Current Journal of Neurology

Letter to Editor

Curr J Neurol 2020; 19(2): 85-6

Cholinergic neuromuscular hyperactivity in a patient with anti-muscle-specific tyrosine kinase myasthenia gravis

Received: 11 Dec. 2019
Accepted: 01 Feb. 2020

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Keywords
Fasciculations; Myasthenia Gravis; Electromyography; Ultrasonography

Approximately 7% of patients of generalized myasthenia gravis (MG) have antibodies against muscle-specific tyrosine kinase (MuSK-Ab).[1] Albeit MG patients with MuSK-Ab have almost the same clinical features to patients with acetylcholine-receptor-antibody (AChR-Ab); they show several clear characteristics such as predominant bulbar and neck weakness, more frequent myasthenic crisis, and more occurrence of muscle atrophy.[2,3]

In addition, MuSK-Ab-positive MG patients exhibit unpredictable responses to acetylcholinesterase inhibitors (AChEIs), including worsening of weakness, frequent cramp, and fasciculations, and decreased therapeutic responsiveness to AChEIs.[4] Which these responses attribute to the cholinergic neuromuscular hyperactivity.[5] At electrodiagnosis, this phenomenon previously demonstrated as repetitive compound muscle action potentials (R-CMAPs) in a MuSK-Ab-positive MG patient taking the standard dose of AChEI.[5,6]

Synaptic R-CMAPs , caused by excess acetylcholine in the neuromuscular synapse, occur in several conditions, such as congenital AChE deficiency, slow-channel congenital myasthenic syndrome, and organophosphate poisoning and acetylcholinesterase inhibition.[7]

A 26-year-old man presented with fluctuating diplopia, ptosis, and dysphagia started four months before. Neurological examination revealed bilateral facial muscle weakness and near-complete ophthalmoplegia. The muscle strength of the upper and lower extremities was 5/5 based on the Medical Research Council (MRC) grade. On 3-Hz slow repetitive nerve stimulation (RNS), more than 20% decrement in anconeus and trapezius muscles was seen. With

How to cite this article: Okhovat AA, Fatehi F. Cholinergic neuromuscular hyperactivity in a patient with anti-muscle-specific tyrosine kinase myasthenia gravis. Curr J Neurol 2020; 19(2): 85-6.

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the diagnosis of MG, he received intravenous prednisolone 50 mg daily, and Mestinon 60 mg immunoglobulin (2 g/kg for five days), four times a day (qid). One week after the start of pyridostigmine (Mestinon), the patient was revisited; he complained of profound generalized fasciculations (Video 1, Part I) and worsening of weakness. 3-Hz slow RNS was positive with repetitive CMAPs (R-CMAPs) in abductor pollicis brevis (APB) (Figure 1 and Video 1, Part II), abductor digiti minimi (ADM), and Anconeus muscles.

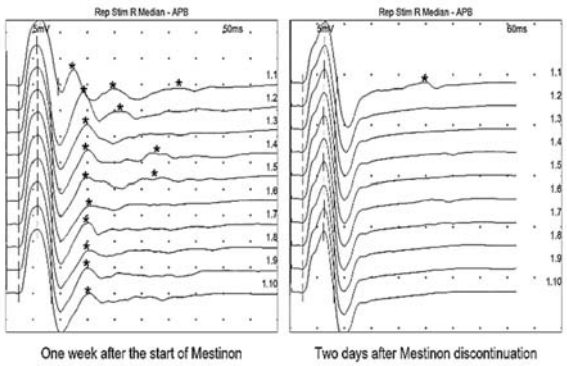

Figure 1. Slow repetitive nerve stimulation (RNS) before and after Mestinon consumption. Repetitive compound muscle action potentials (R-CMAPs)
*Disappeared after Mestinon discontinuation

Needle electromyography (EMG) (Video 1, Part III) and muscle ultrasound (Video 1, Part IV) revealed several fasciculations in different muscles. Considering the evolution of new symptoms instantly after the initiation of Mestinon, it was discontinued, and the fasciculations mostly improved two days after the cessation of Mestinon. In the follow-up, the anti-MuSK-Ab level was 48 nmol/l.

Video 1. Profound generalized fasciculations after use of Mestinon, completely disappear after discontinuation (Part I). Patient's RNS (Part II). Patient's EMG (Part III), and patient's muscle sonography revealed several fasciculations in different muscles disappear after mestinon discontinuation (Part IV).

Response to Mestinon in the Anti-MuSK MG is unpredictable, including the overt worsening of MG symptoms, suggestive of cholinergic neuromuscular hyperactivity.[6] In this patient, we observed electrophysiological and ultrasound changes of cholinergic neuromuscular hyperactivity. It is helpful to consider R-CMAPs in slow RNS as a measure for cholinergic neuromuscular hyperactivity, especially in anti-MuSK MG patients.[4]

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

None.

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