What Is Different about Teratoma-Associated Anti-LGI1 Encephalitis? A Long-Term Clinical and Neuroimaging Case Series

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Keywords
Anti-leucine-rich glioma-inactivated 1 encephalitis · Rapidly progressive dementia · Faciobrachial dystonic seizures · Diagnostic biomarkers · Teratoma

Abstract

\textbf{Introduction:} Anti-leucine-rich glioma-inactivated 1 (LGI1) encephalitis is clinically heterogeneous, especially at presentation, and though it is sometimes found in association with tumor, this is by no means the rule. \textbf{Methods:} Clinical data for 10 patients with anti-LGI1 encephalitis were collected including one case with teratoma and nine cases without and compared for clinical characteristics. Microscopic pathological examination and immunohistochemical assay of the LGI1 antibody were performed on teratoma tissue obtained by laparoscopic oophorocystectomy. \textbf{Results:} In our teratoma-associated anti-LGI1 encephalitis case, teratoma pathology was characterized by mostly thyroid tissue and immunohistochemical assay confirmed positive nuclear staining of LGI1 in some tumor cells. The anti-LGI1 patient with teratoma was similar to the non-teratoma cases in many ways: age at onset (average 47.3 in non-teratoma cases); percent presenting with rapidly progressive dementia (67% of non-teratoma cases) and psychiatric symptoms (33%); hyponatremia (78%); normal cerebrospinal fluid results except for positive LGI1 antibody (78%); bilateral hippocampal hyperintensity on magnetic resonance imaging (44%); diffuse slow waves on electroencephalography (33%); good response to immunotherapy (67%); and mild residual cognitive deficit (22%). Her chronic anxiety and presentation with status epilepticus were the biggest differences compared with the non-teratoma cases. \textbf{Conclusion:} In our series, anti-LGI1 encephalitis included common clinical features in our series: rapidly progressive dementia, faciobrachial dystonic seizures, behavioral disorders, hyponatremia, hippocampal hyperintensity on magnetic resonance imaging, and residual cognitive deficit. We observed some differences (chronic anxiety and status epilepticus) in our case with teratoma, but a larger accumulation of cases is needed to improve our knowledge base.

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Introduction

Autoimmune encephalitis (AE) is an immunopathologic encephalopathy mediated by autoantibodies. Antileucine-rich glioma-inactivated 1 (LGI1) encephalitis is characterized by rapidly progressive dementia (RPD), faciobrachial dystonic seizures (FBDS), hyponatremia, and hyperintensity of bilateral hippocampus on magnetic resonance imaging (MRI) [1]. However, “typical” clinical features above were absent in 38 anti-LGI1 encephalitis patients: only 42% (16/38) presented with RPD; 47% (18/38) suffered from FBDS; 35% (13/37) had no hyponatremia; and 26% (9/35) showed normal structural MRI [2]. Therefore, anti-LGI1 encephalitis was commonly misdiagnosed as its mimickers, including Creutzfeldt-Jakob disease [3], herpes simplex encephalitis [4], Hashimoto’s encephalopathy [5], neurodegenerative disease [6], and stroke [7].

Correlations between the presence of tumors and paraneoplastic limbic encephalitis, an important subtype of AE have been indicated. Cancer of the lung (50%), testis (20%), and breast (8%) were the three most common tumors, alongside other rarer cancers like Hodgkin’s disease (4%), ovarian teratoma (4%), and thymoma (2%) [8]. The most specific correlation is between anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis and ovarian teratoma [9]. In a descriptive clinical report including 81 anti-NMDAR encephalitis patients, ovarian teratoma was found in 56% of patients >18 years old, 31% of patients >14 and ≤18 years old, and 9% of patients ≤14 years old [10]. However, only less than 10% of anti-LGI1 encephalitis was comorbid with tumors, including thymus, thyroid, lung, and renal cell tumors [11, 12]. Even though tumors were detected in 13% of a series of 166 patients with LGI1 IgG positivity [13], to our best knowledge, no correlation between teratoma and LGI1 encephalitis has been reported.

Here, we report a case of anti-LGI1 encephalitis comorbid with teratoma; pathological association was indicated by immunohistochemistry, and partial or focal positive nuclear staining of LGI1 was appreciated in some tumor cells. The patient has been followed for 18 months, and the clinical features of this rare case to nine anti-LGI1 encephalitis cases without teratoma were also summarized and compared to facilitate the accurate and early diagnosis of anti-LGI1 encephalitis, to improve our clinical acknowledgement of anti-LGI1 encephalitis, especially with teratoma.

Materials and Methods

Clinical Data

Ten patients diagnosed with anti-LGI1 encephalitis (one with ovarian teratoma and nine without) between January 2013 and July 2019 were included. Data were abstracted from patient records, including age of onset, symptoms at onset and during disease course, serum sodium levels (normal range 136–145 mmol/L), glucose (normal range 3.9–6.1 mmol/L), thyroid function indexes thyroid-stimulating hormone (TSH) (normal range 0.35–4.94 µU/mL), free triiodothyronine (FT3) (normal range 1.71–3.71 pg/mL), free thyronine (FT4) (normal range 0.70–1.48 ng/mL), rheumatic antibody detection, immunity assay, cerebrospinal fluid (CSF) results, AE antibody panel (NMDA, LGI1, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid 1 [AMPA1], AMPA2, gamma-aminobutyric acid-B [GABA_B], contactin-associated protein 2 [CASPR2]) of serum and CSF, presence of comorbid tumor, MRI, electroencephalography, neuropsychological assessment, response to therapy, and clinical course.

For neuropsychological assessment, we used the following evaluation scales: (1) Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA): cognitive impairment was determined when the score was under 26 and 24, respectively; (2) Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD): anxiety or depression was considered while the score was equal or over 7 and further divided to mild (7–14), moderate (14–21), and severe (>21); (3) modified Rankin Scale (mRS).

For CSF results, we defined normal as cell count <8 cells/mL, protein level ≤0.30 g/L, glucose normal range 2.22–3.89 mmol/L. For onset, we defined acute within 2 weeks, subacute as 2 weeks to 2 months, and chronic as >2 months for the time from onset to peak.

Neuroimaging Scanning Protocol

All MRI sequences were performed on the 3.0-T MR scanner (Discovery MR750, GE Healthcare, Milwaukee, WI, USA) with a 32-channel phased-array head coil. All subjects underwent a standard structural brain scan and detailed scanning protocol has been stated in our published work [14].

Pathological and Immunohistochemistry Examination of Ovarian Teratoma Tissue

The teratoma tissue was fixed by 4% paraformaldehyde, embedded by paraffin, and sliced using a microtome. Immunohistochemical analyses were performed using a rabbit polyclonal antibody against LG1 (diluted 1:200, BIOSS, Beijing, China). The immunostaining protocol for LG1 detection was described previously [15]. The study was approved by our Committee on Human Research, and all patients signed informed content to participate.

Results

Clinical Presentation of Anti-LGI1 Encephalitis with Teratoma

The patient was a 48-year-old woman with past medical history of nodular goiter and abdominal mass. She...
began to suffer from anxiety 6 months prior to diagnosis and has been treated with anxiolytics with no effect and with gradual deterioration. In the 2 months prior to admission, she had been hyperglycemic, and for the prior month had suffered from short-term memory dysfunction and drowsiness.

She was transferred to the neurology department because of cognitive impairment from the endocrinology department once glucose control was established. The patient frequently forgot whether she had taken her medication, where her bed was located, and who had visited her. MMSE was 13 (shown in Table 1), and she could not complete the MoCA because of irritability. Laboratory data confirmed slightly decreased sodium level of 135.4 mmol/L, increased glucose level (12.48 mmol/L), but normal thyroid function indexes (TSH, FT3, and FT4), anti-thyroid antibodies (thyroglobulin antibody, thyroid peroxidase antibody, and thyrotropin receptor antibody), blood routine tests, urinalysis, liver and renal function, myocardial infarction markers, coagulation functions, and rheumatic antibody detection results and immunity results. On day 6 after admission, lumbar puncture was performed with normal routine and biochemical testing results. AE antibody panel of serum and CSF was performed. On day 7, she developed visual hallucinations, showing diffuse slow waves on electroencephalography and bilateral hippocampal hyperintensity on T2-weighted imaging/fluid-attenuated inversion recovery (T2WI/FLAIR) (shown in Fig. 1). Methylprednisolone (200 mg/day) was given immediately.

On day 8, she was transferred to intensive care unit because of convulsive status epilepticus (SE) for 20 min unresponsive to diazepam (10 mg i.v.) twice and phenobarbital (200 mg I.M.). Endotracheal intubation was followed by antibiotic therapy, midazolam, fentanyl and levetiracetam (LEV) initially followed by LEV monotherapy once she had been seizure-free for 24 h. The diagnosis of anti-LGI1 encephalitis was confirmed by positive antibodies both in serum (1:32) and CSF (1:3.2). Considering her hyperglycemia and seizures were controlled, methylprednisolone was maintained at 200 mg/day with combined intravenous immunoglobulin (0.4 mg/kg/day, i.v.) 5 days).

On day 13, she returned to the neurology ward with cognitive impairment, visual hallucinations, irritability, and seizure-free. On day 25, the patient could answer simple questions and complained of stomachache (right lower quadrant). Abdominal computed tomography indicated a possible teratoma. Gynecologic oncologists recommended elective surgery after encephalitis was stable.

| Scales | Time after admission |
|--------|---------------------|
|        | day 6 | day 32 | month 3* | month 4 | month 5 |
| MMSE   |        |       | 26      | 24     | 27      |
| Total  | 13     | 19    | 26      | 24     | 27      |
| Orientation | 5 | 7    | 10      | 9      | 9       |
| Memory | 2      | 3     | 3       | 3      | 3       |
| Attention and calculation | 2 | 1    | 1       | 1      | 5       |
| Recalling | 0 | 0    | 3       | 2      | 1       |
| Language | 4 | 8    | 9       | 9      | 9       |
| MoCA   |        |       | 28      | 29     |         |
| Total  | N/A    | 20    | 24      | 28     | 29      |
| Visuospatial and executive function | N/A  | 4     | 5       | 5      | 5       |
| Naming | N/A    | 3     | 3       | 3      | 3       |
| Attention | N/A | 4    | 4       | 4      | 6       |
| Language | N/A  | 3     | 3       | 3      | 3       |
| Abstraction | N/A | 2    | 1       | 2      | 2       |
| Delayed recall | N/A | 0    | 2       | 5      | 4       |
| Orientation | N/A | 4    | 6       | 6      | 6       |
| HAMA   | 8      | 2     | 4       |        |         |
| HAMD   | 12     | 0     | 3       |        |         |

N/A, MoCA was not performed because the patient was too irritated. MMSE, Mini-Mental State Examination; MoCA, Montreal cognitive assessment; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; BI, Barthel Index; ADAS-Cog, Alzheimer’s Disease Assessment Scale-Cognitive section. * One month after surgery.
One week later, neuropsychological assessment was performed with MMSE of 19 and MoCA of 20 (shown in Table 1). She was discharged with continued oral prednisone acetate, LEV, and olanzapine.

At month 1 follow-up, the patient complained of impaired short-term memory and spatial disorientation, without hallucinations. She was intermittently unaware of where she was and why she had come. She had to write down her daily plan and what she did every day. She was partially reliant on a caregiver. Repeated MRI (3 months after onset) showed reduced swelling of bilateral hippocampus on T2WI/FLAIR. She underwent laparoscopic oophorocystectomy, and mature teratoma was confirmed by pathological examination: part of the ovarian tissue was filled with colloidal substance, most of which was goiter, meanwhile with a few components from multiple embryonal layers. Immunohistochemistry showed partial or focal positive nuclear staining of LGI1 in tumor cells (shown in Fig. 2).

At month 2–4 follow-up, her spatial disorientation recovered, she complained of anxiety when facing daily activities such as answering phone calls originally, and her short-term memory gradually improved and she could recall what she had done every day. She could live independently and return to work. Neuropsychological assessment showed improved cognitive function and mood scales (shown in Table 1). LGI1 antibody titer in blood was 1:32 (1 month after surgery).

At month 5 follow-up, she still complained of short-term memory impairment and was afraid of being alone. Neuropsychological assessment scores returned to normal (shown in Table 1). Repeated structural and functional MRI indicated improvement: hyperintensity on T2WI/FLAIR was restricted to the right hippocampus without swelling; no progressive brain atrophy; diffusion-weighted imaging and diffusion tensor imaging showed slightly decreased blood flow on the left temporal lobe.

Fig. 1. Serial MRI of the patient with teratoma at different disease stages. a–d were taken 1 month after cognitive impairment onset. Bilateral hippocampal hyperintensity was shown obviously on T2 (a) and T2-FLAIR (b), without restricted diffusion (c) and enhancement (d). e, f were repeated images 3 months after cognitive impairment onset, which presented reduced swelling of the bilateral hippocampus on T2 (e) and T2-FLAIR (f) sequence, slightly better than the initial one. g–j were taken 5 months after cognitive impairment onset. T2 (g) and T2-FLAIR (axial (h) and coronal (i)) only presented slightly right hippocampal hyperintensity without swelling, and no progressive cerebral atrophy was observed comparing with the former two reviews. Arterial spin labeling (j) showed slightly decreased blood flow on the left temporal lobe.
were symmetric bilaterally and normal; arterial spin labeling showed slightly decreased blood flow in her left temporal lobe (shown in Fig. 1).

At month 6–12 follow-up, she still complained of memory impairment but gradually got used to the working environment and recovered to the original working and daily living state. At month 18 follow-up, she had almost gone back to normal, and the serum LGI1 antibody turned negative.

Comparison of Clinical Manifestations in Anti-LGI1 Encephalitis Cases with and without Teratoma

Our case with teratoma shared many clinical features with those without teratoma (NT cases), including (1) age at onset of 48, near the average of 47.3 years in the NT cases; (2) hyponatremia and normal CSF cell count and protein, as seen in 78% of the NT cases; (3) hippocampal hyperintensity on T2WI/FLAIR, as seen in 89% of the NT cases; (4) cognitive impairment and sleep disorder, along with residual cognitive impairment >1 year after admission, seen in 67% of the NT cases; (5) immunotherapy was effective and good prognosis: mRS score was 1 in the patient with teratoma, as compared to ≤2 in 67% of the NT cases (shown in Table 2).

However, there are also three points in which the patient with teratoma differed from those without. First, the prodromal chronic anxiety: only 1 patient in the NT cases had acute anxiety beginning simultaneously with FBDS. Second, her persistent anxiety until 9 months from onset: the acute anxiety of the NT patient had resolved by 2 months follow-up. Third, her convulsive SE during disease course, rather than FBDS, as was seen in 38% of the NT cases.

Prognosis of the Anti-LGI1 Encephalitis with and without Teratoma

One patient in the NT cases was lost to follow-up, the other eight were followed for an average of 26.1 ± 12.0 months. Similar to the case with teratoma, immune therapy (methylprednisolone pulse therapy, intravenous immunoglobulin, plasma exchange, and/or immunosuppressant) was effective in 78% of the NT cases. One patient died of pneumonia because of comorbid myasthenia gravis, and 1 patient died of hepatic failure due to chronic schistosomiasis liver disease and hepatitis B, deteriorated after methylprednisolone pulse therapy followed by oral azathioprine. None of the patients relapsed within the follow-up period.

Discussion

Anti-LGI1 encephalitis is a subtype of AE with heterogeneous clinical manifestations, rarely comorbid with tumor [12]. We firstly reported a case of anti-LGI1 encephalitis with teratoma and derived two possible differential features (chronic anxiety and SE) to anti-LGI1 encephalitis without teratoma.

We think that anti-LGI1 encephalitis was associated with the teratoma in our case for several reasons: (1) immunohistochemistry staining confirmed positive nuclear staining of LGI1 in some tumor cells; (2) teratoma tissue mainly consisted of the thyroid gland, which easily promotes the generation of various antibodies as antigens [16] (additionally, thyroid cancer can be comorbid with anti-LGI1 encephalitis) [11, 12]; (3) after removal of the teratoma, her cognitive function recovered greatly at the first month and almost fully at the third month after surgery. Although the serum LGI1 antibody titer remained (1:32), it gradually decreased to undetected level at the 18-month follow-up. No study about the dynamic change...
| Clinical characteristics | Without teratoma, N (%) | With teratoma, N (%) |
|--------------------------|-------------------------|----------------------|
| N                        | 9                       | 1                    |
| Female, n/N (%)          | 3/9 (33%)               | Yes                  |
| Age at onset, years ± SD (range) | 47±16 (19–67)     | 48                  |
| Disease onset            | 9                       |                      |
| Acute, n (%)             | 6 (67)                  |                      |
| Subacute, n (%)          | 3 (33)                  |                      |
| Chronic                  | 0                       | Yes                  |
| Clinical symptoms        | 9                       |                      |
| Onset symptoms           | 9                       |                      |
| Behavioral disorders, n (%) | 2 (22)              |                      |
| FBDS, n (%)              | 2 (22)                  |                      |
| Cognitive impairment, n (%) | 1 (11)             |                      |
| Behavioral disorders + cognitive impairment, n (%) | 1 (11) |                      |
| RBD, n (%)               | 1 (11)                  |                      |
| Dizziness                | 1 (11)                  |                      |
| Anxiety                  | 0                       | Yes                  |
| Anxiety + FBDS, n (%)    | 1 (11)                  |                      |
| Symptoms through entire disease course | 9 (89) |                      |
| Seizures, n (%)          | 8 (89)                  |                      |
| Generalized convulsions, n/N (%) | 4/8 (50)          |                      |
| FBDS, n/N (%)            | 3/8 (38)                |                      |
| Focal seizure, n/N (%)   | 1/8 (13)                |                      |
| SE                       | 0                       | Yes                  |
| Cognitive impairment, n/N (%) | 6 (67)            |                      |
| Hallucination, n (%)     | 3 (33)                  | Yes                  |
| Sleep disorder, n (%)    | 6 (67)                  | Yes                  |
| Insomnia, n/N (%)        | 3/6 (50)                |                      |
| RBD, n/N (%)             | 2/6 (33)                |                      |
| Drowsiness, n/N (%)      | 1/6 (17)                | Yes                  |
| Ancillary test results   | 9                       |                      |
| Evidence of tumor        | 0                       | Yes                  |
| Hyponatremia, n (%)      | 7 (78)                  | Yes                  |
| CSF, n (%)               | 7 (78)                  |                      |
| Cell count <8 cells/mL, n/N (%) | 7/7 (100)        | Yes                  |
| Protein ≤0.58 g/L, n/N (%) | 7/7 (100)           | Yes                  |
| Positive LGI1 antibody immunoassay, n (%) | 9 (100) |                      |
| Serum, n/N (%)           | 2/9 (22)                |                      |
| CSF, n/N (%)             | 2/9 (22)                |                      |
| Serum + CSF, n/N (%)     | 5/9 (56)                | Yes                  |
| EEG, n/N (%)             | 6 (67)                  |                      |
| Background slowing, n/N (%) | 3/6 (50)         | Yes                  |
| Background slowing + epileptic discharges, n/N (%) | 1/6 (17) |          |
| Normal, n/N (%)          | 2/6 (33)                |                      |
| MRI                      | 9 (100)                 |                      |
| Hippocampal lesion       | 8 (89)                  |                      |
| Bilateral, n/N (%)       | 4/8 (50)                | Yes                  |
| Unilateral, n/N (%)      | 4/8 (50)                |                      |
| Normal, n (%)            | 1 (11)                  |                      |
| Pharmacological therapy, n (%) | 9 (100)         |                      |
| MPT, n (%)               | 5 (56)                  |                      |
| MPT + IVIG, n (%)        | 1 (11)                  | Yes*                 |
| MPT + immunosuppressant, n (%) | 2 (22)             |                      |
| MPT + IVIG + immunosuppressant | 0                   |                      |
| MPT + IVIG + plasma exchange | 0                 |                      |
| MPT + immunosuppressant + plasma exchange, n (%) | 1 (11) |                      |
| Neuropsychic evaluation results, n (%) | 6 (67) |                      |
| Cognitive function, n (%) | 6 (67)                  |                      |
| MMSE ≤ 24, n/N (%)       | 3/6 (50)                | Yes                  |
| MoCA ≤ 26, n/N (%)       | 1/6 (17)                | Yes                  |
| Normal, n/N (%)          | 2/6 (33)                |                      |
| Follow-up, n (%)         | 8 (89)                  |                      |
| mRS evaluation, n (%)    | 8 (89)                  |                      |
| <2, n/N (%)              | 6/8 (75)                | Yes                  |
| ≥2, n/N (%)              | 2/8 (25)                |                      |
| Residual symptoms or death, n (%) | 8 (89)         |                      |
| No symptom, n/N (%)      | 3/8 (38)                |                      |
| Short-term memory impair, n/N (%) | 2/8 (25)       | Yes                  |
| FBDS, n/N (%)            | 1/8 (13)                |                      |
| Death, n/N (%)           | 2/8 (25)                |                      |

"Yes" means the LGI1 encephalitis patient with teratoma had the symptom. LGI1, leucine-rich glioma-inactivated 1; FBDS, faciobrachial dystonic seizures; RBD, rapidly eye movement behavior disorder; CSF, cerebrospinal fluid; EEG, electroencephalography; MRI, magnetic resonance imaging; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; MPT, methylprednisolone pulse therapy; IVIG, intravenous immunoglobulin. * Reduced methylprednisolone dose.
of serum or CSF antibody titer after teratoma removal surgery was reported in AE patients, but the correlation of antibody titers and clinical diagnosis, prognosis, and relapse was confirmed by a retrospective study of anti-NMDAR encephalitis [17].

The most representative and high-incidence subtype of AE associated with teratoma was anti-NMDAR encephalitis. Unlike NMDA receptors, which are the extra-cellular domain of the GluN1 subunit [18], LGI1 is not a structural component of a receptor or ion channel but is rather secreted by neurons, explaining why the incidence of tumor is much lower in anti-LGI1 encephalitis. Nevertheless, LGI1 forms a trans-synaptic complex with pre-synaptic proteins [19], so anti-LGI1 encephalitis may still be comorbid with tumors such as teratoma.

Summary data from our case series indicate similar clinical manifestations as seen in many larger series. These specific manifestations are probably early diagnostic clues to anti-LGI1 encephalitis, including (1) acute or sub-acute onset of RPD in relatively older aged population [2], (2) FBDS [2], (3) hyponatremia [2], and (4) hyperintensity of hippocampus on T2WI/FLAIR [2].

More importantly, our anti-LGI1 encephalitis case with teratoma presented several specific features that might differentiate it from other subtypes of AE but perhaps even cases of anti-LGI1 encephalitis without teratoma. First, her chronic onset of anxiety has never been reported in other subtypes of AE by our best knowledge. For anti-NMDAR encephalitis, 86% of 100 cases presented headache, fever of a nonspecific viral-like illness as prodromal symptom [20], and developed psychiatric symptoms and short-term memory loss in less than 2 weeks [21]. Seventy-seven percentage of 22 anti-GABA B R encephalitis patients presented recurrent seizure at onset [22]. In 76 LGI1 antibody-positive patients, only 2.6% presented isolated anxiety as an initial symptom with median duration time of 2 months [23].

Second, seizure is one of the most common symptoms of AE, with various manifestations among different subtypes. The incidence of seizure in anti-NMDAR and anti-GABA B R encephalitis is the highest, followed by anti-LGI1 and anti-AMPA encephalitis, whereas the most typical seizure type with diagnostic specificity is FBDS in anti-LGI1 encephalitis, seen in almost half of confirmed cases, but not seen in our case with teratoma [2]. Anti-NMDAR encephalitis has more seizure types at onset: 43% had generalized tonic-clonic seizures, 43% had focal seizures, and 14% had both [24]. SE is more common in anti-GABA receptor (GABAR) encephalitis, based on the limited literature: seen in 58% of 12 anti-GABA R encephalitis cases [25] and 27% of 11 confirmed GABA B R encephalitis subjects [26], compared with only 6% of 100 anti-NMDAR encephalitis patients [27] and 5% of 19 anti-LGI1 encephalitis patients [28]. Interestingly, our case with teratoma developed SE on her 8th day of admission. We think there are two interpretations, (1) SE may be more typical in anti-LGI1 encephalitis with teratoma and (2) the patient’s immunotherapy started relatively late, 1 month after onset of RPD, facilitating the development of SE.

Third, RPD is the most common symptom in anti-LGI1 encephalitis, and residual cognitive dysfunction was more common than other AE. Ninety-seven percent of 38 anti-LGI1 encephalitis patients developed memory disturbances during the course of disease and 86% of them had persistent amnesia for events happened during disease course at 2-year follow-up [2]. The persistent short-term memory impairment until 5 months following the acute stage in our patient was highly consistent with reported anti-LGI1 encephalitis. Sixty-two percentage of 85 voltage-gated potassium channel-IgG-positive patients with central involvement had residual cognitive disturbances [13], and 23% of 76 patients with LGI1 antibody-positive had moderate or severe cognitive impairment at 2-year follow-up [23]. Recovery from cognitive symptoms is quicker and more complete in other forms of AE. Seventy-five percentage of 100 patients with anti-NMDAR encephalitis showed full recovery or very mild functional deficits (mRS 1–2, MMSE 25–28) at median 17-month follow-up [20]. Serial observation of patients with anti-GABA B R encephalitis indicated that 35% recovered fully and 40% improved markedly, except for recurrent seizures in 50% of 20 cases comorbid with small-cell lung cancer [29]. Our case suggested that the cognitive deficits in anti-LGI1 encephalitis might need longer time to recover than those in anti-NMDAR or GABA B R encephalitis.

Conclusion

We first reported a case of anti-LGI1 encephalitis with teratomas, characterized by chronic onset of mood disorders, followed by RPD, SE, and psychiatric symptoms. Our case illustrated again that early diagnosis is vitally important because early initiated immunotherapy might avoid deterioration and need for intensive care unit management. Further illumination of specific clinical biomarkers of anti-LGI1 encephalitis with teratoma will require collection of more cases.
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Statement of Ethics

The study was approved by the Huazhong University of Science and Technology (HUST) Ethics Committee on Human Research (TJ-IRB20191006). All patients signed informed content to participate. All patients signed informed content for publication of the details of their medical case and any accompanying images. All procedures in our study were done with all patients’ informed consent in compliance with the Helsinki Declaration.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

Cun Li and Hong-bin Cai collected all the clinical data. Xu Zhao performed and read all the MRI scans. Xin-cong Xi and Cun Li followed up the cases. Qing Zhou and Hui-ya Luo did IHC assay of the LGI1 antibody. Zhou-ping Tang provided advice on neuropsychological assessment. Cun Li wrote the first draft of the manuscript, Hui-cong Kang and Heidi E. Kirsch contributed to main idea of the manuscript. All authors contributed to the revision of the manuscript and approved the submission.

Data Availability Statement

The data that support the findings of this study are available on reasonable request from the corresponding author because at this time, the data also form part of another ongoing study.
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