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CASE REPORT AENSI PUBLICATIONS

Leucine-rich glioma-inactivated-1 antibody encephalitis in a 56-year-old lady with altered mental status and unexplained seizure: A case report

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ABSTRACT

BACKGROUND: Leucine-rich glioma-inactivated 1 (LGI1) antibody encephalitis is a type of autoimmune encephalitis, diagnostic facility for which is not widely available. **OBJECTIVE:** The aim of the study is to describe the diagnostic pearls of a case of LGI1 antibody encephalitis. **METHOD:** Clinical evaluation and laboratory tests including autoimmune encephalitis antibody panel of the patient were done. **RESULTS:** A 56-year-old lady presented with a 10-month history of sleep disturbance and irrelevant talking along with tremulous movements and seizures affecting arms and face (faciobrachial dystonic seizure; FBDS). After excluding the differential diagnoses CSF was studied for autoimmune encephalitis panel of which LGI1 came positive. Following treatment with intra-venous methyl prednisolone and plasmapheresis the seizure was controlled and the patient was doing better. **CONCLUSIONS:** Autoimmune encephalitis needs to be considered and screened for in patients with suggestive clinical presentation as treatment is often rewarding with remarkable clinical improvements. FBDS is a characteristic seizure that points towards the diagnosis of LGI1 encephalitis.

Keywords: LGI1 antibody encephalitis, autoimmune encephalitis, unexplained seizure

INTRODUCTION

Encephalitis with unclear etiology was frequently labeled as ‘viral’ or ‘idiopathic’ when laboratory and imaging facilities were not widely available (Linnoila et al., 2014). With the advancement of medical science, it is now apparent that many of them are actually autoimmune in nature. The prevalence and incidence of autoimmune encephalitis were comparable to infectious encephalitis in developed countries (Dubey et al., 2018). Specific clinical syndromes of autoimmune encephalitis have been defined that are related to antibodies targeting different neuronal surface antigens (Hermetter et al., 2018). Of them, Leucine-rich glioma-inactivated 1 (LGI1) antibodies are associated with a clinical syndrome where faciobrachial dystonic seizure (FBDS), limbic encephalitis, hyponatremia, sleep disorder and myoclonia are characteristic features (Hermetter et al., 2018). Diagnosis of this autoimmune encephalitis is a new avenue for the neurologists of our country as until recently, and antibody detecting tests were not available here. Proper detection and management of these conditions are rewarding as improvements are often dramatic. Here we present our experience of diagnosing and treating a patient with LGI1 antibody encephalitis.

CASE SUMMARY

A 56-year-old lady attended our health facility to evaluate a 10-month history of sleep disturbance and irrelevant talking along with tremulous movements and convulsions for 3 months. Her illness started acutely with insomnia and hallucinations with irrelevant talking that were gradually deteriorating. She was treated with Lorazepam and Quetiapine in variable doses that reduced

her symptom intensity. For the past three months, she was experiencing tremulous movements of both hands, which were fine, symmetrical and brief, usually occurring in action. She also had convulsions affecting arm and face which repeatedly occurred about 8-10 times a day (figure-1: to see the video: scan QR code; used for scientific commitments only with informed consent). It was associated with fall and post-ictal confusion with emotional lability. Convulsions were not associated with unconsciousness, tongue bite, or urinary incontinence. She was treated with Sodium valproate and Levetiracetam but there was no improvement. She noticed difficulty standing from a sitting position and slowness of movement for the last one month. There was no history of fever, unconsciousness, visual disturbance or double vision, difficulty swallowing, nasal regurgitation, bowel or bladder involvement or any sensory symptoms. Her medical records were remarkable for the presence of repeated hyponatremia.

On examination, she was apathetic but cooperative, had slurred speech and rigidity of the limbs along with slow, short stride and reduced arm swing. The rest of the neurological and systemic examinations were unremarkable. The patient obtained a score of 22 out of 30 in the Mini mental state examination (MMSE).

Figure 1: The video of faciobrachial dystonic seizure (FBDS) of the patient can be seen by scanning the QR code (Used for scientific commitments only with informed consent)

Blood counts and baseline biochemistry results were normal with normal renal, hepatic and thyroid function (Table-1). Computed tomography (CT) scan and magnetic resonance imaging (MRI) was unrevealing. Electroencephalogram (EEG) revealed slow background suggesting mild global cerebral dysfunction. Biochemistry and cytology of cerebrospinal fluid (CSF) were normal (glucose 4.62 mmol/L, protein 19.8 mg/dl, cell count 02/cm^3, 100% lymphocytes). CSF culture revealed no growth of any pathogenic organisms. CSF was also studied for autoimmune encephalitis panel including N-methyl-D-aspartate (NMDA), gamma-aminobutyric acid B (GABA B), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), LGI1 and Contactin-associated protein-like 2 (CASPR2) antibodies of which LGI1 came positive.

She received treatment with intravenous methylprednisolone (1g per day for 5 days) followed by plasmapheresis (4 sessions over 7 days). Her seizure was controlled during discharge and now she is under regular follow up.

DISCUSSION AND CONCLUSIONS

A wide diversity of pathologic processes characterized by various antibodies against intracellular proteins and neuronal surface proteins comprises autoimmune encephalitis (Esposito et al., 2019). It emerged as an essential new entity in the last few years. Now it is increasingly recognized as a treatable cause of encephalitis, although population based incidence and prevalence data are lacking in most countries (Ahmad et al., 2012). This is at least in part due to the unavailability of tests detecting neural autoantibodies allowing confirmation of diagnosis and differentiation from other forms of encephalitis (Dubey *et al.*, 2018). Even though the cost is still high and not widely available, these tests can be done in our country.

LGI1 antibody is directed against a neuronal surface protein mainly expressed in hippocampus and neocortex (Irani et al., 2010). The antibodies inhibit the ligand-receptor interaction between LGI1 and ADAM22/23 (Ohkawa et al., 2013). The binding of antibodies disrupt this interaction and interferes in normal function (Petit-Pedrol et al., 2018). Evidence supports the direct pathogenicity of LGI1 antibodies because of their binding ability to native, surface-exposed LGI1 epitopes and excellent response to immune-modifying therapy, including plasma exchange (Irani et al., 2010; Sonderen et al., 2016).

To suspect an etiology like autoimmune encephalitis in a patient presenting with subacute onset of memory deficits, metal status alteration or psychiatric problems, we need at least one of the following features that include new focal central nervous system (CNS) findings, seizures not explained by a previous seizure disorder, CSF pleocytosis or MRI features of encephalitis. In addition, reasonable exclusion of the alternative causes is necessary for such suspicion (Graus et al., 2016). The present case presented with subacute onset of altered mental status and had a characteristic new-onset seizure. As a result, after excluding alternative diagnosis, we sent for panel of CSF antibodies, suspecting an autoimmune cause.

In a recent review of autoimmune encephalitis cases with positive LGI1 antibodies, the main manifestations were FBDS, cognitive disorder, epilepsy, metal disorders, sleep disorder and hyponatremia (Wang et al., 2017). The present case had characteristic FBDS which is very specific to anti-LGI1 encephalitis and pointed towards the diagnosis. In addition, MRI abnormalities were reported in a series of Chinese patients, where abnormalities were found involving hippocampus, basal ganglia and insula (Li et al., 2018). But MRI findings are not diagnostic and may not be present in all cases.

LGI1 encephalitis is treated with steroids and plasma exchange/intravenous immunoglobulin (Bien and Holtkamp, 2017). The effectiveness of this treatment is around 80% and improvement is noted within 2 weeks of treatment. There is an early response in terms of seizure control, but cognition improves slowly. The residual long-term memory deficit may be present in many patients (Rodriguez et al., 2020). In non-responders, second-line treatment consists of Cyclophosphamide or Rituximab (Lee et al., 2016; Renard et al., 2016). Our patient had rapid control of seizures in response to IV methylprednisolone in conjunction to plasmapharesis.

In conclusion, autoimmune encephalitis needs to be considered as the differential diagnosis of patients presenting with subacute onset of altered mental status and unexplained seizure. FBDS is a characteristic seizure that points towards the diagnosis of LGI1 encephalitis. Diagnostic facilities are now available in our settings, and treating these conditions is rewarding.

AVAILABILITY OF DATA AND MATERIALS

The datasets of the current study will be available from the corresponding author on reasonable request.

COMPETING INTEREST

All the authors declare that there is no competing interests.

ETHICS COMMITTEE APPROVAL

The study was approved by the Institutional review committee (IRB) of NINS.

FUNDING

Any authority did not fund the study.

AUTHORS' CONTRIBUTION

MH (1) and MNU were involved in the management of the patient. MH (3) recorded the data and prepared the manuscript. MH (1) and MNU reviewed the manuscript.

List of abbreviation

AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CASPR2	Contactin-associated protein-like 2
CNS	Central nervous system
CSF	Cerebrospinal fluid
EEG	Electroencephalogram
FBDS	Faciobrachial dystonic seizure
GABA B	gamma-aminobutyric acid B
LGI1	Leucine-rich glioma-inactivated 1
MMSE	Mini mental state examination
NMDA	N-methyl-D-aspartate

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