



Anti-LGI1 Limbic Encephalitis—Case Report

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Abstract

Limbic encephalitis is characterized by acute or subacute changes in mood and behaviour, by recent memory changes, seizures and cognitive dysfunction. In this article, the authors present a case report of a 53-year-old woman that resorted to consultation with clinical presentation suggestive of major depressive episode. However, the worsening of symptoms despite treatment and the testimony of seizures put on the trail of another diagnosis. She was admitted in Neurology Service of home area hospital, where she was diagnosed with Autoimmune Limbic Encephalitis (Anti-LGI1 positive). Currently, the patient keeps mensal immunotherapy and daily treatment with levetiracetam and valproic acid, without new seizures. However, she maintains memory and behavioural changes which interfere substantially with her daily functioning. The Family Physician had an essential role not only in the diagnosis of Limbic Encephalitis, but also in helping the patient, through holistic and longitudinal care, to accept and adapt to her illness and related limitations, relieving the suffering.

Subject Areas

Neurology, Psychiatry & Psychology

Keywords

Limbic Encephalitis, Encephalitis, Autoimmune Diseases

1. Introduction

The limbic area of the brain controls many types of activities including memory, learning, and emotions such as sexual desire, love, anger, sadness and jealousy. The main regions of the limbic area include the hippocampus, thalamus, hypothalamus and amygdala [1].

There are several causes of Limbic Encephalitis (LE), and often the underlying cause is not found. Most forms of encephalitis fall into 2 main categories: infectious encephalitis

litis; autoimmune encephalitis. Any infection of the brain can potentially cause an inflammation of the limbic area. But a number of viruses seem to target this area particularly, such as the herpes simplex virus (HSV) [1]. There are broadly two forms of Autoimmune LE: Paraneoplastic Limbic Encephalitis (PLE) and Non-Paraneoplastic Limbic Encephalitis (NPLE). Most individuals with PLE will turn out to have a cancer of the lung, thymus gland, the breast or the testis. NPLE has only been clearly recognised in the last few years. The specific antibody targets may explain the variation of the clinical presentation. Voltage-gated potassium channel complex antibody targets proteins that are tightly linked in with the potassium channels in brain. The majority of these antibodies target LGI1 (leucine-rich glioma inactivated 1). LGI1 is a protein that appears to be important in controlling brain's electrical activity. Antibodies against other protein in the voltage-gated potassium channel/LGI1 complex, such as Caspr2 (contactin-associated protein 2) and contactin-2, have been shown to also cause Autoimmune LE. AMPAR (α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic-acid receptor) and GABABR (Gamma-aminobutyric-acid receptor) antibodies are now known to be less common causes Autoimmune LE. NMDAR (N-Methyl-D-Aspartate Receptor) antibodies usually cause encephalitis involving several brain regions, but it can rarely cause LE [2] [3].

LE is characterized by acute or subacute changes in mood and behaviour, by recent memory changes, seizures and cognitive dysfunction. In addition, electroencephalography (EEG) often shows focal or generalized slow wave or epileptiform activity, and magnetic resonance imaging (MRI) findings reveal hyperintense signals of the medial temporal lobes in T2-weighted or Fluid attenuation inversion recovery (FLAIR) images. However, the definitive diagnosis of encephalitis is pathological, but in practice it is established based on clinical presentation and by changing in analytical and imaging exams [4] [5].

NPLE seems to have a better prognosis than PLE since a substantial proportion of NPLE may have a good response to immunotherapy, particularly if it is promptly initiated. The importance of early correct diagnosis and prompt treatment is emphasized by evidence that patients with a delay in the initiation of immunotherapy are less likely to respond to treatment [6].

The aim of this article was to facilitate recognition of the clinical features of LE, in order to sensitize clinicians to this entity, for rapid diagnosis and prompt treatment initiation.

2. Case Report

Woman, 53-year-old, 9th grade, auxiliary of pharmacy. Pathological Background: Anxiety and Sleep Disorders and Obesity. Chronic medication: alprazolam 0.5 mg bid and trazodone 50 mg id.

The patient resorted, in January 2014, to her Family Health Unit with clinical presentation suggestive of major depressive episode, referring as psychosocial stress factors work overload and conflicts with her husband. Clinical examination without altera-

tions. It was prescribed hemogram and thyroid function, both normal, and venlafaxine 75 mg id, alprazolam 0.5 mg bid and ethyl loflazepate 2 mg in SOS.

In February 2014, the patient referred worsening of symptoms, particularly in memory and “mind blocked”. During the appointment, the patient had stereotyped movements of the hands and mouth, without perception of these movements, no response to verbal stimulation or memory during this period (10 seconds). Brain computed tomography (CT) was requested, which was normal, and EEG recorded a crisis with paroxysmal activity with left frontotemporal predominance. It was requested urgent evaluation by Neurology in the home area Hospital, where she was admitted in that same day.

The further study (**Table 1**) revealed alterations suggestive of Autoimmune LE (Anti-LGI1), having performed inpatient treatment with metilprednisolone and intravenous immunoglobulin.

During hospitalization, the patient presented uninhibited behaviour, with suggestive and seductive speech partially improved with the introduction of valproic acid and quetiapine.

She also presented confabulatory speech and visual hallucinations: “drops of water falling from the ceiling” and “figures behind her back.” The assessment by Neuropsychology revealed mnesic dysfunction and frontal deficits.

Currently, the patient keeps mensal immunotherapy and daily treatment with levetiracetam and valproic acid, without new seizures. However, she maintains memory and behavioural changes, which interfere substantially with her daily functioning, being not capable to return to her habitual job.

3. Discussion

Anti-LGI1 LE is a *rare* neurological disorder, with few cases published in scientific literature.

Table 1. Exams performed during the internment in Neurology Service of home area Hospital.

Exams	Results
<i>MRI</i>	Figure 1 —“hypersignal and expansion of the temporal amygdala and left hippocampal head, turning up the cortex of the adjacent temporal pole... changes suggestive of post-critical edema or subacute encephalitis...”
<i>Video-EEG</i>	“Electrophysiological changes that suggest epilepsy with focal seizures starting from deep focus, probably temporal or frontal, uncertain lateralization, most likely left”
<i>CT Brain Angiography</i>	Normal
Immunological study	Anti-LGI1 antibody positive
Blood, urine and cerebrospinal fluid analysis	
Endoscopic exams of digestive tract	Exclusion of neoplastic lesions and viral infections
Imaging Studies	

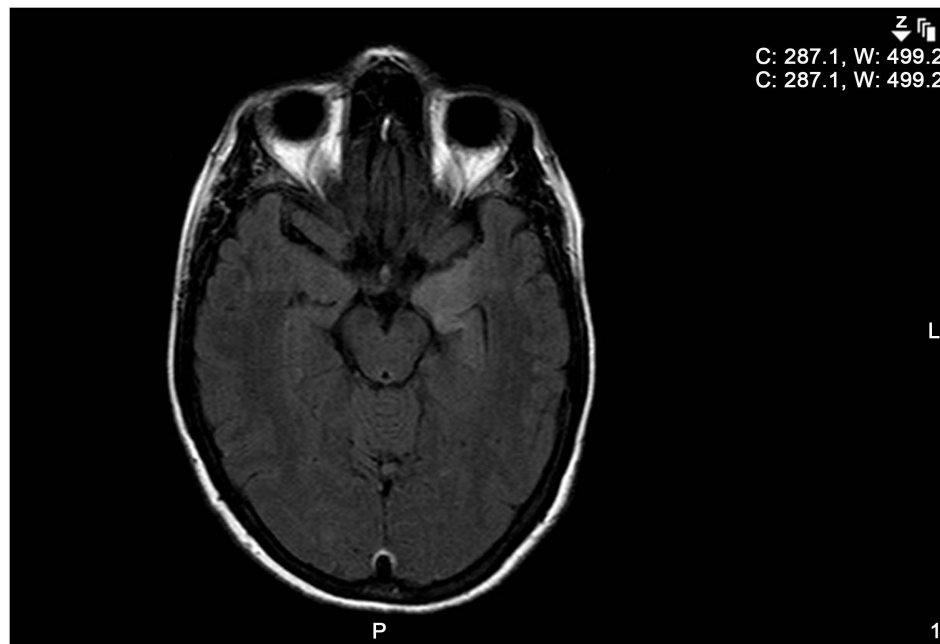


Figure 1. Axial fluid attenuation inversion recovery (FLAIR) MRI of the brain showing a bright signal temporal amygdala and left hippocampal head, turning up the cortex of the adjacent temporal pole, consistent with limbic encephalitis (arrow).

In this case report, the prompt diagnosis of LE was possible due to the testimony of stereotyped movements made by the patient, who never revealed changes in objective examination, raising the suspicion of a possible organic etiology. In fact, the clinical presentation manifested by the patient could easily be confused with an anxiety or depressive disorder. In addition, the patient presented personal psychiatric background and psychosocial stressors that would justify several of the presented symptoms.

Despite the rapid diagnosis of LE and the prompt initiation of treatment with methylprednisolone and intravenous immunoglobulin, clinical improvement was incomplete. The patient had a highly responsible job in a local pharmacy for more than 20 years. However, the mnemonic dysfunction and the frontal deficits maintained by the patient, barred the return to her work activity, which was a difficult situation to accept by the patient. The Family Physician had an essential role not only in the diagnosis of LE, but also in helping the patient, through holistic and longitudinal care, to accept and adapt to her illness and related limitations, relieving the suffering.

4. Conclusions

The initial stages of the LE may be similar to a depressive or anxiety disorder. A high level of suspicion is required in order to achieve the correct diagnosis.

In the recent years, it has been increasingly recognised that in a group of LE antibodies are directed against the scaffolding protein LGI1, which is part of the voltage gated potassium channel (VGKC) complex on neural synapses. Patients present with seizures and subacute history of neuropsychiatric symptoms, including psychosis and changes

in memory, cognition, and behaviour. Faciobrachial dystonic seizures can be observed, which are highly characteristic for LGI1 encephalitis. MRI shows medial temporal abnormalities in more than half of the cases. Cerebrospinal fluid evaluation is usually normal. Hyponatremia is frequently associated and may confuse the initial diagnosis. Early recognition and prompt initiation of immunotherapies are of great importance. The clinical improvements often correlate with the antibody levels [7].

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