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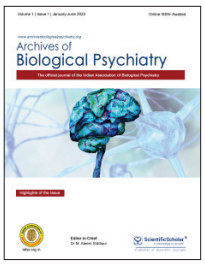

Case Report *Neuropathology*

Anti-LGI1 autoimmune limbic encephalitis presenting with psychiatric manifestations – An under-recognized entity: A rare case report

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ABSTRACT

Leucin-rich glioma-inactivated protein 1 (LGI1) encephalitis is the second most common cause of autoimmune encephalitis; it is a rare and poorly recognized phenomenon. Unlike the typical presentation of LGI1 type of limbic encephalitis in regard to age (30–70 years) as well as gender (M>F), we are describing a case of an adolescent female who presented to us with psychiatric manifestations and initial insignificant neuro-imaging, which led to misdiagnosis and thus delay in her treatment. This case study highlights how the clinician must think ahead of the prevalence patterns and entertain rare possibilities in such atypical cases.

Keywords: Autoimmune, Behavioral changes, Electroencephalogram, Limbic encephalitis, Neuroimmunology

INTRODUCTION

A subtype of autoimmune encephalitis is limbic encephalitis (LE), the inflammatory damage not being limited to the limbic region.[1] The term LE was originally used by Corsellis *et al.* in 1968, and since then, the illness has presented a persistently difficult diagnostic conundrum.[2] Indeed, a prolonged workup of LE is the current norm, with one case series of 20 patients noting the median time from symptom onset to a formal diagnosis being 4 weeks, with a range from 2 to 104 weeks.[3] In 2010, the first description of anti-LGI1 autoimmune encephalitis was published. It is the most frequent cause of immune-mediated LE and the second most common cause of autoimmune encephalitis after anti-N-methyl-D-aspartate receptors encephalitis.[4] Acute to subacute onset of cognitive impairment and convulsions, faciobrachial dystonic seizures (FBDSs), and behavioral disturbances are the hallmarks of LGI1-antibody encephalitis.[5] Improvements in diagnostic methods over time, including serological and neuroimaging, have made it easier to identify and comprehend this mysterious disorder.[6,7] The usual age ranges from 27 to 75 years (median age, 51.5 years), with a male-to-female ratio of 7:3 respectively.[8] This study reports the clinical information, diagnostic process, and therapeutic approach of an adolescent female (unusual age and gender as per the prevalence) with anti-LGI1 encephalitis. We hope to contribute to the growing body of knowledge about this fascinating disorder and emphasize the significance of prompt and targeted management strategies in improving patient outcomes.

CASE REPORT

A 19-year-old female, unmarried student, presented to the hospital along with her parents with chief complaints of forgetfulness, behavioral changes in the form of inappropriate laughter, unprovoked anger outbursts, and anxiety symptoms for the past two months. She had intermittent confusion and short-term memory loss. She had crying spells, generalized body weakness, multiple body aches, and decreased energy levels to carry out routine activities. After a thorough evaluation, the patient was found to have a history of fever, remittent type, not associated with chills and rigor, 1.5 months ago, which lasted for around 10 days, following which her behavioral changes started. Initial investigations showed raised C-reactive protein levels (30.5 mg/dL) with normal leukocyte count. The behavioral changes were followed by a single episode of abnormal jerky body movements associated with stiffening of limbs along with uprolling of eyeballs and clenching of teeth with post-ictal confusion, not associated with bladder/bowel incontinence. This episode occurred 1 month later from the onset of symptoms, during sleep, and lasted for 30 seconds. Ten days after the episode, the patient was started on sodium valproate (1000 mg) and clobazam (10 mg) before she presented to our hospital. The patient's initial medications and investigations were reviewed. The patient had been treated with multiple medications, both from a general physician as well as a psychiatrist, in the form of antidepressants and antipsychotics, written records of which could not be retrieved. As per verbal recall and picture of medication strips shown by the attendants, she was found to be on tablet risperidone up to 2 mg/day for a month along with tablet escitalopram 15 mg/day for 20 days. According to the patient's father, on presentation, she continued with risperidone without any improvement. She also had secondary amenorrhea since the start of the medications. During the hospital stay, she had impulsive outbursts of aggression and self-harm. The neurological examination was unremarkable. On mental status examination (MSE), she had a staring gaze, delayed reaction time, a monotonous tone of speech, and blunt affect. No disorder of thought or perception was elicited. Her cognitive symptoms were assessed which showed impaired recent memory but intact remote memory. Higher mental functions were intact, but the five-minute recall was absent. Her parents and relatives attributed it to malingering. Further routine investigations revealed no significant abnormality. Tablet sodium valproate and tablet clobazam were stopped, as per the neurologist's opinion. Tablet aripiprazole 10 mg was started in view of behavioral changes and considering amenorrhea due to risperidone, which showed only some improvement. Magnetic resonance imaging (MRI) brain done three weeks ago did not reveal any abnormal findings. During the current hospital stay, keeping the possibility of organic etiology in mind and consultation with a neurologist, an MRI brain was repeated. It revealed bulky bilateral medial temporal lobes and hippocampi and showed a T2/fluid-attenuated inversion recovery hyperintense signal, which was suggestive of autoimmune encephalitis. Cerebrospinal fluid (CSF) was sent for complete analysis along with qualitative herpes simplex virus 1 and 2-DNA testing and anti-thyroid peroxidase antibodies; it was all negative. The thyroid profile and serum electrolytes were within normal limits. Ultrasound abdomen was done to rule out ovarian teratoma/tumors, which showed insignificant findings. Electroencephalogram (EEG) showed focal epileptiform activity from the bilateral temporal area. CSF sample was sent for neuroimmunology testing, which revealed a strong positive for leucine-rich glioma-inactivated protein 1 (LGI1), thus confirming the diagnosis of autoimmune LE. The patient received IV solumedrol 1g for five days. Behavior symptoms in the form of anger outbursts and impulsivity started showing improvement third day onwards, and her interactions improved. By the fifth day, her sleep and appetite had improved. The patient was shifted to oral prednisolone 60mg once daily after 5 days of intravenous steroids. She was discharged after seven days of starting steroid therapy and was sent on oral prednisolone. Aripiprazole was continued. Steroids were gradually tapered on follow-up visits in the outpatient department, and there was marked improvement within the next six to eight weeks. Aripiprazole was reduced to 5 mg/day. At eight weeks, the patient continued to show improvement.

DISCUSSION

Leucine-rich glioma-inactivated protein 1 (LGI1) is a protein causing AE, which was originally reported in 2010. It is a subacute condition that manifests as memory loss and epileptic seizures, among other signs of LE.[9] As per the observational study conducted in South India,[10] it is prevalent between the ages of 30 and 80 (median age 60), and patients belonging to the anti-LgI1 subgroup were mostly older males and more likely presented with movement disorder or spontaneous movements and FBDSs which was not the scenario in our patient; making this case report unique.

Up to 84% of the time, changes in brain MRI are discovered,[11] which, in our case, were found on repeat scans despite insignificant findings a few weeks ago. Similar changes in serial MRI findings have been previously quoted.[12] Part of this diagnostic difficulty is due to the heterogeneity of the symptoms of LE and the project of differentiating it from different conditions of LE.[13] It is increasingly recognized as a potentially treatable condition that is often misdiagnosed as dementia/delirium or dissociative disorders; diagnostic delay often worsens outcomes. The subacute development, in days or weeks, of short-term memory deficits is considered the hallmark of the disorder, but this deficit is surprisingly overlooked in some patients, either because they seem to be extremely confused or because other symptoms overshadow it. The EEG almost

always reveals epileptic activity in single or both temporal lobes with focal or generalized slow activity.[14] Our patient did not respond very well to antipsychotics as well as antiepileptics but very well to steroids, as also reported in previous studies.[8,10] Long-term cognitive deficits can be prevented by early management, keeping in mind a suspicion of organic etiology despite atypical presentation. Unlike the typical presentation of the LGI1 type of LE in regards to age (30–70 years) as well as gender (M>F), this case study highlights how clinician has to think ahead of the prevalence patterns and entertain rare possibilities in such atypical cases. In India, the epidemiology of autoimmune encephalitis is unknown. This necessitates greater knowledge of the various forms of autoimmune encephalitis and their differing clinical, biochemical, electrophysiological, and radiographic manifestations. In addition, this has significant therapeutic and prognosis consequences.

CONCLUSION

The present case report detailed the clinical, imaging, and laboratory characteristics of an adolescent female with diverse symptoms. The delay in the recognition of such cases increases the lag in starting appropriate treatment avoiding which shortens the hospital course and prevents long-term neurological consequences.

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