CASE REPORT

LGI1 encephalitis: a disease of jerks and confusion

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SUMMARY

Limbic encephalitis is a group of immune-mediated disorders that includes the classic paraneoplastic encephalitic syndrome and the recently described non-paraneoplastic autoimmune encephalitis most of which target the extracellular antigens. We present a case of 70-year-old man who presented with rapidly progressive cognitive decline and refractory faciobrachial dystonic seizures and demonstrated seropositivity for leucine-rich, glioma-inactivated protein 1 antibodies. After immunomodulation, the patient had dramatic improvement in the cognitive functioning and in seizure control.

BACKGROUND

Limbic encephalitis (LE) is conventionally associated with antibodies triggered by neoplasms with clinical presentation of rapidly progressive cognitive decline, seizures and psychiatric disturbances. A new group of autoimmune encephalitis which is not associated with malignancy and is characterised by antibodies that target extracellular domains of neural antigens have been described. These target the neuronal surface or synaptic proteins and include NMDA, α -amino-3-hydroxy-5-methylisoxazoleproionic acid and γ -aminobutyric acid B receptors. Leucine-rich glioma-inactivated protein 1 (LGI1) and contactin-associated protein-like 2 are recently described target proteins which were previously grouped under antibodies against voltage-gated potassium channel complex. We describe a case of LGI1 antibody-associated encephalitis which responded excellently to immunotherapy.

CASE PRESENTATION

A 70-year-old man presented with progressive cognitive decline and behavioural changes including apathy, episodes of confusion and anxiety for the previous 2 months. He also reported of episodes of sudden turning of the head and posturing of the left hand which lasted for few seconds to minutes. These episodes occurred 5–10 times in a span of 1 hour and progressively the frequency increased to 15–20 per hour. The neurologic examination and neuropsychological evaluation confirmed that patient had significant dysfunction of frontal and temporal lobar functions.

The patient's clinical condition had progressively deteriorated from a fully functioning bank official to now being fully dependent for all his activities of daily living (ADL). Patient was given a trial of three antiepileptic drugs for the repeated episodes of head turning with hand posturing, but despite these, the frequency of these episodes increased.

His behaviour also progressively worsened with increasing confusion, agitation and aggression.

INVESTIGATIONS

The routine laboratory studies were normal except for persistent hyponatremia. He underwent MRI of the brain which did not reveal any abnormality. CSF analysis revealed five cells all lymphocytes with normal glucose and protein. Screening for herpes simplex virus 1 and 2, *Cryptococcus* and *Mycobacterium tuberculosis* was negative. Positron emission tomography (PET) of the whole body and brain revealed no evidence of malignancy. The basal ganglia showed evidence of hypermetabolism bilaterally. (figure 1).

DIFFERENTIAL DIAGNOSIS

In view of the clinical presentation of rapidly progressive dementia with antiepileptic drug refractory faciobrachial dystonic seizures, a working diagnosis of LE was kept and extensive diagnostic testing was undertaken to search for occult malignancy. Whole body and brain PET scan also was performed, but it did not show any evidence of neoplasm. CT scan of the chest, abdomen and pelvis did not reveal any evidence of cancer. Serological markers for autoimmune encephalitis were also absent. Patient serology for LGI1 antibody by indirect immunoassay was positive.

TREATMENT

The patient was started on immunomodulation in the form of intravenous methylprednisolone pulse followed by a 5-day (400 mg/kg/day) course of intravenous immunoglobulin (IVIg). FBDS remitted after the institution of immunomodulatory drugs. He also had improvement in his cognitive functions. The patient was put on maintenance dose of mycophenolate mofetil and is currently doing well.

OUTCOME AND FOLLOW-UP

After the institution of immunomodulatory drugs, the FBDS remitted. He also had improvement in his cognitive functions and started doing his ADL independently. The patient was put on oral steroids and maintenance dose of mycophenolate mofetil and is currently doing well.

DISCUSSION

Our patient presented with rapidly progressive cognitive decline and refractory FBDS which disabled the patient. Investigations revealed that the patient was seropositive for LGI1 antibody, and he was treated with immunomodulatory drugs after which he had dramatic improvement.

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Figure 1 Transaxial fused PET/CT images reveal hypermetabolism in the bilateral basal ganglia.

LGI1 antibody-associated encephalitis is usually characterised by amnesia, behavioural and psychiatric disturbances, seizures, hyponatremia and, in some cases, autonomic dysfunction and sleep abnormalities. One of the characteristic features of patients with encephalitis with LGI1 antibodies is the presence of FBDS. These are characterised by episodes of posturing involving hemifacial and ipsilateral upper extremity which lasts briefly (usually less than 3 s). Irani *et al*¹ postulated that FBDS usually precedes the LGI1 antibody LE and is a specific clinical marker for the presence of this form of encephalitis. It is still not clear if FBDS is a type of seizure as it is usually unaccompanied by EEG correlate. The recent literature suggests that it is a form of subcortical seizure arising as a result of abnormal basal ganglia functioning based on studies where there was evidence of abnormal basal ganglia metabolism on FDG-PET studies. Flanagan *et al*² conducted a retrospective study and studied the MRI findings of patients of LGI1 encephalitis and reported a radiological correlate to help diagnosis of FBDS. Our patient also presented with antiepileptic drug refractory FBDS along with cognitive decline which responded only to immunomodulation. The

duration of these episodes in our patient varied from few seconds to minutes. A prolonged duration reaching up to minutes has been described by Irani *et al*.³ There was evidence of hypermetabolism in bilateral basal ganglia, although MRI of the brain was normal. The patient in the present case presented with rapidly progressive dementia, FBDS and hyponatremia, but had no sleep disorder or autonomic dysfunction. The patient's diagnosis was confirmed by the presence of seropositivity for LGI1 antibodies in the blood. As reported in the literature, even after extensive evaluation, there was no evidence of malignancy in our patient. After the institution of steroids and IVIg, our patient had dramatic recovery in his cognitive functions, and also the FBDS remitted.

Our case demonstrates the need to have high-index suspicion for LGI1 antibody-associated encephalitis in patients who present with rapidly progressive dementia along with FBDS as early treatment with immunomodulatory drugs can reverse the disease.

Learning points

- ▶ LGI1 encephalitis presents with rapidly progressive dementia and FBDS.
- ▶ In all patients of rapidly progressive dementia, potentially reversible aetiology like autoimmune encephalitis should be ruled out.
- ▶ Timely diagnosis and intervention can lead to the total reversal of the manifestations.

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