Case Report

Encephalitis due to antibodies to voltage gated potassium channel (VGKC) with cerebellar involvement in a teenager

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Abstract

Encephalitis due to antibodies to voltage gated potassium channel (VGKC) typically presents with limbic encephalitis and medial temporal lobe involvement on neuroimaging. We describe a case of 13 year girl female with encephalitis due to antibodies to VGKC with signal changes in the cerebellar dentate nuclei bilaterally and clinical features that suggested predominant cerebellar involvement. These have never been reported previously in the literature. Our case expands the phenotypic spectrum of this rare condition.

Key Words

Antibodies to voltage gated potassium channel, anti-VGKC, encephalitis, voltage gated potassium channel, VGKC

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Case Summary

A 13 year old previously healthy and developmentally normal female presented with 3 days of fatigue and muscle aches. One day prior to admission to our institution, she developed unsteadiness and inability to walk. This was followed by alteration of sensorium that progressed to stupor and bilateral 6th nerve palsies. Magnetic resonance imaging (MRI) of brain showed hyperintensities involving the dentate nuclei bilaterally [Figure 1]. She had no clinical seizures and electroencephalograms on multiple occasions failed to reveal epileptiform discharges or electrographic seizures. Extensive infectious and rheumatological work-up was negative. Antibodies to voltage gated potassium channel (VGKC) were positive and elevated at 0.05 nanomole per liter in serum (normal < or = to 0.02). Paraneoplastic work up was otherwise negative including extensive search for an occult malignancy. She received corticosteroids, intravenous immunoglobulin, and rituximab. Her sensorium improved gradually and mental status returned to baseline. She had significant dysarthria, truncal and gait ataxia, dysmetria, and nystagmus. Although these cerebellar signs improved, she was left with residual deficits. Repeat MRI showed resolution of the previously seen signal changes in the dentate nuclei [Figure 2].

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Discussion

Anti-VGKC antibodies have been implicated in a variety of neuronal hyper-excitability disorders including Issacs' syndrome (acquired neuromyotonia), Morvan's syndrome (neuromyotonia with cognitive impairment, sleep disturbances and dysautonomia), and limbic encephalitis (encephalopathy, seizures, sleep disorder, hyponatremia, and signal changes in the medial temporal lobes on MRI).[1] Unusual symptoms like chorea and chronic pain syndrome have also been reported.[2,3] These antibodies have been documented in some patients with long-standing epilepsies refractory to conventional anti-convulsants though the causality is not proven.[4] Patients with limbic encephalitis with anti-VGKC antibodies typically have medial temporal lobe signal changes though lesions in claustrum and basal ganglia have also been reported.[5,6]

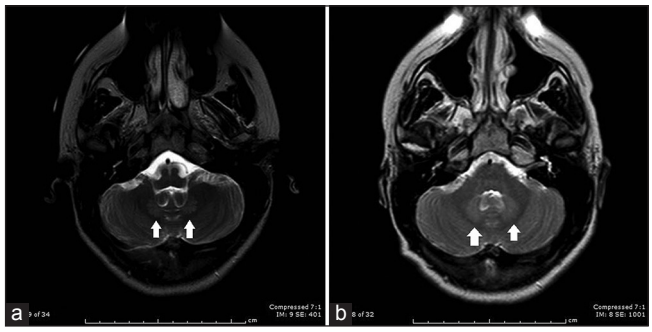

Figure 1: (a and b) Signal changes involving the dentate nuclei bilaterally

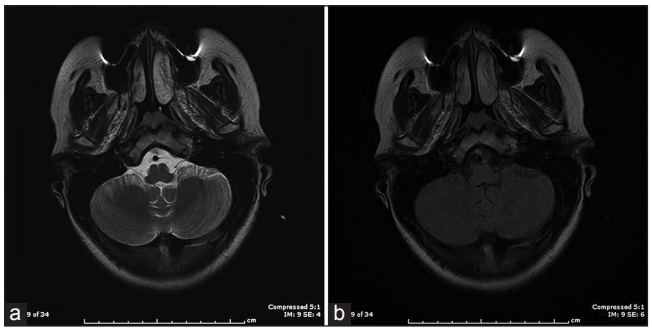

Figure 2: (a and b) Resolution of the signal changes in the dentate nuclei after treatment

It is now understood that anti-VGKC antibodies are not directed against the VGKC itself, but against other cell surface antigens that form part of the VGKC complex; the various known antigenic targets being leucine-rich glioma-inactivated protein 1 (LGI1, typically associated with limbic encephalitis and central nervous system hyper-excitability disorders), contactin-associated protein 2 (Caspr2, typically associated with peripheral nervous system hyper-excitability disorders), and contactin 2 (no known phenotype).[7] Additional undiscovered targets may be responsible in those who have anti-VGKC antibodies but are LG1, Caspr2, and contactin 2 negative. Unfortunately, our patient did not have testing for any of these targets which is available only on a research basis. However, it should be emphasized that neither the diagnosis nor the management of our patient would have been affected even if any of these targets were to be positive.

Patients with encephalitis due to anti-VGKC antibodies have been documented to have had ataxia as one of the clinical features. However, none have been previously reported with abnormal cerebellar findings on MRI or with preponderance of cerebellar signs. On a cellular level, there is evidence to support rationale for dentate nuclei involvement. Although seen widely throughout the brain, certain subtypes of the potassium channels have a proclivity for the cerebellum and in particular the deep nuclei like the dentate.[8,9] Voltage-gated potassium channel subunits Kv3.1b and Kv3.3 have been localized within the dentate nuclei in animal models and are hypothesized to play a role in motor control.[9] Our patient expands the phenotypic spectrum of anti-VGKC antibody encephalitis.

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