Peripheral Nerve Hyperexcitability Following Titanium Marker Placement

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INTRODUCTION

Peripheral nerve hyperexcitability (PNH) is characterized by spontaneous and continuous muscle activity, caused by hyperactive motor nerve terminal or neuromuscular junction. PNH can be associated with a variety of peripheral nerve disorders that can be inherited, autoimmune, metabolic or toxic.[1] Here we describe a patient of PNH following titanium marker placement during a breast biopsy.

CASE PRESENTATION

A 48 year-old Caucasian female with no prior medical history was noted to have microcalcifications in her left breast on mammogram. Biopsy revealed fibrocystic disease with no evidence of malignancy. During biopsy, a titanium marker was placed in the left breast for repeat imaging. One week later she developed stiffness in her heels while walking, followed by sensations of tingling in bilateral hands, bilateral feet and chest tightness. Within the following month, she noticed widespread muscle tightness that was prominent at the initiation of limb movement and became less noticeable with repeated motion. Frequent muscle spasms also appeared in her lower extremities. Her exam revealed increased tone in bilateral lower extremities, mild weakness in distal arms and legs, diffuse hyporeflexia, and prominent fasiculations in eyelids, tongue, and all extremities. Her lab work was significant for an elevated creatine kinase level of 885 U/L (reference range: 30-220 U/L) and a low vitamin B12 level of 193 pg/mL (reference range: 221-700 pg/mL). Acetylcholine receptor and muscle specific receptor tyrosine kinase antibodies were negative. Electromyogram (EMG) showed persistent continuous motor unit activity during attempted relaxation, doublets and triplets, myokymic discharges and cramp potentials in essentially all examined muscles, indicative of PNH. Motor unit potential configurations were difficult to analyze due to overriding spontaneous activity but appeared unremarkable. An extensive work up including inflammatory markers, heavy metal screening, serum paraneoplastic antibody panel, including voltage gated potassium channel antibodies, glutamic decarboxylase antibodies, computed tomography of chest; abdomen and pelvis was unrevealing. Cerebrospinal fluid analysis was normal. She was treated with carbamazepine 200 mg twice daily which led to significant symptomatic relief within 1 week. Patient also took B12 supplementation with correction of B12 levels subsequently.

The titanium marker was removed at 3 months, which led to no clinical improvement. The dose of carbamazepine was steadily increased to 200 mg four times a day and was associated with improvement in fasciculations, stiffness and gait. At 10 months, repeat EMG demonstrated a partial improvement in the amount of spontaneous discharges. She was treated with 5 cycles of plasmapheresis which led to short-lived improvement of stiffness, fasciculations and gait. Prednisone at a daily dosage of 40 mg was initiated, resulting in improvement of stiffness and weakness. Subsequently prednisone dose was gradually tapered. At 66 months following the initial onset, she remained minimally symptomatic on a combination regime of prednisone 10 mg per day and carbamazepine 200 mg four times a day.

DISCUSSION

Peripheral nerve hyperexcitability syndrome commonly results from ion channel dysfunction from either decreased potassium conduction or persistent sodium channel activity, or enhanced neuromuscular junction transmission from acetylcholinesterase inhibition. In our patient, an extensive work up for known causes of PNH was unrevealing. While the possibility of coincidence cannot be totally excluded, the close temporal relationship between titanium marker placement and onset of PNH may indicate an association. There have been reports of PNH occurring secondary to heavy metal exposure such as gold, platinum, mercury, lithium, and manganese.[2-6] The mechanism of PNH in these cases is typically due to toxicity resulting in ion channel dysfunction or acetylcholinesterase inhibition.[2-6]

Titanium is used extensively in surgical and radiological procedures due to its sustainability and biocompatible properties. It has been demonstrated that titanium may

alter the kinetics of voltage-gated potassium channel currents resulting in changes in neuron excitability.[7] However, a direct toxicity of ion channel may not be the underlying mechanism of PNH in our patient, as removal of the titanium marker did not lead to significant improvement. Recent studies also suggested that metals such as titanium, nickel, mercury and gold could trigger systemic autoimmune or autoinflammatory syndromes in humans.[8-9] The observed clinical improvement with prednisone and plasmapheresis treatment in our patient is supportive of an immune mediated etiology. Given the widespread use of titanium in surgical and radiologic procedures, clinicians should consider inquiring about titanium or other metal exposure in PNH syndromes.

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