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IMMUNOTHERAPY-RESPONSIVE CHOREA AS THE PRESENTING FEATURE OF LGI1-ANTIBODY ENCEPHALITIS

We describe 2 patients who presented with subacute chorea as the initial feature of autoimmune encephalitis associated with antibodies against leucine-rich glioma inactivated 1 (LGI1), a component of the voltage-gated potassium channel (VGKC) complex.

Case 1. Case 1 was a 77-year-old man who presented with apathy and continuous choreiform movements in the left leg, spreading over 8 weeks to all limbs, primarily the legs and head. A month later he presented to the medical team who treated him for mild hyponatremia without improvement of the chorea. CT and MRI did not show any abnormality. Two weeks later, he developed progressive memory loss followed by confusion and disorientation. On this occasion, his sodium was 118 mmol/L and corrected by fluid restriction and demeclocycline with dramatic improvement in his conscious state. However, his chorea persisted (video on the *Neurology*® Web site at www.neurology.org) and cognitive assessment revealed anterograde amnesia evident by delayed story recall (fifth centile), and executive dysfunction evident by reduced letter fluency and difficulty with proverbs. There were no seizures and no other neurologic signs. EEG showed mild slowing without epileptiform or lateralizing activity. Other routine tests and CSF were normal; antinuclear, antiphospholipid, antiendomysial, NMDAR, CV2/CRMP5, and other paraneoplastic antibodies were negative. Seven years before he had 2 generalized convulsions, and 3 years before was treated successfully for prostate cancer (latest PSA 1.7 μg/L). Whole body FDG-PET was normal. While genetic testing was being considered for late-onset hereditary chorea, VGKC complex antibodies were detected at 407 pM (normal <100 pM), with LGI1 but not CASPR2 immunoreactivity. This finding prompted treatment with prednisolone (60 mg alternate days), followed by 5 days of IV immunoglobulin. The chorea stopped within 2 weeks of treatment and his sodium normalized without other intervention. Six weeks after immunotherapy, there was significant improvement in delayed story recall (85th centile) with residual executive dysfunction as evident by poor performance in letter fluency, Stroop, and Trail Making tasks. Clinical improvement was accompanied by a reduction in antibody titers, which peaked at 655 pM and fell to 231 pM 16 weeks postimmunotherapy.

Case 2. Case 2 was a 60-year-old man who presented with a 5-month history of apathy and troubling chorea involving his head and all limbs. CT brain was normal and blood tests showed a sodium level of 125 mmol/L. Initial tests were negative for Huntington disease, ASOT, NMDAR, and antinuclear and paraneoplastic antibodies. Two months after his initial presentation, he developed progressive memory loss, frequent temporal lobe seizures, and 2 generalized seizures. Brain MRI showed high T2/fluid-attenuated inversion recovery signal within both mesial temporal lobes. CSF analysis showed 16 white cells with normal protein. EEG showed diffuse slowing. VGKC complex antibodies were elevated at 1,915 pM with specificity for LGI1. CT chest was normal. Treatment with IV immunoglobulin and prednisolone (100 mg alternate days) produced an improvement in the chorea and cognition, with no further seizures reported. He had residual retrograde amnesia with normal performance on delayed story recall but impaired executive function (reverse digit span = 3; Stroop Task 4th centile). At 2 years, his MRI normalized and VGKC complex antibodies were undetectable.

Discussion. VGKC complex antibodies have been associated with neuromyotonia, Morvan syndrome, limbic encephalitis, and certain forms of epilepsy.[1] It is now clear that the antibodies bind to proteins complexed with VGKC, and antibodies to LGI1, and to a lesser extent CASPR2, account for many CNS presentations.[2,3]

Although extrapyramidal symptoms have been reported with VGKC complex antibodies,[4] in our patients chorea was the presenting complaint and appeared to predate limbic encephalitis by several weeks. Whether LGI1 is the sole antigenic target in these patients is unknown. Both patients eventually developed obvious cognitive difficulties whereas temporal lobe seizures developed only in patient 2, with the highest antibody titer.

Even though we did not detect striatal changes on MRI, it is of note that basal ganglia hypermetabolism was previously shown using PET or SPECT in patients with LGI1 antibodies and faciobrachial dystonic seizures, which can also precede limbic encephalitis.[5] Interestingly, both patients had residual executive dysfunction despite significant memory improvement, further suggesting the involvement of a subcortical neuronal network.

In both cases genetic testing was considered for late-onset hereditary chorea and diagnosis was delayed by several weeks. Despite this latency, the chorea and memory deficits responded well to immunotherapy. It is thus likely that prompt recognition and initiation of immunotherapy may prevent the longer-term sequelae of VGKC complex antibody encephalitis. VGKC complex antibodies, espe-

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Supplemental Data

cially those directed against LGI1, should be considered in patients with a combination of late-onset chorea and personality or cognitive change. In this respect an early diagnostic clue is hyponatremia, which should be specifically sought.

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