Objective: To describe the first case (to our knowledge) of voltage-gated potassium channel–complex protein antibody encephalitis with kinesigenic dyskinesia and cramp-fasciculation syndrome.

Design: Case report.

Setting: Hospitalized care.

Patient: A 38-year-old man with a history of bronchial asthma, eczema, vitiligo, and immune complex mesangiopathic glomerulonephritis presented with abnormal movements.

Main Outcome Measures: Clinical examination, magnetic resonance imaging, single-photon emission computed tomography, electromyography and nerve conduction studies, video-electroencephalographic monitoring, plasmapheresis exchange therapy, and intravenous immunoglobulin administration.

Results: Clinical examination revealed paroxysmal kinesigenic dyskinesia and fasciculations. Magnetic resonance imaging of the brain revealed a left caudate and left putamen increased signal lesion on T2-weighted and fluid-attenuated inversion recovery sequences as well as increased flow in the same region on single-photon emission computed tomographic scans. Electromyography and nerve conduction studies revealed significant afterdischarges, cramp potentials, and continuous motor activity. The video-electroencephalographic monitoring revealed no epileptiform discharges. The patient dramatically improved after 5 plasmapheresis exchange treatments and a course of intravenous immunoglobulin at 2 gm/kg over 5 divided doses.

Conclusion: To our knowledge, this is the first report of paroxysmal kinesigenic dyskinesia with voltage-gated potassium channel–complex protein antibody encephalitis associated with the cramp fascication syndrome.

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Video available online at www.archneurol.com
On admission, he was fully alert and oriented but had trouble with immediate recall and tasks that required concentration (eg, serial 7s). He had slight forward flexed posture but otherwise had full strength, sensation, and coordination. He demonstrated multiple episodes of kinesigenic dyskinesia, which were always initiated by sudden movement (most often by reaching for objects or attempting to get up from a sitting position). The movements were at times bilateral and at times unilateral. He would flex at the elbow and wrist and extend his knees while dorsiflexing his foot. His face involved the orbicularis oculi, buccinator muscles, and lower facial musculature. The episodes were stereotyped and lasted 3 to 10 seconds (video, http://www.archneurol.com). He had full recollection of the events and had no loss of consciousness or confusion. He had 20 to 30 episodes per hour. He also demonstrated fasciculations at rest, most prominently of the quadriceps and gastrocnemius muscles.

Magnetic resonance imaging of the brain with gadolinium revealed increased fluid-attenuated inverse recovery signal of the head of the left caudate and the middle of the left putamen (Figure 1). The lesions enhanced with gadolinium (Figure 1C). Single-photon emission computed tomography demonstrated increased uptake in similar regions (Figure 2). Autoantibody and paraneoplastic evaluation revealed an elevated voltage-gated potassium channel (VGKC) antibody titer (0.97 n mole/L; reference value, <0.02 n mole/L) and an elevated ganglionic acetylcholine receptor antibody titer (0.45 n mole/L; reference value, 0.02 n mole/L). Electromyography and nerve conduction studies using the cramp-fasciculation protocol revealed significant afterdischarges with 3-Hz stimulation, significant cramp potentials with 5-Hz stimulation, and continuous motor activity with 10-Hz stimulation (Figure 3). The serum sodium level on admission was 128 mEq/L (to convert to millimoles per liter, multiply by 1.0). A 72-hour continuous video-electroencephalographic monitoring system revealed nonspecific slowing but no epileptiform activity. The results of a complete malignancy workup, including total-body positron emission tomography, were negative.

Levetiracetam therapy (1000 mg twice a day) was initiated and was continued throughout the course of the patient’s evaluation. The patient underwent 5 plasma exchanges during the first week. There was no clinical im-
provemem. The third week, 5 intravenous immunoglobulin infusions of 2 mg/kg were administered over 4 to 5 hours with 30 mg of prednisone. On the 10th day (third intravenous immunoglobulin infusion), the kinesigenic dyskinesia decreased dramatically to only 1 to 2 very mild episodes per day. The patient no longer had spontaneous fasciculations. Topiramate (100 mg every night) was added to his regimen the last week of treatment. At the 8-week follow-up visit, his VGKC antibody level was undetectable.

To our knowledge, this is the first reported case involving both VGKC complex protein antibody encephalitis and fasciculations associated with kinesigenic dyskinesia. Because of the patient's history of 2 autoimmune diseases—vitiligo and immune complex mesangipathic glomerulonephritis—and negative cancer evaluation findings, we believed that the VGKC encephalitis and the peripheral cramp-fasciculation syndrome were on an autoimmune basis. He had the typical clinical presentation for the VGKC antibody spectrum disease, including seizures and memory and cognitive impairment, supported by the laboratory findings of a slow electroencephalogram, hypoatremia, and an elevated antibody titer. Two other patients have been described with caudate and putaminal lesions associated with this syndrome.1,2 Two clinically similar cases have also been reported,3,4 but, unlike our patient, both patients had clear antibodies present clinically with fewer nervous system symptoms of peripheral nerve hyperexcitability that have been described in association with VGKC antibody spectrum diseases (neuromyotonia or Isaacs syndrome, cramp-fasciculation syndrome, and Morvan syndrome).5,6 He did, however, have prominent fasciculations, especially in the lower extremities.

Until recently, VGKCs were thought to be the antigenic target in these patients.6 The work by Lai et al7 and Irani et al8 has demonstrated that the antigenic targets are proteins that form a complex with these VGKCs, ie, leucine-rich glioma-inactivated 1 and contactin-associated protein 2. Leucine-rich glioma-inactivated 1 associates with the VGKC KV1.1 and KV1.2 VGKCs at the neural juxtaparanodal region. Contactin-associated protein 2 associates with both KV1.1 and KV1.2 VGKCs at the neural juxtaparanodal region, and patients with contactin-associated protein 2 antibodies present clinically with fewer nervous system symptoms and more features of peripheral nervous system dysfunction. Of note, none of the patients described in these 2 articles had dyskinesia or evidence of basal ganglia lesions on magnetic resonance images. Although the exact mechanism is unknown, it is probable that these antibodies cause dysfunction of the VGKCs and increase their excitability. In our patient, this hyperexcitability of VGKC may have led to the loss of inhibition of the globus pallidus, with consequent disinhibition of the motor thalamus. The specific VGKCs (KV1.1 and KV1.2) are known to be hyperpolarizing to neurons of the striatum and may have been affected in this case.12,14

Figure 3. Electromyography and nerve conduction studies demonstrating cramp potentials (left) and continuous motor unit activity (right) during tibial repetitive nerve stimulation at 5 Hz and 10 Hz, respectively.

To our knowledge, this is the first reported case involving both VGKC complex protein antibody encephalitis and fasciculations associated with kinesigenic dyskinesia.
Kinesigenic dyskinesia may include dystonia, ballism, chorea, or athetosis. It is induced by sudden voluntary movement and may occur (secondary form) as a result of a wide variety of conditions, including trauma, metabolic abnormalities, multiple sclerosis, kernicterus, and central nervous system infections.\textsuperscript{15-17} The literature supports treatment of this condition with a variety of immunosuppressive strategies.\textsuperscript{3,6,8,9,17-19} Our patient was treated with plasmapheresis, intravenous immunoglobulin, and anticonvulsant agents. We are not sure which of the modalities that were used were effective in his treatment.

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