Neurology Asia 2024; 29(3) : 805 – 813

Characteristics and prognosis of LGI1 antibody encephalitis

Ruixue Zhang, Lei Bao, Hongjuan Shi, Qingjie Li

Department of Neurology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China

Abstract

Objectives: To investigate clinical manifestations and outcomes of patients with LGI1 autoimmune encephalitis. *Methods:* A total of 12 patients who were diagnosed with LGI1 autoimmune encephalitis were retrospectively analyzed between 2018 and 2022 at the Department of Neurology of the Affiliated Hospital of Xuzhou Medical University. Clinical characteristics, laboratory examinations, electroencephalograms, brain magnetic resonance images and prognosis were assessed. The clinical data were collected by searching through electronic medical records. *Results:* Among 12 patients, 8 were male and 4 were female. The average age at disease onset was 61.8 years (24–83). The most common clinical symptoms were seizures (n=10), cognitive dysfunction (n=8), and mental behavioral disorders (n=8). A total of 9 cases had hyponatremia. Brain MRI and electroencephalographic were abnormal in 7 patients each. All patients were treated with first line immunotherapy. Most patients responded well and 3 patients relapsed on follow-up.
Conclusion: Characteristic features of LGI1 antibody encephalitis include subacute onset cognitive impairment, seizures, faciobrachial dystonic seizures (FBDS), and mental and behavioral abnormalities. Especially, FBDS and hyponatremia suggest LGI1-antibody encephalitis. Therefore, early identification and immunotherapy may prevent cognitive impairment and improve prognosis.

Keywords: Autoimmune encephalitis, LGI1, FBDS, cognitive function

INTRODUCTION

Anti-leucine-rich glioma inactivated 1(LGI1) antibody encephalitis, which is relatively rare in clinic, is the second most common cause of autoimmune encephalitis (AE) following anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, similar to other Asian studies.[1] The common manifestations of anti-LGI1 encephalitis are cognitive impairment or rapidly progressive dementia, psychiatric and behavior disorders, generalized or partial epileptic seizures, often as faciobrachial dystonic seizures (FBDSs), and refractory hyponatremia. Since LGI1 antibody encephalitis is characterized by acute or subacute onset of cognitive dysfunction, the disease has often been misdiagnosed as a psychiatric illness.[2] LGI1 antibody encephalitis often, in addition, present chronic courses, of between 1 and 5 years, unlike other autoantibody-mediated encephalitis. These more insidious courses often lead to a delayed diagnosis, and hence late commencement of immunotherapy, poor prognosis and cognitive sequelae. It is of major clinical importance to all neurologists because these patients present with a wide variety of neuropsychic characteristics and typically respond to immunotherapy. In order to improve the awareness and knowledge of this disease, we report here the clinical features, laboratory examinations, electroencephalograms and brain magnetic resonance images of patients with LGI1 antibody encephalitis in our hospital.

METHODS

Ethics

The study was approved by the Clinical Research Ethics Committee of the Affiliated Hospital of Xuzhou Medical University. The protocols were in accordance with the Declaration of Helsinki. All patients provided informed consent for the use of their medical records.

Address correspondence to: Qingjie Li, Department of Neurology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, 221004, China. Tel: 86-15996969166, email: xyfysnlqj@126.com

Date of Submission: 11 November 2023; Date of Acceptance: 1 April 2024

https://doi.org/10.54029/2024ytn

Study participants

This study comprised of 12 patients who were diagnosed with LGI1 antibody encephalitis from October 2018 to March 2022, at the Department of Neurology in the Affiliated Hospital of Xuzhou Medical University, Jiangsu, China. The inclusion criteria of LGI1 antibody encephalitis were: (1) clinical symptoms such as cognitive impairment, mental disorders, FBDS, and hyponatremia; (2) the presence of positive LGI1 antibody in the serum or cerebrospinal fluid (CSF) ; and (3) reasonable exclusion of other disorders. All included patients underwent serum and CSF autoimmune encephalitis-related antibodies detection, including N-methyl-D-aspartate receptor (NMDAR), LGI1, contactin-associated protein-2 (CASPR2), γ-aminobutyric acid type B (GABAB), and α-amino-3-hydroxy- 5-methyl-4-isoxazolepropionic acid receptor (AMPAR), and other intracellular protein-related antibodies (CV2, Hu, Yo, Ri, PNMA2, and amphiphysin). All patients also received other laboratory tests, such as standard biochemistry, thyroid function, viral antibodies (syphilis, HIV, herpes simplex virus 1, 2, and herpes zoster virus), and tumor biomarkers. All patients had undergone electroencephalography (EEG) and brain MRI for neurological assessment during clinical evaluation. All patients were followed up for at least 1 year after being discharged from the hospital. The clinical data, including demographic, clinical manifestation, laboratory examination, EEG, MRI, details of treatments and prognosis were reviewed by searching the electronic medical records.

RESULTS

From October 2018 to March 2022, 76 patients were suspected of having potential autoimmune encephalitis. According to the inclusion criteria of LGI1 antibody encephalitis, a total of 12 consecutive patients were recruited for inclusion in the study. A flowchart that describes patient selection is shown in Figure 1. Among the 12 patients in our study, 8 were male, 4 were female, and the average age was 61.8 years (24–83). The time from initial symptoms to definite diagnosis (positive antibody titer) was a median of 50 (range 5–150) days. Table 1 describes the clinical characteristics of all patients included in our study in detail. The most common clinical manifestations of LGI1 antibody encephalitis were seizures (n=10), mental behavioral disorders (n=8), such as visual hallucinations, mood lability, anxiety, impulsivity, paranoia, and cognitive dysfunction (n=8), mainly manifested as recent memory deficit and spatial disorientation. The most frequent initial symptom was seizures, including FBDS, tonic-clonic seizures, and status epilepticus. Among them, FBDS was the most obvious manifestation.

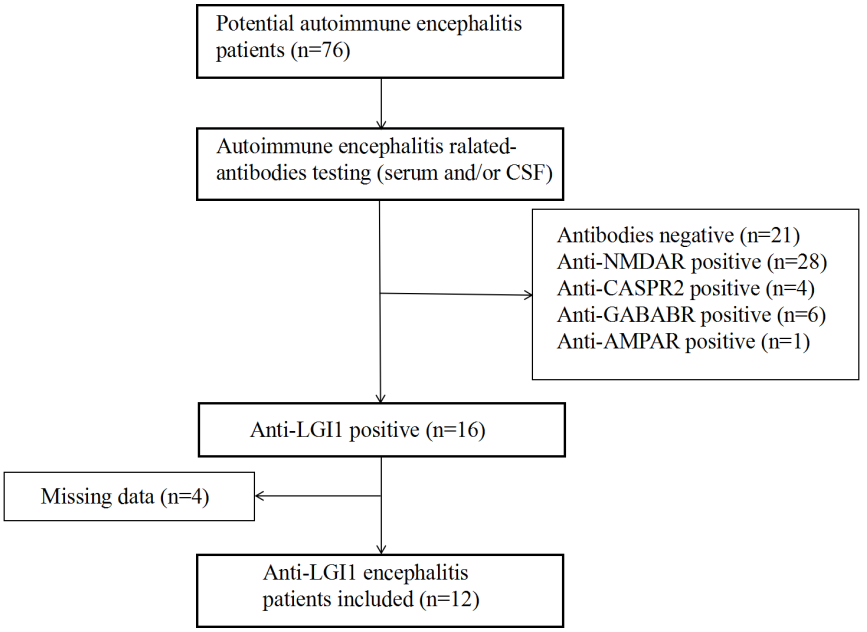

Figure 1. The flowchart of patients selection.

Table 1: Clinical characteristics of patients with LGI1-antibodies

	Age (years)	Gender	Onset to diagnosis (days)	Neurological symptoms	ICU admission	Cancer
Patient 1	66	Female	100	FBDS(30/d), tonic-clonic seizures, cognitive dysfunction, psychiatric symptoms, sleep disorders, impaired consciousness , urinary and fecal incontinence	Yes	No
Patient 2	54	Male	31	FBDS(20/d), tonic-clonic seizures, status epilepticus, cognitive dysfunction, sleep disorders	No	No
Patient 3	24	Female	5	Dizziness, vomiting, ataxia	No	No
Patient 4	61	Male	40	FBDS(10/d), cognitive dysfunction	No	No
Patient 5	64	Female	13	Status epilepticus, tonic-clonic seizures, psychiatric symptoms	Yes	No
Patient 6	76	Male	28	FBDS(20/d), cognitive dysfunction, sleep disorders, psychiatric symptoms, visual hallucination, urinary and fecal incontinence	No	No
Patient 7	77	Male	150	FBDS(5/d), cognitive dysfunction, psychiatric symptoms, hallucination, sleep disorders	No	No
Patient 8	83	Male	120	FBDS(10/d), status epilepticus, tonic-clonic seizures, cognitive dysfunction, psychiatric symptoms, hallucination, impaired consciousness	No	No
Patient 9	66	Male	15	Dizziness, FBDS(5/d), sleep disorders, psychiatric symptoms	No	No
Patient 10	61	Male	30	Cognitive dysfunction, psychiatric symptoms	No	No
Patient 11	50	Male	10	Status epilepticus,	No	No
Patient 12	60	Female	58	Status epilepticus, tonic-clonic seizures, cognitive dysfunction, impaired consciousness, psychiatric symptoms	No	No

The average frequency of FBDS was 14 per day (range 5–30). Other common symptoms were sleeping disorders (n=5), hallucination (n=3), and conscious disturbance (n=3). Three patients also suffered from autonomic dysfunctions, including urinary and fecal incontinence and vomiting.

CSF examination, EEG and MRI were performed in all patients before immunotherapy. All patients were positive for the LGI1 antibody in CSF, although the antibody titer was significantly lower than that in the serum, and negative for other autoimmune encephalitis antibodies. Only one patient had increased white blood cell counts (78 × 106 /L) in CSF, 7 patients had increased protein levels (0.51-1.30 g/L, the normal value was 0.15-0.45 g/L), 9 patients had increased IgG, and sugar was slightly higher in 2 patients. There were 9 cases of hyponatremia, hypochloremia or both, 5 of which were refractory hyponatremia. Intracellular protein-related antibodies (CV2, Hu, Yo, Ri, PNMA2, and amphiphysin), thyroid function, viral antibodies and tumor biomarkers were in the normal range in all 12 patients (Table 2). Seven patients had abnormal EEG signals, involving unilateral or bilateral slow waves, sharp waves, and sharp-slow waves originated from the temporal, frontal, and parietal lobe (Fig. 2). Whereas no abnormal EEG signals were detected during FDBS. Brain MRI of seven patients identified abnormalities

Table 2: Laboratory data of patients with LGI1-antibodies

	LGI1-antibody level		Blood sodium (mmol/L)	Blood chlorine (mmol/L)	CSF			EEG	MRI
	Serum	CSF			WBC (106 /L)	Protein (g/L)	Glucose (mmol/L)		
Patient 1	1:100	1:3.2	125.5	87.7	2	0.41	4.54	Normal	Normal
Patient 2	1:32	1:3.2	125.6	87.5	4	0.68	4.44	Slow wave (right temporal lobe)	Left basal ganglia
Patient 3	1:10	1:1	139.8	101.7	78	1.30	2.90	Normal	Bilateral frontal lobe
Patient 4	1:32	1:1	137	96.3	3	0.51	3.51	Diffuse slow wave (bilateral frontal parietal temporal lobe)	Right hippocampus
Patient 5	1:100	1:3.2	129.1	84.6	3	1.23	3.51	Spike-slow, slow wave (bilateral temporal lobe)	Bilateral hippocampus
Patient 6	1:100	1:1	136	93.8	3	0.51	3.16	Spike, spike-slow, slow wave (bilateral frontal lobe)	Normal
Patient 7	1:100	1:32	136.4	97.3	2	0.30	3.97	Slow wave (bilateral temporal lobe	Bilateral hippocampus
Patient 8	1:1000+	1:100+	122.7	84.6	1	0.85	2.72	Normal	Normal
Patient 9	1:100	1:1	121.5	82.9	3	0.30	3.15	Normal	Normal
Patient 10	1:32	1:1	140.8	103.2	2	0.32	3.19	Normal	Normal
Patient 11	1:32	1:3.2	131.8	104	1	0.30	3.94	Slow wave (right temporal lobe)	Right temporal lobe
Patient 12	1:100	1:1	124.8	84.4	4	0.63	3.33	Spike, spike-slow, slow wave (right temporal lobe)	Right hippocampus

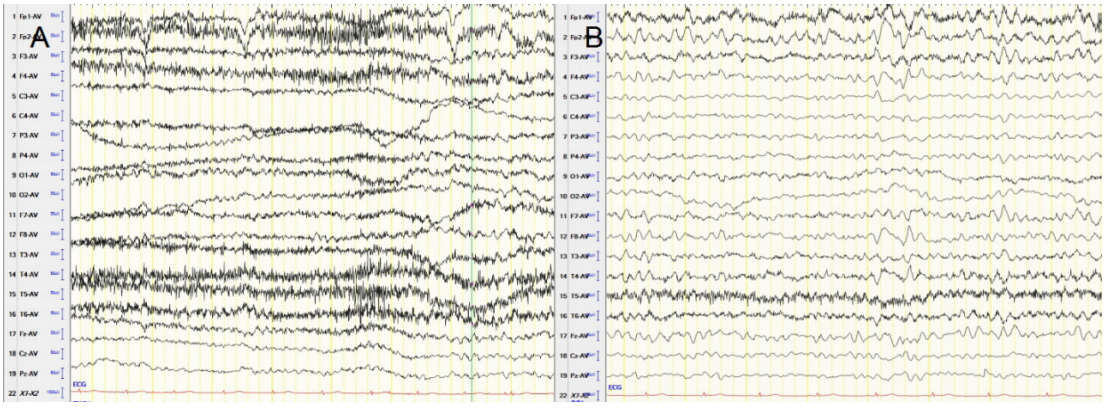

Figure 2. EEG of LGI1-antibody encephalitis. (A) The EEG was normal during FDBS; (B) The EEG showed interictal bilateral temporal and frontal lobe slow, sharp and sharp-slow wave complex.

in the hippocampus (n=4), temporal lobe (n=1) , and basal ganglia (n=1), and frontal lobe (n=1) (Figure 3).

All patients were treated with methylprednisolone intravenously (0.5-1g/d for 3-5 days), followed by oral prednisone (60 mg/d, gradually decreased and then ceased) in 9 patients. Five patients also received treatment with intravenous immunoglobulin (0.4 g/kg/d for 5 days). Most patients responded well to immunotherapy, especially FBDS and psychiatric symptoms. Antiseizure medications (ASMs)

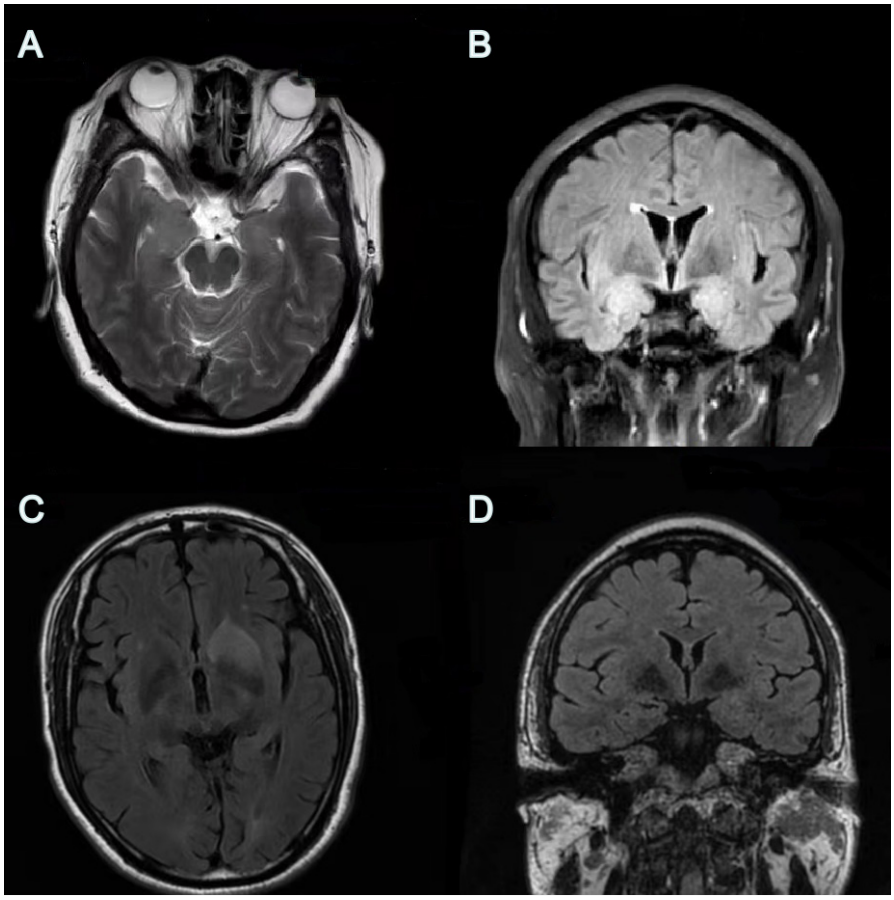

Figure 3. Brain MRI of LGI1-antibody encephalitis. (A, B) Bilateral abnormal signals in the hippocampus. (C) High signal in the left basal ganglia. (D) Atrophy in the right hippocampus.

including sodium valproate, levetiracetam, oxcarbazepine, lamotrigine, and perampanel were given in 10 patients with epileptic seizures before immunotherapy, and 3 had reduced seizures but not fully controlled. To date, 3 patients in our study have experienced a relapse, no patient has developed a tumor after a median follow-up of 1 year.

DISCUSSION

AE is a generic term for a heterogeneous group of disorders caused by a misdirected immune response against self-antigens expressed in the central nervous system. Owing to growing awareness of these disorders and more widespread diagnostic capacities, the incidence of autoimmune encephalitis rose over the last 20 years. Neuronal surface- or synaptic protein-related antigens of autoimmune encephalitis include NMDAR, LGI1, CASPR2, GABAB, and AMPAR. LGI1- antibody encephalitis is one of the most frequent cell surface target antigen mediated AE.[1,3] LGI1 is a synaptic glycoprotein encoded by the epilepsy-related gene lgi1, which is mainly expressed primarily in the hippocampus and temporal cortex.[4] It links epilepsy-related receptors ADAM22 and ADAM23, and organizes a transsynaptic protein complex that includes presynaptic potassium channels and postsynaptic AMPAR.[5] LGI1 antibodies might disrupt this synaptic protein connection and reduce AMPAR–mediated synaptic transmission in the hippocampus. Previous study indicated that loss of LGI1 gene in mice specifically causes the epilepsy, with prominent dystonic, myoclonic, and generalized seizures.[5-7] LGI1gene mutation in human may lead to autosomal dominant lateral temporal lobe epilepsy.[8] In our study, the average age of onset is 61.8 years old and 8 are male, which is consistent with prior report showing that LGI1- antibody encephalitis patients are typically men in their fifth to eighth decades.[9] The unusual demographic of age distribution and male predominance may be associated with environmental triggers and genetic predisposition, such as the recently described HLA-II haplotypes encompassing DRB1*07:01, DQA1*02:01 and DQB1*02:02.[10]

While the clinical manifestations of AE span the spectrum of neurological symptomatology, for patients with auto-antibodies against any individual target there is often a characteristic set of core phenotypic features. Patients with LGI1- antibody encephalitis often show FBDS, autonomic seizures, and generalized tonic–clonic seizures. From our experience, FBDS are the most common characteristic and appear earlier than other symptoms in many patients, while only rare generalized tonic–clonic seizures occur, typically later in disease. Given that FBDS are highly specific and often appear as an initial symptom of LGI1 AE, it is suggested that all patients with FBDS should take LGI1 antibody examination.

Subsequently, in our clinical experience, over half of the patients with LGI1- antibody encephalitis often developed cognitive impairments, typically memory deficits and disorientation, owing to the dense expression of LGI1 antigen in limbic structures, particularly the hippocampus.[11-13] As cognitive dysfunction is often the initial complaint preceded by other symptoms in the LGI1 - antibody encephalitis patients, many patients are committed to psychiatric hospital, which may delay immunotherapy and result in the deterioration of their conditions.[2] Since long-term outcome is mostly determined by cognitive deficits, there is a need for early diagnosis and treatment to prevent cognitive decline. Fortunately, the cognitive impairment might be prevented by early immunotherapy. In addition, patients with LGI1 antibody encephalitis can also exhibit psychiatric symptoms: such as aggression, irritability, mood lability, anxiety, impulsivity, paranoia, hallucinations.[2,14] Sleep disturbances are also common, as described previously, including rapid eye movement sleep behavior disorder, hypersomnia, insomnia fragmented sleep, dream enactment behaviors and sleep-disordered breathing.[9,15] Improved detection and treatment of sleep disorders may reduce morbidity associated with AE and improve long-term outcomes.[15]

Hyponatremia is frequent in patients of our study, which is consistent with previous reports, indicating that the hyponatremia, especially refractory hyponatremia, is a characteristic feature of LGI1 antibody encephalitis. The pathogenic mechanism is likely associated with inappropriate secretion of the antidiuretic hormone, which may be related to the effects of LGI1 antibodies on the hypothalamic paraventricular nucleus and kidney.[16]

The diagnosis of LGI1-antibody encephalitis is often established by the detection of anti-LGI1 antibody in CSF or serum or both. To date, there is also some controversy about whether serum is more sensitive than CSF. In our study, LGI1 antibodies are found to have a higher titer in the serum than in the CSF, which is in line with the findings of a recent review.[17] Therefore, antibody tests in serum should be considered before

lumbar puncture. However, the specific antibody testing usually takes several days. Thus, it is of great importance to diagnose LGI1 antibody encephalitis in the early-stage by clinical features. Determination of antibodies cannot replace the clinical evaluation and should be considered as a supportive test.

Previously, MRI was a preferred radiological modality for the diagnosis of LGI1-antibody encephalitis. Most patients with LGI1-antibody encephalitis have T2-weighted image (T2WI) or fluid-attenuated inversion recovery (FLAIR) hyperintensity in uni- or bilateral medial temporal lobes and/or basal ganglia. Nevertheless, individual patients exhibit negligible MRI findings, notably during the early stage of LGI1-antibody encephalitis. This probably contributed to the delay in diagnosis. Currently, in addition to MRI, 18F-FDG-PET, a novel or distinctive imaging pattern, has been proven to be a more sensitive diagnostic method for LGI1-antibody encephalitis. Comparison between the sensitivity of MRI and 18F-FDG-PET has showed that 18F-FDG-PET exhibited 100% hypermetabolism when the MRI scans were positive, whereas 79% patients had metabolic changes of 18F-FDG in the presence of negative MRI, thus demonstrating that 18F-FDG-PET was apparently superior to MRI in the early diagnosis of LGI1 AE.[18] Other studies also revealed intense FDG uptake in bilateral limbic system at the acute phase of AE, and then decreased and eventually normal according to the clinical improvement after treatment, confirming that 18F-FDG PET has good correlation with activity of AE and is useful for evaluating the treatment response.[19,20] Subsequently, Electroencephalography is also important as a supportive criterion for LGI1-antibody encephalitis, especially when antibody testing and radiology are negative or not available. The most frequent EEG abnormalities were interictal epileptiform discharges, slowing, rhythmic ictal activity in the temporal, frontal or frontotemporal focus.[21]

From experience, immunotherapy is the most effective treatment for LGI1 antibody encephalitis. First-line therapies involve corticosteroids, intravenous immunoglobulin (IVIG) and plasma exchange. Patients with LGI1 antibodies improve remarkably (especially psychiatric symptoms, FBDS and hyponatremia) with appropriate and timely corticosteroids although frequently have significant residual cognitive deficits. Relapses occurred in 3 patients of our study, suggesting that chronic immunotherapy might be useful. In our experience, high-dose intravenous corticosteroids, 0.5-1 g daily for 3–5 days, followed by oral prednisolone for 12–24 months should be maintained, as shorter durations of corticosteroids are often associated with relapses.[22] Over all, acute and long-term immunotherapy is a predictor for better outcome. A randomized placebo controlled clinical trial has confirmed the efficacy of IVIG in LGI1- antibody encephalitis, as the majority cases demonstrated more than 50% reduction in seizure frequency following 6 weeks of IVIG.[23] In clinical, plasma exchange is only used in patients, who show a limited or inadequate response to corticosteroids, and/ or IVIG. Whereas some patients often require more aggressive therapies (rituximab, cyclophosphamide). Given the trial in the relatively late course of patients with LGI1- antibody encephalitis suggested that early rituximab may be effective. Modified Rankin Scale scores improved and relapses decreased significantly in patients with rituximab treatment.[24] However, the effect of rituximab in a study was equivocal, possibly on account of small sample size and long treatment delays.

To date, the effect of ASM for LGI1 antibody encephalitis with FBDS is variable. Experiences from prior studies have suggested that FBDS appear exquisitely responsive to immunotherapy yet only minimally responsive to ASMs.[22,25] Furthermore, significant side effects including localized rash, erythroderma, Stevens-Johnson syndrome were significantly associated with exposure to ASMs in patients with LGI1 antibody encephalitis[9], while fewer side effects of immunotherapy were observed. Whenever possible, immunotherapy is preferred in these patients, and ASMs are reserved only for generalised convulsions.

The overall prognosis of LGI1-antibody encephalitis is favorable. There is an immediate and often complete cessation of FBDS after the start of immunotherapy. However, improvement of cognitive disorders are slower and often incomplete. Recent studies characterizing long-term outcome show that 70% of the anti-LGI1 patients have cognitive sequelae.[26,27] As cognitive deficits are decisive for long-term outcome, and relapses occur in almost one third of the anti-LGI1 patients, thus there is a need for early and chronic immunotherapy to improve prognosis.

By way of generalisation, LGI1-antibody encephalitis is rare and an under-recognized condition. In addition to LGI1 antibody test in serum or CSF, characteristic clinical manifestation, such as: FBDS, hyponatremia

can make accurate diagnosis. Especially, FBDS commonly precedes other symptoms of LGI1 AE, representing an important diagnostic clue. Given that LGI1-antibody encephalitis is mostly non-paraneoplastic, and thought to be responsive to immunotherapy, it is suggested that any rapidly progressive encephalopathy of unclear etiology, particularly if accompanied by FBDS, cognitive deficits and refractory hyponatremia, should raise concern for an immune-mediated process. Early recognition and immediate immunotherapy may possibly prevent cognitive decline and improve outcomes.

REFERENCES

1. Goodfellow JA, Mackay GA. Autoimmune encephalitis. *J R Coll Physicians Edinb* 2019;49(4):287-94. doi: 10.4997/JRCPE.2019.407.
2. Jang Y, Lee ST, Lim JA, *et al*. Psychiatric symptoms delay the diagnosis of anti-LGI1 encephalitis. *J Neuroimmunol* 2018;317:8-14. doi: 10.1016/j.jneuroim.2018.02.005.
3. van Sonderen A, Thijs RD, Coenders EC, *et al*. Anti-LGI1 encephalitis: Clinical syndrome and long-term follow-up. *Neurology* 2016;87(14):1449-56. doi: 10.1212/WNL.0000000000003173.
4. van Sonderen A, Schreurs MW, Wirtz PW, Sillevis Smitt PA, Titulaer MJ. From VGKC to LGI1 and Caspr2 encephalitis: The evolution of a disease entity over time. *Autoimmun Rev* 2016;15(10):970-4. doi: 10.1016/j.autrev.2016.07.018.
5. Fukata Y, Lovero KL, Iwanaga T, *et al*. Disruption of LGI1-linked synaptic complex causes abnormal synaptic transmission and epilepsy. *Proc Natl Acad Sci U S A* 2010;107(8):3799-804. doi: 10.1073/pnas.0914537107.
6. Chabrol E, Navarro V, Provenzano G, *et al*. Electroclinical characterization of epileptic seizures in leucine-rich, glioma-inactivated 1-deficient mice. *Brain* 2010;133(9):2749-62. doi: 10.1093/brain/awq171.
7. Yu YE, Wen L, Silva J, *et al*. Lgi1 null mutant mice exhibit myoclonic seizures and CA1 neuronal hyperexcitability. *Hum Mol Genet* 2010;19(9):1702-11. doi: 10.1093/hmg/ddq047.
8. Kalachikov S, Evgrafov O, Ross B, *et al*. Mutations in LGI1 cause autosomal-dominant partial epilepsy with auditory features. *Nat Genet* 2002;30(3):335-41. doi: 10.1038/ng832.
9. Irani SR, Michell AW, Lang B, *et al*. Faciobrachial dystonic seizures precede Lgi1 antibody limbic encephalitis. *Ann Neurol* 2011;69(5):892-900. doi: 10.1002/ana.22307.
10. Mueller SH, Farber A, Pruss H, *et al*. Genetic predisposition in anti-LGI1 and anti-NMDA receptor encephalitis. *Ann Neurol* 2018;83(4):863-9. doi: 10.1002/ana.25216.
11. Arino H, Armangue T, Petit-Pedrol M, *et al*. Anti-LGI1-associated cognitive impairment: Presentation and long-term outcome. *Neurology* 2016;87(8):759-65. doi: 10.1212/WNL.0000000000003009.
12. Bastiaansen AEM, van Steenhoven RW, de Bruijn M, *et al*. Autoimmune encephalitis resembling dementia syndromes. *Neurol Neuroimmunol Neuroinflamm* 2021;8(5):e1039. doi: 10.1212/NXI.0000000000001039.
13. Heine J, Pruss H, Scheel M, *et al*. Transdiagnostic hippocampal damage patterns in neuroimmunological disorders. *Neuroimage Clin* 2020;28:102515. doi: 10.1016/j.nicl.2020.102515.
14. Endres D, Pruss H, Dressing A, *et al*. Psychiatric manifestation of anti-LGI1 encephalitis. *Brain Sci* 2020;10(6):375. doi: 10.3390/brainsci10060375.
15. Blattner MS, de Bruin GS, Bucelli RC, Day GS. Sleep disturbances are common in patients with autoimmune encephalitis. *J Neurol* 2019;266(4):1007-15. doi: 10.1007/s00415-019-09230-2.
16. Li LH, Ma CC, Zhang HF, Lian YJ. Clinical and electrographic characteristics of seizures in LGI1-antibody encephalitis. *Epilepsy Behav* 2018;88:277-82. doi: 10.1016/j.yebeh.2018.08.019.
17. Ghimire P, Khanal UP, Gajurel BP, *et al*. Anti-LGI1, anti-GABABR, and Anti-CASPR2 encephalitides in Asia: A systematic review. *Brain Behav* 2020;10(10):e01793. doi: 10.1002/brb3.1793.
18. Liu X, Shan W, Zhao X, *et al*. The clinical value of (18) F-FDG-PET in autoimmune encephalitis associated with LGI1 antibody. *Front Neurol* 2020;11:418. doi: 10.3389/fneur.2020.00418.
19. Tripathi M, Tripathi M, Roy SG, *et al*. Metabolic topography of autoimmune non-paraneoplastic encephalitis. *Neuroradiology* 2018;60(2):189-98. doi: 10.1007/s00234-017-1956-2.
20. Seniaray N, Verma R, Ranjan R, Belho E, Mahajan H. Metabolic imaging patterns on 18F-FDG PET in acute and subacute LGI1 autoimmune limbic encephalitis. *Clin Nucl Med* 2021;46(1):e27-e28. doi: 10.1097/RLU.0000000000003258.
21. Celicanin M, Blaabjerg M, Maersk-Moller C, *et al*. Autoimmune encephalitis associated with voltage-gated potassium channels-complex and leucine-rich glioma-inactivated 1 antibodies - a national cohort study. *Eur J Neurol* 2017;24(8):999-1005. doi: 10.1111/ene.13324.
22. Uy CE, Binks S, Irani SR. Autoimmune encephalitis: clinical spectrum and management. *Pract Neurol* 2021;21(5):412-23. doi: 10.1136/practneurol-2020-002567.
23. Dubey D, Britton J, McKeon A, *et al*. Randomized placebo-controlled trial of intravenous immunoglobulin in autoimmune LGI1/CASPR2 epilepsy. *Ann Neurol* 2020;87(2):313-23. doi: 10.1002/ana.25655.
24. Irani SR, Gelfand JM, Bettcher BM, Singhal NS, Geschwind MD. Effect of rituximab in patients with leucine-rich, glioma-inactivated 1 antibody-associated encephalopathy. *JAMA Neurol* 2014;71(7):896-900. doi: 10.1001/jamaneurol.2014.463.
25. Thompson J, Bi M, Murchison AG, *et al*. The importance of early immunotherapy in patients with faciobrachial dystonic seizures. *Brain* 2018;141(2):348-56. doi: 10.1093/brain/awx323.
26. Muniz-Castrillo S, Haesebaert J, Thomas L, *et al*. Clinical and prognostic value of immunogenetic

characteristics in anti-LGI1 encephalitis. *Neurol Neuroimmunol Neuroinflamm* 2021;8(3):e974. doi: 10.1212/NXI.0000000000000974.

27. Bastiaansen AEM, van Sonderen A, Titulaer MJ. Autoimmune encephalitis with anti-leucine-rich glioma-inactivated 1 or anti-contactin-associated protein-like 2 antibodies (formerly called voltage-gated potassium channel-complex antibodies). *Curr Opin Neurol* 2017;30(3):302-9. doi: 10.1097/WCO.0000000000000444.