Case Report

LGI1 Encephalitis: From Diagnosis to Treatment - A Case Report

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Received: 03-03-2024; **Revised:** 02-04-2024; **Accepted:** 08-04-2024; **Published on:** 15-04-2024.

ABSTRACT

Anti-leucine-rich glioma-inactivated 1 encephalitis is an autoimmune encephalitis which is also considered as a subtype of limbic encephalitis characterised by acute or subacute cognitive impairment, faciobrachial dystonic seizures, psychiatric disturbances and hyponatremia. Here we present a case of a 52 year old male with anti- LGI1 limbic encephalitis along with acute changes in mental status, hyponatremia and faciobrachial dystonic seizure who showed improvement with steroid treatment. Our case demonstrated the need to have high suspicion for LG1 antibody associated encephalitis in patients who present with rapidly progressive dementia along with FBDS which is reversible and treatable. Early treatment with immunomodulatory drugs can reverse the disease. Most importantly we should follow up the patient for a long time to monitor the possibility of recurrence.

Keywords: LGI1 encephalitis, hyponatremia, faciobrachial dystonic seizure.

INTRODUCTION

Anti leucine-rich glioma inactivated 1 (LGI1) encephalitis is a rare autoimmune encephalitis (AE), characterized by acute or subacute cognitive impairment, faciobrachial dystonic seizures, psychiatric disturbances and hyponatremia. It is also considered a subtype of limbic encephalitis usually occurring without any detectable paraneoplastic.[1] It is the most common autoimmune limbic encephalitis (LE) and the second most common autoimmune encephalitis (AE) after anti-N-methyl-d-aspartate receptor (NMDAR) encephalitis.[2] The limbic system is comprised of the hippocampus, hypothalamus, cingulate gyrus, amygdala, and limbic cortex.[3] Leucine-rich glioma-inactivated (LGI) proteins 1–4 have roles in synaptic transmission and myelination and LGI1 is one of the novel autoantigens in autoimmune encephalitis.[4] They are secreted proteins consisting of an LRR (leucine-rich repeat) domain and a so-called epilepsy-associated or EPTP (epitempin) domain.[5] In these cases antibodies usually target voltage-gated potassium channels (VGKC) or glutamic acid decarboxylase and are, therefore, accepted as immunotherapy responsive syndromes.[6] A variety of immunotherapies have been shown to be potentially effective (eg, corticosteroids and intravenous immunoglobulins (IVIg), although no definitive treatment guidelines are available for optimal management, and the choice of the immunosuppressive drug is generally an empirical decision of the treating physician.[7] Most patients affected by anti-LGI1 encephalitis are men between the ages of 50 and 70 years.[2] Here we present a case of a 52 year old male with anti- LG1 limbic encephalitis along with acute changes in mental status, hyponatremia and FBDS who showed improvement with steroid treatment.

CASE REPORT

A 52 year old male patient came with complaints of jerky movements of left upper limb, head turning to one side with irrelevant talk lasting for few seconds, duration of symptom lasted for 1 week. At admission he was conscious, oriented. Initially he was given dual anti-platelet, anti-epileptic and advised to take MRI brain. He had a history of diabetes for past 3 months and hypothyroidism for six years, no history of autoimmune diseases and no family history of dementia or other neurological diseases. The routine laboratory studies were normal except for a decrease in serum sodium level (129mmol/L). His MRI brain (See fig1) showed enlarged left hippocampus with ill defined gyriform pattern of diffusion high signal and low ADC showing T2/FLAIR hyper-intensity. Increased perfusion in ASL images noted in the region showed possibility of post ictal edema. Discrete FLAIR hyper-intensities in bilateral frontal white matter-small vessel ischemic changes. No evidence of focal space occupying lesions. Video EEG showed left fronto temporal slowing. Chest CT and abdomen was normal. In view of new onset seizures, altered behaviour and MRI findings possibility of LG1 encephalitis was considered hence CSF study was done. His CSF study showed total WBC count 2cells/UL, sugar 101mg/dL, protein 45mg/dL, chloride 120mmol/L, ADA 18 U/L, lactate S 34mg/dL. The CSF infectious panel was negative. However, serum VGKC was strongly positive for leucine-rich glioma-inactivated protein 1 (LG1) (see fig2). Serum MOG report was negative. In ward he developed multiple episodes of jerky movements and was treated with oxcarbazepine, valproic acid along with injdexona 4mg. IV Steroid was given for a total of 4 days. He started to improve clinically and was discharged with valproic acid 200mg, oxcarbazepine 300mg and oral prednisolone 40mg. Now he is on a tapering dose of steroid.

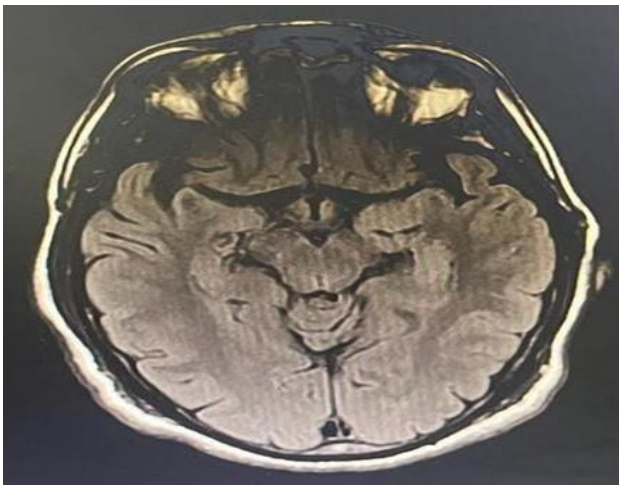

Figure 1: MRI brain showing enlarged left hippocampus with ill defined gyriform pattern of diffusion high signal and low ADC showing T2/FLAIR hyperintensity. Increased perfusion in ASL images noted in the region- possibility of post ictal edema. Discrete FLAIR hyperintensities in bilateral frontal white matter-small vessel ischemic changes

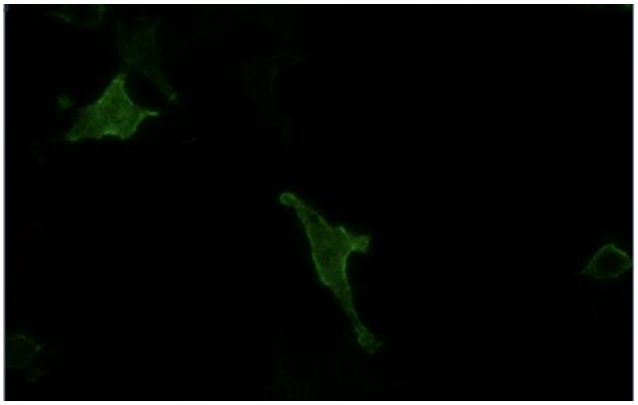

Figure 2: immunofluorescence image showing LG1 strong positive. Results of LG1 antibody in serum (1:10 titer dilution)

DISCUSSION

Our patient presented with jerky movements of left upper limb, head turning to one side with irrelevant talk lasting for few seconds. Investigations revealed that the patient was seropositive for LG1 antibody. He was then treated with immunomodulatory drug. The patient had dramatic improvement to medicine.

LG1 antibody-associated encephalitis is characterised by amnesia, behavioural and psychiatric disturbances, seizures, hyponatremia, also with autonomic dysfunction and sleep abnormalities. Prior to the encephalitis syndrome patients frequently have highly repetitive, unilateral faciobrachial dystonic seizures (FBDS). These are characterised by episodes of posturing involving hemifacial and ipsilateral upper extremity which lasts usually less than 3s.[8]LG1 predominantly occurs in hippocampus and entorhinal cortex.[9]

LG1 which is the target antigen for LG1 antibody mediated limbic encephalitis.LG1 is a secretory synaptic glycoprotein mainly distributed in temporal cortex and cornuammonis 3, a hippocampal subfield that has been implicated in memory coding.[10]In a study of evaluation of cognitive deficits and structural hippocampal damage in encephalitis with LG1 antibody conducted by Carsten et al concluded that anti LG1 encephalitis is associated with cognitive deficits and disability as a result of structural damage to the hippocampal memory system and this damage might be prevented by early immunotherapy.[11]

With cognitive impairment seizure is also one of the major clinical feature in LG1 encephalitis. Disruption of LG1 linked synaptic complex causes abnormal synaptic transmission and epilepsy.[9] FBDS are a recently recognised immunotherapy-responsive disorder. They are characterised by unilateral, short lived dystonic posturing of the upper limb and face accompanied by autoantibodies to leucine-rich glioma-inactivated 1 (LG1) a component of the voltage-gated potassium channel complex (VGKC-complex).[12] LGI1 is the glycoprotein released by presynaptic membrane, and it can interact with presynaptic membrane ADAM metallopeptidase domain 22 and presynaptic membrane ADAM metallopeptidase domain 23 to affect the signal transduction between the synapses by the VGKCs and postsynaptic membrane α-amino-3-hydroxy-5-methyl-4-isoxazole propionate receptors.[1] This combination is necessary for inhibition of signal conduction. LGI1 antibody reduces the interaction of LGI1–ADAM and aggregation of AMPAR (reversibly). Protein gene disruption of LGI1 causes temporal lobe epilepsy.[6] Early recognition and immunosuppressive treatment of FBDS can prevent progression to limbic encephalitis and the development of cognitive deficits. Our case has typical FBDS characteristics. The patient had a remarkable response to given treatment and FBDS was completely under control after treatment with steroid.

Anti-LG1 encephalitis can mimic a variety of other pathologic processes because of its diverse clinical features, presenting a diagnostic challenge for clinicians. The signal pattern of MTL lesion was typical for LE, which usually manifests as T2-FLAIR hyperintensity in the acute phase and mesial temporal sclerosis on follow-up imaging.[2] Here the patient was having T2/FLAIR hyperintensity in the left hippocampal and discrete FLAIR hyperintensities in bilateral frontal white matter.

CONCLUSION

Our case demonstrated the need to have high suspicion for LGI1 antibody associated encephalitis in patients who present with rapidly progressive dementia along with FBDS which is reversible and treatable. Early treatment with immunomodulatory drugs can reverse the disease. FBDS which improved faster than cognitive impairment and hyponatremia. Most importantly we should follow up the patient for a long time to monitor the possibility of recurrence.

Source of Support and Conflicts of Interest

The authors would like to thank the managements of Lourdes hospital and St.Joseph's College of Pharmacy for their support and encouragement. The authors report no conflicts of interest.

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