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CASE REPORT

LGI1 Autoimmune Encephalitis: A Cause of Delirium that is Easily Missed

***Harriet Crosby*[1*] *and Tarun Solanki*[2]**

[1]*Trainee Speciality Registrar in Geriatric Medicine, Department of Care of Older People, Musgrove Park Hospital, Somerset Foundation NHS Trust, UK*

[2]*Consultant in Geriatric Medicine, Department of Care of Older People, Musgrove Park Hospital, Somerset Foundation NHS Trust, UK*

***Corresponding author:** *Dr. Harriet Crosby, Department of Care of Older People, Musgrove Park Hospital, Taunton, TA1 5DA, United Kingdom*

Introduction

Leucine-rich glioma inactivated-1 (LGI1) autoimmune encephalitis is a rare but important cause of delirium in adults over fifty. We present two cases highlighting the diagnostic challenges of anti-LGI1 encephalitis.

Case Description

Case 1

A 78-year-old woman presented with acute confusion, short term memory loss and intermittent jerking movements in her right arm. She had a past medical history of pulmonary embolism, anxiety and 3-month history of cognitive decline. Investigations revealed a new hyponatraemia (122 mmol/L (136-145)) with osmolalities consistent with syndrome of inappropriate secretion of antidiuretic hormone (SIADH). She had a normal CT and MRI brain.

She was discharged home and re-admitted two months later with drowsiness and intermittent right arm and face spasms - faciobrachial dystonic seizures (FBDS), and white cell count of 10.7 10^{*}9/L (4-10), CRP 111 mg/L (0-5) and sodium of 121 mmol/L. CT showed an area of low attenuation in the right temporal lobe and a subsequent MRI showed T2 and FLAIR hyperintensities within the same region. Cerebrospinal fluid (CSF) analysis demonstrated normal white blood cells 0 × 10^{*}6/L, raised protein 0.79 g/L (0.15-0.45) and no organisms. Fourteen days after CSF was collected it reported positive LGI1 antibodies. She was initiated on methylprednisolone and levetiracetam followed by plasma exchange. FBDS resolved but she remained cognitively impaired with a modified Rankin Score (mRS) of 5.

Case 2

A 78-year-old male presented to the hospital acutely confused looking for his deceased wife. He had a past medical history of squamous cell carcinoma of the tongue and normal cognitive function. Investigations revealed white blood cells 10.37 10^{*}9/L, CRP 6 and a new hyponatraemia (125 mmol/L). A CT head was normal. MRI brain showed T2 and FLAIR hyperintensities within the medial cortex of left temporal lobe. CSF analysis demonstrated raised white bloods cells 10 × 10^{*}6/L, raised protein 0.77 g/L and no organisms. LGI1 antibodies were identified in the serum and CSF. Initiation with methylprednisolone led to a good recovery with mild residual cognitive impairment and a mRS of 2 (Table 1).

Conclusion

The two cases illustrate the diagnostic challenges of anti-LGI1 encephalitis. Delays in diagnosis, as seen in Case 1, can lead to prolonged cognitive impairment. In contrast, Case 2 benefitted from early treatment initiation based on the suggestive MRI findings.

Anti-LGI1 encephalitis is a rare autoimmune condition, with a reported annual incidence of 0.4-0.83/

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Table 1: Summary of clinical features of LGI-1 autoimmune encephalitis present in both cases compared to the prevalence of clinical features in four other studies of anti- LGI1 encephalitis.

Clinical Features of Anti- LGI1 Encephalitis	Case 1	Case 2	Lai et al., 2010[1]	Sonderen et al., 2016[9]	Wang et al., 2017[2]	Qiao et al., 2021[7]
Number of patients	1	1	57	38	11	117
Subacute cognitive decline	+	+	100%	97%	100%	70%
Psychiatric disorder	+	+	Not mentioned	90%	45.5%	31.6%
Hyponatraemia	+	+	60%	65%	45.5%	65%
Seizure	-	-	82%	90%	54.5%	51.2%
Faciobrachial dystonic seizures	+	-	Not mentioned	47%	72.7%	35.9%
Favourable outcome (mRS 0-2)	-	+	78%	67%	100%	100%

million, most commonly affecting adults over fifty [3]. Its pathophysiology remains largely unknown, but is associated with malignancy in up to 11% of cases [4]. Prompt recognition and initiation of treatment are crucial for improved patient outcomes [5].

Key clinical features include subacute cognitive decline, psychiatric manifestations, hyponatraemia, seizures, specifically FBDS. The presence of FBDS should raise suspicion for this condition, present in 50% of cases, even in the absence of abnormal brain imaging [6]. There is conflicting evidence about sensitivities of CSF and serum LGI1 antibodies, so both samples should be sent for an accurate diagnosis. MRI may show increased T2 and FLAIR hyperintensities in bilateral temporal lobes and hippocampus, but can be normal in up to a third of cases [7]. Electroencephalogram (EEG) may be abnormal is up to two third of cases [8]. FBDS may precede cognitive impairment and is usually responsive to immunotherapy whilst cognition can take months to improve [4]. Relapses are common, affecting up to 35% of patients, and can present up to 8 years after initial disease [9]. Treatment is with immunotherapy agents, including high dose methylprednisolone, immunoglobulins and plasma exchange.

Anti-LGI1 encephalitis should be considered in elderly patients presenting with unexplained subacute cognitive impairment, refractory hyponatraemia and especially if they exhibit FBDS. Performing a lumbar puncture, regardless of brain imaging results, is recommended when there is a high clinical suspicion [10]. Increased awareness among healthcare professionals is vital to ensure early recognition and appropriate management of this challenging condition.

Key Points

- Leucine-rich glioma-inactivated 1 (LGI1) antibody encephalitis is a rare but important form of autoimmune encephalitis (AE) which is treatable with favourable outcomes
- Consider LGI1 AE diagnosis in patients who present with any of the following key features: subacute cognitive decline, psychiatric disorder, refractory hyponatraemia, generalised seizure or facial-brachial dystonic seizures
- Consider MRI, lumbar puncture and antibody serology if high index of clinical suspicion and do not delay immunotherapy treatment

Conflicts of Interest

None declared.

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