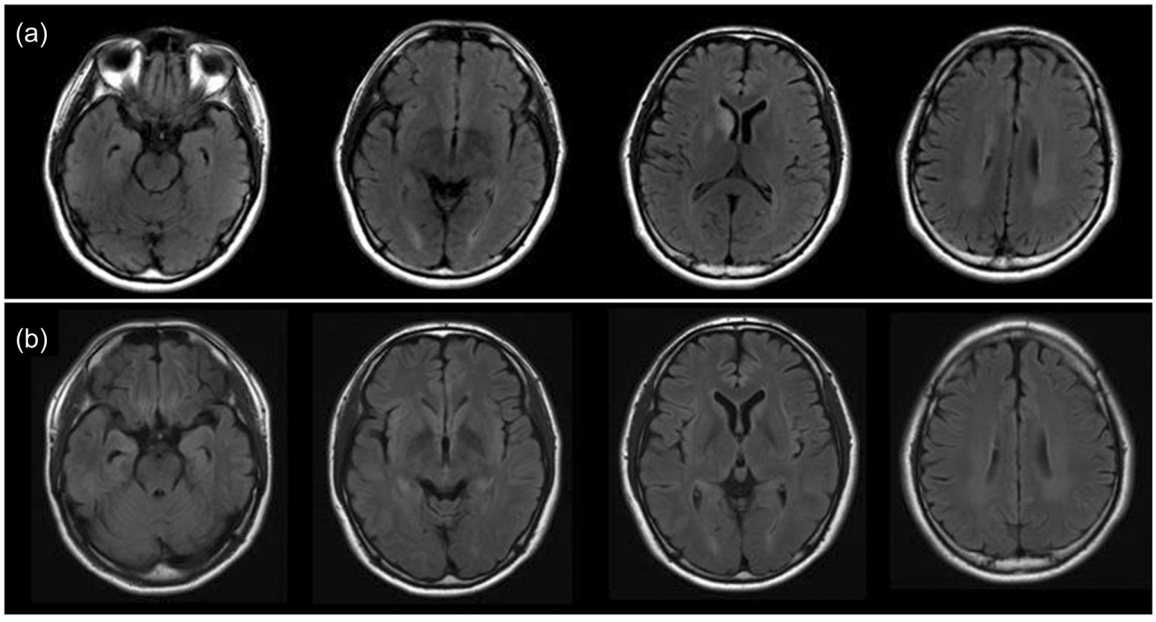

FIGURE 1 Neuroradiological findings. (a) Fluid-attenuated inversion recovery magnetic resonance imaging reveals swelling and hyperintensity in the right caudate nucleus and putamen. (b) The abnormal findings have resolved after methylprednisolone pulse therapy.

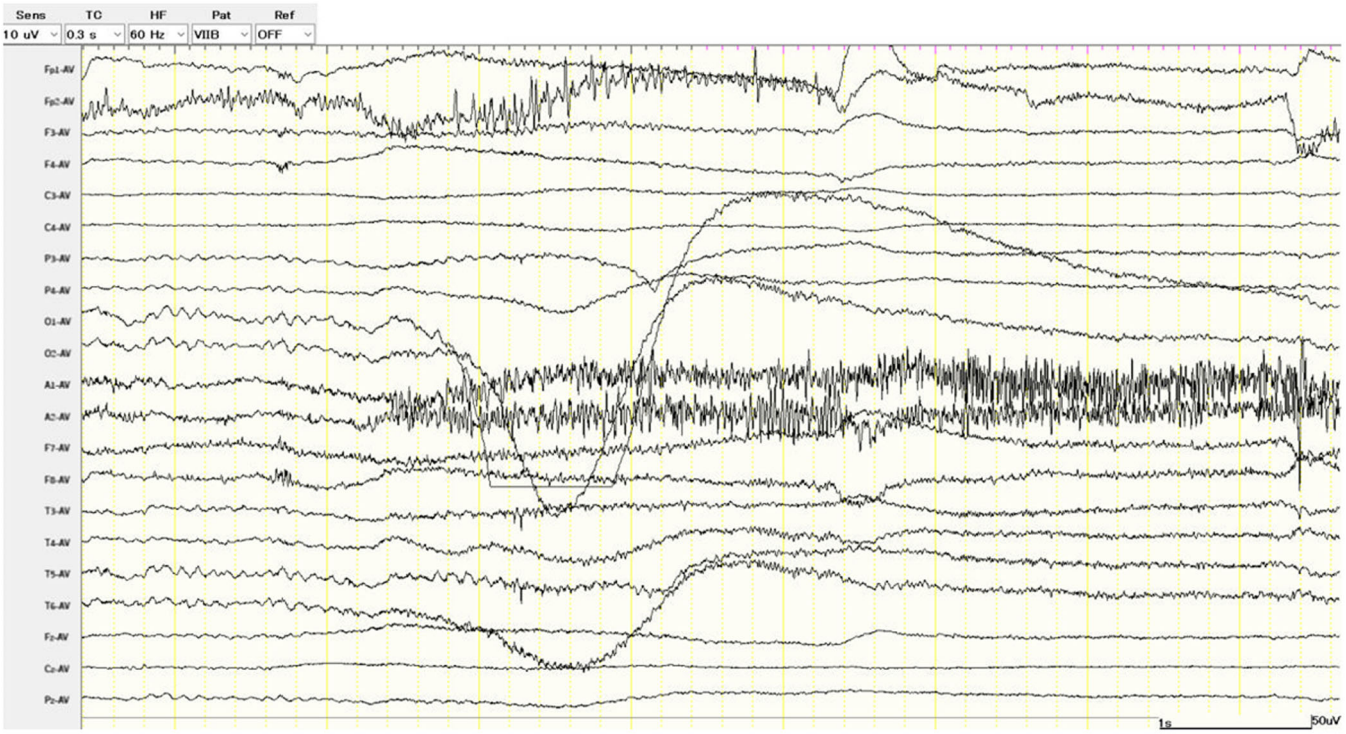

FIGURE 2 Electroencephalography findings. There are no ictal changes on electroencephalography, although motion artifacts are observed during seizures on the left side of the upper limb.

and the patient was discharged. Thereafter, he continued to take 15 mg of methylprednisolone, and his symptoms did not recur.

DISCUSSION

In the present case of anti-LGI1 encephalitis, the patient initially developed anxiety and panic symptoms and subsequently developed psychotic symptoms. In the early stage, seizures, such as FBDSs, did not appear, and the patient visited the emergency department and psychiatric clinic, where he was diagnosed with panic disorder. Although he exhibited FBDSs at the visit to our hospital, he had been experiencing only psychiatric symptoms for approximately 2 months, including anxiety, panic symptoms, and psychosis. Notably, even the symptoms of FBDSs were described by the patient in terms of delusions of control.

To date, only a few cases of anti-LGI1 encephalitis with isolated psychiatric symptoms in the initial phase have been reported.[6–8] Porpiglia et al. reported a case of a 70-year-old man who presented with isolated psychiatric symptoms, such as severe insomnia, hyperactivity, euphoria, and disinhibition, for 2 years and was diagnosed with mania.[6] Notturno et al. reported the case of a 71-year-old woman who presented with isolated psychiatric symptoms, such as agitation, irascibility, and anxiety, for several days and was diagnosed with a delusional disorder.[7] Moon et al. reported the case of a 41-year-old woman who presented with anxiety for 4 months, followed by hallucinations 6 months later, and was diagnosed with schizophrenia.[8] Taken together, the present and the previous cases indicate diversity in the characteristics, age of onset, and the duration of isolated psychiatric symptoms.[6–8]

In the present case, the main symptoms at the first visit to our hospital were hallucinations and delusions, and acute psychotic disorder was also a differential diagnosis. Anti-NMDA receptor encephalitis tends to develop more frequently in young women and is associated with tumors.[1] Therefore, such clinical information prompts consideration of autoimmune encephalitis. On the other hand, in anti-LGI-1 encephalitis, there is no extreme sex-related bias, with the proportion of male patients ranging from approximately 40% to 67%; moreover, the age of onset ranges from the teens to the 80s.[2–4,9] Therefore, if mild or no neurological symptoms, such as seizures, are present, autoimmune encephalitis may be easily overlooked. Furthermore, in patients with anti-LGI1 encephalitis with FBDSs, ictal changes may not be seen on EEG,[10,11] and FBDSS may even be misdiagnosed as psychogenic seizures.[11] In fact, the previous reports showed that patients developing isolated psychiatric symptoms in the initial phase were diagnosed with psychiatric disorders,[6–8] and there was a long interval before anti-LGI1 encephalitis was diagnosed.[6,8]

The MRI findings of anti-LGI1 encephalitis are characterized by abnormal findings in the medial temporal lobes,[1] although approximately half the cases of anti-LGI1 encephalitis accompanied by FBDSs do not show abnormal findings in the medial temporal lobes.[11] In addition, abnormal findings in the basal ganglia on MRI are associated with the onset of FBDSs.[11] In the present case, abnormal findings only in the basal ganglia could be related to the onset of

FBDSs, and mild amnesia caused by attention deficits due to dysfunction of the frontal-subcortical circuits.[12]

A limitation of this report was that the patient may have had a false-positive test result for anti-LGI-1 antibody, which was measured once before methylprednisolone pulse therapy using only CSF samples.

Patients with autoimmune encephalitis who exhibit only psychiatric symptoms in the initial phase and receive treatment based on a diagnosis of acute-onset psychiatric disease may take time to receive appropriate treatment. Psychiatrists should consider anti-LGI1 encephalitis in patients with acute-onset psychiatric symptoms.

AUTHOR CONTRIBUTIONS

Takuma Numazawa examined the patient, analyzed the data, and drafted the manuscript. Ryota Kobayashi analyzed the clinical and neuroradiological data and drafted the manuscript. Toshinori Shirata, Toshiyuki Kondo, and Hiroyasu Sato examined the patient and revised the manuscript. Keiko Tanaka analyzed the data and revised the manuscript. Akihito Suzuki encouraged the study and revised the manuscript. All the authors have read and approved the final version of this manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

ETHICS APPROVAL STATEMENT

This study was approved by the Ethical Review Committee of Yamagata University Faculty of Medicine.

PATIENT CONSENT STATEMENT

Written informed consent for the publication of this report was obtained from the patient.

CLINICAL TRIAL REGISTRATION

N/A

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