Case Report: Psychiatric and Behavioral Disturbance in LGI1- Antibody Encephalitis

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Background

Autoimmune Limbic Encephalitis (ALE) is a clinical syndrome presenting with rapid neuropsychiatric decline and cognitive deficits (1). Leucine-rich glioma-inactivated 1 (LGI-1) antibody encephalitis is a rare form of ALE, in which an anti-neuronal antigen or anti-synaptic surface protein forms, causing inflammation of the limbic system [2,3].

- The cognitive profile of LGI-1 antibody encephalitis includes deficits in short-term memory, spatial orientation, and psychiatric and behavioral symptoms.
- There is a male predominance and the age of onset is often over 60 [1]. Associations with thymoma have been reported, but LGI-1 encephalitis is rarely associated with a tumor (1). Hyponatremia is also a common feature [4]. In cases of ALE such as LGI-1 antibody encephalitis, the inflammation of medial temporal lobes may be observable on MRI; however, this finding is neither sensitive nor specific [1].

Diagnostic criteria:

1) Subacute onset (rapid progression of < 3 months) of working memory deficits, seizures, or psychiatric symptoms suggesting limbic system involvement

2) Bilateral brain abnormalities on T2-weighted FLAIR MRI, highly restricted to the medial temporal lobes

3) Reasonable exclusion of other alternative causes

4) At least one of the following:

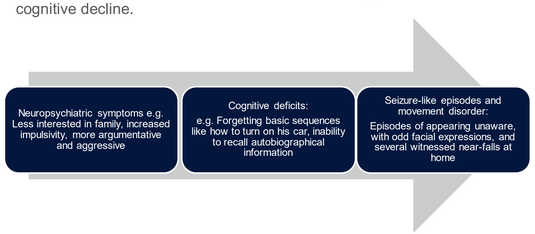
- CSF pleocytosis (WBC>5cells/mm^3)
- EEG with slow-wave activity involving the temporal lobes[5]\

Treatment includes steroids, plasmapheresis, immunotherapy, tumor resection (if applicable), and symptomatic management.

- Treatment outcomes:
  - Seizures usually completely resolve.
  - Residual cognitive and memory impairment is common
  - At least one relapse occurs in 12.5-35.3% of cases [4]

Case

A 68-year-old man with no past psychiatric history presented to the Ontario Shores Centre for Mental Health Sciences due to aggressive behaviors and cognitive decline.



An EEG was performed at another hospital, which did not detect seizure activity. It was initially hypothesized that his behavioral concerns and cognitive decline were secondary to a major neurocognitive disorder.

Assessment

Initial Impression

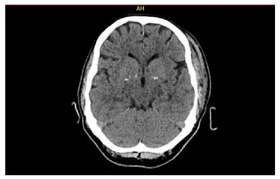
- MMSE score at admission was 20/30 and MOCA score was 17/30. In the first few days, some odd facial movements were noted. The patient had trouble recalling autobiographical information and establishing a timeline of events. At some times, his thought content was odd and delusional or with confabulation.
- The patient was increasingly aggressive, exit-seeking, and intrusive with staff and co-patients. He displayed word-finding difficulty and had trouble following instructions, becoming disoriented on the unit often. He had several episodes where he appeared to space out and then would say something nonsensical/unrelated to the situation he was in. As his behavioral issues worsened, he exhibited delusional thought content, grandiosity, and several near-falls.
- Neuropsychological Assessment several weeks later revealed impairment in orientation, verbal and visual memory, semantic fluency, executive switching, and sustained attention.

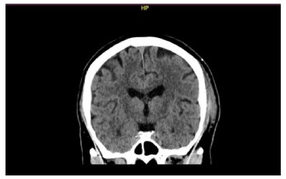
Differential diagnoses

- Infectious (HSV 1/2, VZV, Enterovirus, WNV, Syphilis, TB, Bartonella henselae)
- Autoimmune (antibodies: Hu, CRMP5/CV2, Ma2, NMDAR, AMPAR, LGI1, CASPR2, GAD65, GABA-BR, DPPX, mGLUR5, AK5, Neurexin-3 alpha
- Tumors, including thymoma, small cell lung cancer, testicular tumors, breast cancer, Hodgkin Lymphoma, glioma
- Lewy body dementia, vascular dementia, temporal lobe vasculopathy

Labs and testing

- The only abnormal lab finding on his initial workup was hyponatremia, with a sodium of 129.
- MRI brain with GAD showed atrophy of the temporal lobe, and EEG confirmed episodes of facio-brachial dystonic seizures.
- CT chest was negative for malignancy including thymoma.
- CT brain without contrast was normal
- Further testing showed LGI1-antibodies in serum





Discussion

Treatment Plan

- The patient received a course of steroids without improvement
- He was then treated with IVIG alone, and did start to show moderate improvement.
- Plasmapheresis was not done due to issues with central line.
- Later he received 2 doses of Rituximab 2 weeks apart.
- Cognitive and behavioral optimization strategies were encouraged to improve performance.

Follow-up

- After treatment with Rituximab, the patient still had difficulty recalling autobiographical information but successfully recalled information he previously could not.
- Thought content was logical and goal-directed.
- MRI and EEG were normal. Seizures ceased, as confirmed by EEG.
- Hyponatremia resolved
- Neuropsychological reassessment revealed impairment in attention, language, and executive switching ability. Processing speed and orientation also improved but were variable.
- MMSE score improved to 26 and MOCA score had improved to 23. Patient had a notable improvement in executive functioning. his insight was improved and he was less preoccupied with previous delusional thoughts
- 3 months after initial diagnosis and beginning treatment, his MOCA score was 28.
- Family and staff observed improved cognition and behavior, and he was discharged home.
- Treatment outcome was consistent with the literature regarding post-treatment functioning in patients with autoimmune encephalitis

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