LETTER TO THE EDITOR

To the Editor

Myotonic Discharges in Anti-MuSK Myasthenia

Keywords: Myasthenia, Anti-MuSK, Myotonia

A 63-year-old woman of Malaysian–Chinese origin presented with subacute progressive dysarthria and dysphagia. She had a history of left stage II Her2-positive breast cancer with metastasis only to an adjacent lymph node, treated with mastectomy, chemotherapy, and radiation the year before presentation. She was only on Herceptin at the time of neurological symptoms, which was discontinued shortly thereafter. She was not on a statin. Over the subsequent 8 months her dysphagia progressed, requiring gastrostomy tube placement. A trial of pyridostigmine was negative. She developed dyspnea and required nocturnal ventilator assistance, but was not intubated. She received a course of intravenous immunoglobulin, without benefit.

MRI brain was performed twice, 7 months apart, and was normal. CT of the chest, abdomen, pelvis, and neck was unremarkable. Bloodwork, including B12, thyroid-stimulating hormone, and creatine kinase, was normal. Acetylcholine receptor antibody (AchRAb) testing was negative. Paraneoplastic autoantibody panel testing was negative, including LGI1 and CASPR2. CSF examination was normal. Needle electromyography (EMG) demonstrated myotonic discharges in the left extensor indicis and tibialis anterior, and repetitive stimulation of ulnar nerve recording from abductor digiti minimi was normal. Muscle biopsy of the right tibialis anterior showed type 1 muscle fiber atrophy without other abnormality. Genetic testing for myotonic dystrophy type 1 and 2 and for mutations in the SCN4A gene were negative. Pompe dried blood spot was negative.

On presentation to our institution 1 year after symptom onset, she had diffuse cachexia without fasciculations, and dyspnea at rest. Speech was unintelligible owing to flaccid dysarthria, and the patient communicated in writing. She denied any fluctuation throughout the day or over time. She had bilateral ptosis, worse on the left, with fatigability. She had bilateral adduction paresis and horizontal diplopia in all directions of gaze. She had bilateral facial weakness and tongue weakness without fasciculations. Jaw jerk was normal. She had weakness of neck flexion (MRC scale 4+/5), and symmetric weakness of deltoids (4/5), biceps (4+/5), triceps (4/5), distal upper extremity (4/5), and hip flexors (4/5). There was no percussion, grip, or eye closure myotonia.

Repetitive simulation of the right facial nerve recording nasalis and right accessory nerve recording trapezius demonstrated decrement of 18%-20%. Myotonic discharges were present in the right extensor indicis (see online Supplementary Video), but not in the right deltoid, biceps, triceps, or tibialis anterior. There was no other electrophysiological evidence of myopathy.

Given the progressive bulbar weakness, abnormalities on repetitive stimulation, and negative AchRAb testing, testing for antibodies against muscle-specific receptor tyrosine kinase (MuSK) was performed and was positive. The patient was treated with plasma exchange and prednisone, and began to slowly improve. Three months after treatment she no longer required respiratory support, was cleared for oral intake of thickened liquids, and had markedly less dysarthria. Her ptosis and diplopia resolved, but she had ongoing milder facial and limb weakness. Myotonic discharges were no longer seen in the right extensor indicis on repeat EMG, although we did not sample further at this time and therefore no conclusions on response of myotonia to treatment could be made.

Our patient had a 1-year history of progressive predominantly bulbar weakness, and was eventually diagnosed with anti-MuSK myasthenia. Anti-MuSK myasthenia has a higher prevalence in women, has prominent craniobulbar weakness, and has a higher frequency of respiratory crises.[1] Electrical myotonia in anti-MuSK myasthenia has previously been reported in a single series of two patients, although other causes of myotonia were not fully ruled out.[2] Other studies have reported myotonic discharges in patients with both myotonic dystrophy and myasthenia gravis.[3,4] The differential diagnosis of myotonia includes myotonic dystrophy type 1 and 2, myotonia congenita, and paramyotonia.[5] However, these disorders are almost universally associated with both clinical and electrical myotonia. Acid maltase deficiency and other rare causes of myotonia (e.g. statin medications) may only have electrical myotonia.[6] In our case, myotonic dystrophy type 1 and type 2 and SCN4A mutations were ruled out, as were other plausible causes of myotonia.

The mechanism behind electrical myotonia in anti-MuSK myasthenia remains speculative. Electrical myotonia is felt to occur owing to dysfunction in muscle membrane channels, with abnormal function of both chloride and sodium channels implicated, and could arise from either neuromuscular junction or muscle dysfunction. One previous study found neuromyotonia and fasciculations in two patients with anti-MuSK antibodies, and hypothesized a role of anti-MuSK in nerve terminal hyperexcitability.[7] In addition, MuSK is expressed extrasynaptically in skeletal muscle of mice, and mediates the expression of genes in myoblasts and myotubes via bone morphogenetic proteins, which inhibit calcium signaling induced by muscarinic AchR.[8] Therefore, disruption of calcium signaling by MuSK antibodies, or an as-of-yet undefined role in the regulation of sodium or chloride channels in the muscle membrane, could lead to electrical myotonia.

Our finding suggests that in a patient with progressive bulbar weakness and electrical myotonia, testing for anti-MuSK myasthenia should be considered, in order to make a prompt diagnosis, avoid unnecessary investigations, and initiate early therapy.

Disclosures

The authors have nothing to disclose.

Statement of Authorship

RAJ was involved in patient management and writing of the manuscript. GI, AG, and CDK contributed to patient management and critical revision of the manuscript.

Supplementary Materials

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