Voltage-Gated Potassium Channel/LGI1 Antibody–Associated Encephalopathy May Cause Brief Psychotic Disorder

To the Editor: Voltage-gated potassium channel (VGKC) antibody–associated encephalopathy has been identified as a potentially immunotherapy-responsive form of limbic encephalitis.[1] A recent study showed that the target antigen in this condition is in fact LGI1, a secreted neural protein that functions as a ligand for 2 epilepsy-related proteins, ADAM22 and ADAM23.[2] Limbic encephalitis is typically a paraneoplastic syndrome with a poor prognosis. Thus, identifying those patients with potentially reversible symptoms is important. Patients typically present with symptoms of hippocampal and temporal lobe dysfunction such as memory loss, confusion, and seizures.[1,3–5]

Here, we report the case of a patient with VGKC-associated encephalopathy who presented with a brief psychotic disorder and responded well to subsequent immunotherapy.

Case report. Mr A, a 25-year-old toolmaker, developed a brief psychotic disorder over a period of 4 weeks. Initially, he showed an

increase in energy, drive, and speech production. His concentration was reduced, but there were no specific problems with memory. The patient felt that symbols on TV had a specific meaning for his life and felt observed. Having read a flier for an HIV clinic, he subsequently developed the delusional belief that he was infected and demanded spinal cord transplantation on admission to the psychiatric ward in December 2008. He reported feelings of reference but no hallucinations. The patient also described odd tingling sensations, slight dizziness, and a feeling like being stabbed in the back.

The neurologic examination results were completely normal. Magnetic resonance imaging (MRI) showed a singular white matter lesion in the right frontal white matter without gadolinium enhancement, which was interpreted as insignificant or as an artifact by the consultant neuroradiologists. Thus, the patient was referred to the psychiatric unit for treatment of brief psychotic disorder. On day 4 of admission, additional difficulties with aphasic symptoms and spatial orientation led to a cerebrospinal fluid (CSF) analysis, which showed lymphocytic pleocytosis (cell count = 72/μL; total protein = 470 mg/L; albumin quotient = 5.6; no quantitative immunoglobulin G [IgG], IgA, or IgM synthesis; IgG index = 0.53; oligoclonal IgG bands were negative).

Subsequently, the patient was transferred to the neurologic intensive care unit (ICU). Antibiotic and antiviral intravenous treatment with ceftriaxone, ampicillin, and acyclovir led to no improvement. Mr A deteriorated, developed increasing mutism and akinesia, suffered from a series of complex partial seizures, and developed an asystole that required emergency cardiac pacemaker implantation.

Extensive immunologic and microbiological investigations produced normal results except for positive anti-VGKC antibodies (187 pM; normal range, 0–100 pM). Follow-up CSF analyses consistently showed a slight lymphocytic pleocytosis (6–38 cells/μL), a transient increase in lactate and impairment of the blood-CSF barrier (total protein = 704 mg/L), and no intrathecal synthesis of immunoglobulins. On the basis of these findings, the diagnosis of limbic encephalitis was made and immunotherapy with intravenous immunoglobulin (Octagam), intravenous methylprednisolone (500 mg/d), and 5 sessions of plasmapheresis over 9 days was initiated. This resulted in a slow but steady recovery over a period of about 10 weeks.

Mr A was then transferred to a specialized hospital for neuropsychiatric rehabilitation. He remained on immunosuppressive therapy with prednisolone 60 mg/d and azathioprine 25 mg/d and subsequently achieved full psychiatric and neurologic remission including normal results on extensive neuropsychological testing after approximately 11 months. His antibody titers decreased to 152 pM 5 months after treatment and to 135 pM 6 months after treatment (reference range, 0–100 pM). The initial electroencephalogram (EEG) after the patient's transferral to the neurologic ICU showed a generalized slowing with baseline theta activity and intermittent bitemporal spikes. The EEG findings improved significantly following therapy, with only discrete intermittent generalized slowing and no spikes at 1.5-year follow-up. A follow-up MRI was not initiated because the initial MRI report was judged to be normal by consultant neuroradiologists in the acute phase of the disease.

To our knowledge, this is the first report of a VGKC-associated encephalopathy causing a presenting clinical syndrome of brief psychotic disorder and showing good response to immunotherapy. The clinical presentation of the first 5 weeks was that of a brief psychotic disorder, but indicators of an organic cause slowly accumulated as the disease progressed.

CSF analysis is not a part of the routine investigations in patients with brief psychotic disorder in most countries. The clinical presentation of our case is well compatible with the diagnosis of brief psychotic disorder, and there were no relevant neurologic findings on initial presentation. Therefore, this case illustrates that when typical causes of brief psychotic disorder such as drug abuse are absent, CSF and blood samples should be tested for VGKC and other neuropil antibodies. This notion is further supported by evidence that up to 80% of patients with VGKC antibody–associated encephalopathy may improve with specific treatment.[6]

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