An Adult Man with Altered Mental Status, Bizarre Behavior, and Abnormal Limb Movements

Stephen V. Marcoux, MD; Ha N. Lam, MD; Christine E. Petrich, MD†; and Nicholas M. Ray, DO

A man in his 30s with a previous diagnosis of syndrome of inappropriate antidiuretic hormone secretion (SIADH) of unknown etiology and no known prior medical or psychiatric history presented to the emergency department with altered mental status, agitation, bizarre behavior, and abnormal limb movements for the past 6 weeks. He was subsequently admitted to internal medicine for evaluation. The patient was oriented to person and intermittently oriented to place. His review of systems was otherwise negative. The patient had no personal or family history of psychiatric or neurologic disease. His physical examination was notable for intermittent limb flailing. The patient’s initial testing revealed no evidence of neurologic, cardiac, pulmonary, hepatic, or renal disease. Psychiatry was consulted on the day of admission for assistance with the patient’s agitation, hallucinations, and altered mental status.

From collateral sources, it was learned that the patient had previously experienced behavioral disturbances and abnormal limb movements, leading to a hospital admission 9 months prior. During that admission, the patient had undergone extensive testing of his hyponatremia, with serum and urine chemistries consistent with SIADH. Before that hospitalization, the patient’s wife reported that he was employed and had no cognitive, psychiatric, or medical impairment. After the first discharge, the patient continued to have intermittent disorientation, hallucinations, and aggression, leading to unemployment and removal from his home. The patient also endorsed anxiety and depressive symptoms, for which he had initially received fluoxetine and anxiolytics without improvement. According to his wife, the patient had exhibited worsening agitation and disorientation for 6 weeks prior to the current admission.

Upon this second presentation to the hospital, the patient’s initial sodium was 127 mmol/L, which was similar to the value at his previous discharge. Other laboratory abnormalities included mildly elevated liver enzymes and lipase, but all other results, including nutritional, metabolic, hematologic, heavy metals, toxicology, and infectious panel, were negative. Tests for Huntington’s disease and Wilson’s disease...
were also negative. Computed tomography scans of his head, chest, abdomen, and pelvis, along with a magnetic resonance imaging (MRI) scan of his brain, were negative for an acute process. Specifically, the brain MRI revealed no enhancements or lesions. Lumbar puncture revealed no indication of infection or oligoclonal bands. A 30-minute electroencephalogram (EEG) revealed diffuse, nonspecific cerebral slowing.

During the first 9 days of hospitalization, the patient demonstrated disorientation, tangential thinking, intermittent auditory and visual hallucinations, and abnormal limb movements, which are atypical of neurologic etiology. Executive function testing was completed using the Exit 25, CLOX 1, and CLOX2 tests, with scores of 14 (normal is below 5), and 10 and 12 (normal is 15), respectively, consistent with cognitive impairment.1,2 The patient was started on a low dose of risperidone with subsequent titration up to 1 mg twice daily. Given his prolonged altered mental status with acute psychiatric changes, serum autoimmune antibodies were drawn. On day 10 of hospitalization, the patient was transferred to the inpatient psychiatry service for continued management of behavioral disturbances. From days 10 to 17 of the hospital stay, the patient exhibited disorientation, intermittent auditory and visual hallucinations, and intrusive behavior. The risperidone was discontinued and the patient was given haloperidol at a dose of 5 mg twice daily, which was then switched to quetiapine at a dose of 200 mg at night, which better managed his behavior.

**D I A G N O S I S**

**Anti-LGI1 Autoimmune (Limbic) Encephalitis**

On hospital day 17, serum autoimmune antibody testing revealed positive voltage-gated potassium channel antibodies at 741 pmol/L (reference level, 88 pmol/L), with positive titers of anti–leucine-rich glioma inactivated 1 (LGI1) at a ratio of 1:40 (reference level, 1:10). The patient was diagnosed with anti-LGI1 autoimmune (limbic) encephalitis. Neurology was consulted for further treatment. After a course of intravenous (IV) steroids, plasmapheresis, and IV immunoglobulin, the patient ultimately had resolution of hallucinations and agitation with residual intermittent confusion and mild cognitive disability. The patient was discharged to a nursing facility after a 31-day hospital stay.

**DISCUSSION**

Encephalitis has a hospitalization rate of 7.3 per 100,000 people in the United States, with autoimmune encephalitis found in 17% to 32% of hospitalized cases.3 In autoimmune encephalitis, autoantibodies attack either intracellular antigens, antigens attached to the cell membrane, or synaptic structures associated with brain cells.4,7 LGI1 is a synaptic protein that can induce limbic encephalitis when attacked by the autoimmune antibody anti-LGI1 5,7 a voltage-gated potassium channel (VGKC) antibody.9,10 One large study identified anti-LGI1 antibodies as the etiology in 0.1 per 100,000 encephalitis cases,3 with other studies identifying VGKC antibodies as the etiology in only 3.4% of cases.5,7,8 Typical symptoms of autoimmune encephalitis include irritability, depression, hallucinations, delirium, dyskinesias, catatonia, and seizures. Laboratory and imaging evaluations typically find cerebrospinal fluid pleocytosis and oligoclonal bands, hyperintensity within medial temporal lobes on MRI, and diffuse slowing or seizure activity on EEG.5,8,11,13 Symptoms specific to anti-LGI1 encephalitis involve confusion, psychosis, and memory loss in nearly 100% of cases; faciobrachial tonic seizures in 40% of cases; and uniquely hyponatremia in 60% of cases.4,5,7 Anti-LGI1 encephalitis involves cerebrospinal fluid abnormality in 41% of cases, MRI findings in 84% of cases, and EEG abnormality in 76% of cases.5,7 Treatment of anti-LGI1 autoimmune encephalitis includes IV immunoglobulin, steroids, plasmapheresis, or other immunosuppression.5,7,12 Full recovery is seen in roughly 24% of cases, with mild disability in 54% of cases;7 death occurs in approximately 6% of cases.7

The diversity of symptom profiles and etiologies of autoimmune encephalitis often impedes its early diagnosis and management. In this case, no clear-cut etiology of the patient’s symptoms could be identified, and given the persistent hallucinations and agitation, a primary psychiatric diagnosis had to be considered. Imaging did not assist in diagnosis, as MRI revealed no specific organic etiology, and EEG revealed
nonspecific diffuse slowing. The sudden onset of hyponatremia with behavioral and mood disturbance 9 months prior was likely the first manifestation of an encephalitic process, especially without discovery of an etiology of SIADH. This suggests the utility of more frequent use of serum autoimmune antibody panels in patients with unique constellations of symptoms underlying an altered mental status.

Interestingly, mid-level dosing of quetiapine better assisted with the patient’s behavioral disturbance compared with haloperidol and risperidone during the encephalitic infection. Better control of psychosis with mid-level quetiapine dosing rather than with haloperidol or risperidone is unusual in primary psychotic disorders. Perhaps sedation rather than heavy dopaminergic antagonism better assisted with the neurochemical dysregulation of encephalitis. Further study would be beneficial, as evidence for preferential treatment of psychiatric symptoms during encephalitis is limited.

CONCLUSION

This case highlights the necessity of including encephalitic pathology and other reversible causes early in the differential of psychiatric presentations, especially in cases with co-occurrence of unexplainable neurologic manifestations and metabolic abnormalities, specifically suggesting the earlier use of serum autoimmune antibody panels in diagnosis. The case also suggests quetiapine as a possible preferential treatment for behavioral disturbance during encephalitic infection. Most importantly, early recognition and treatment of autoimmune encephalitis can drastically alter a patient’s overall recovery.

REFERENCES