Kinesigenic Dyskinesia in a Case of Voltage-Gated Potassium Channel–Complex Protein Antibody Encephalitis

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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 mesangioptic 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 fasciculation syndrome.


To our knowledge, this is the first description of a patient who had central neurologic signs of seizures, encephalopathy, and kinesigenic dystonia as well as fasciculations and peripheral cramps.

Video available online at www.archneurol.com

REPORT OF A CASE

A 38-year-old man presented with the chief complaint of the sudden onset of “stiffness” of both arms and legs. The problem had begun 8 weeks earlier, when the patient experienced 2 episodes of extreme anxiety that lasted for approximately 30 seconds with no associated loss of consciousness or abnormal movements. A few days after these 2 episodes, he noted the onset of abnormal movements, which were initiated by change of position or startle and would involve either the upper or the lower extremities. The movements occurred up to 40 to 50 times per day and were exacerbated by stress and lack of sleep. The patient subsequently developed clear cognitive decline manifested as difficulty with short-term memory and concentration. The episodes of anxiety increased in frequency and intensity and were followed by 2 witnessed generalized tonic-clonic seizures. The patient was admitted to an outlying hospital and underwent an extensive workup, which included routine magnetic resonance imaging without gadolinium, cerebral arteriography, and routine blood, urine, and cerebrospinal fluid analysis, the results of which were normal. He also had bronchial asthma, eczema, vitiligo, and immune complex mesangiopathic glomerulonephritis. He was taking 500 mg of mycophenolate mofetil (CellCept [2-morpholino-ethyl ester of mycophenolic acid]) twice a day for his renal condition.

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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 nmol/L; reference value, <0.02 nmol/L) and an elevated ganglionic acetylcholine receptor antibody titer (0.45 nmol/L; reference value, 0.02 nmol/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-

Figure 1. Magnetic resonance images of the brain. Fluid-attenuated inverse recovery (FLAIR) sequence (A, axial; B, coronal), gadolinium (gad)-enhanced T1-weighted images (C), and T2-weighted images (D), all demonstrating increased signal intensity in the left caudate and putamen (arrows).

Figure 2. Single-photon emission computed tomographic scans of the brain demonstrating increased flow in the left striatum region (arrows).
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 mesangiocapillary glomerulonephritis—and negative cancer evaluation findings, we believe 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, hyponatremia, and an elevated antibody titer. Two other patients have been described with cاعدate 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 lesions and putaminal lesions associated with this syndrome.1,2 Two other patients have been described with contactin-associated protein 2 antibodies present clinically with fewer nervous system symptoms (limbic encephalitis, seizures, and altered mental status). Contactin-associated protein 2 associates with both VGKC 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 leucine-rich glioma-inactivated 1 and contactin-associated protein 2. The work by Lai et al10 and Irani et al11 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 leucine-rich glioma-inactivated 1 and contactin-associated protein 2. He did, however, have prominent fasciculations, especially in the lower extremities.

Until recently, VGKCs were thought to be the antigenic target in these patients.6,7 The work by Lai et al3,4 and Irani et al11 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 VGKC antibodies present clinically with fewer nervous system symptoms (limbic encephalitis, seizures, and altered mental status). Contactin-associated protein 2 associates with both VGKCs and VGKC 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 excitability 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.
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, kerticterus, and central nervous system infections. The literature supports treatment of this condition with a variety of immunosuppressive strategies. Our patient was treated with plasmapheresis, intravenous immunoglobulin, and anticongulvent agents. We are not sure which of the modalities that were used were effective in his treatment.

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