A Female Patient with Anti-Muscle-Specific Kinase Antibody Positive Generalized Myasthenia Gravis Responded to Salbutamol but not Pyridostigmine: A Case Report

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Abstract

Anti-muscle-specific kinase (MuSK) antibody positive generalized myasthenia gravis (MuSK-MG) is an autoimmune disease, in which deterioration of myasthenic symptoms may occur by cholinesterase inhibitor (ChE-I) treatment. Salbutamol, a sympathetic β2 receptor agonist, was an effective therapeutic drug in congenital myasthenic syndrome patients with MuSK gene abnormalities and in MuSK-MG animal model. Salbutamol was attempted to treat a female MuSK-MG patient who did not respond to ChE-I. Any acute benefit of salbutamol was not observed but her myasthenic symptoms gradually improved over a year without adverse effects. Salbutamol may be a therapeutic drug to alleviate myasthenic symptoms in MuSK-MG patients.

Keywords

Muscle-specific kinase (MuSK), Myasthenia gravis (MG), Salbutamol, Cholinesterase inhibitor, Pyridostigmine

List of Abbreviations

MuSK: Muscle-Specific Kinase; MG: Myasthenia Gravis; ChE-I: Cholinesterase Inhibitor; Ach: Acetylcholine; AChR: Acetylcholine Receptor

Introduction

Anti-MuSK antibody-positive generalized myasthenia gravis (MuSK-MG) is liable to cause bulbar symptoms and respiratory muscle paralysis [1]. The cholinesterase inhibitor (ChE-I) may easily cause hypersensitivity reactions such as fasciculation and deterioration of myasthenic symptoms [1,2] due to a decrease in the cholinesterase activities at neuromuscular junctions in MuSK-MG patients [3]. Pre- and postsynaptic electrophysiological and histopathological abnormalities were observed in a MuSK-MG patient [4] and MuSK-MG model animals [5], in which a reduced quantum content of evoked acetylcholine (ACh) release from the motor nerve terminals was observed. Recently, the sympathomimetic drugs were clarified to promote the release of ACh from the motor nerve terminals [6] and salbutamol, sympathetic β2 receptor agonist, was an effective treatment in patients with congenital myasthenic syndrome (CMS) caused by abnormal MuSK gene [7-9] and MuSK-MG model animals [10]. This time, salbutamol (up to 10 mg/day) was tried on a female MuSK-MG patient who failed to respond to the pyridostigmine treatment. Although there was no immediate effect of salbutamol, her myasthenic symptoms and grip strength gradually improved over a year. Salbutamol may be a therapeutic drug to alleviate myasthenic symptoms in MuSK-MG patients substituting for ChE-Is.

Case Report

A 51-year-old female patient complained difficulty in swallowing and respiratory distress followed by bilateral blepharoptosis and diplopia, since December 2007 (at the age of 42). She was suspected as having anti-acetylcholine receptor (AChR) antibody negative MG at another hospital but the pyridostigmine treatment caused muscle fasciculation and worsened respiratory distress. In June 2008, she admitted to U hospital for diagnosis.

At the time of hospitalization, she had a double vision at left gaze with mild eyelid ptosis. Although she showed easy fatigability of limb muscles, her limb mus-
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Vagal or aversive effects. The neck heaviness, easy fatigueability in the evening and swallowing disturbance gradually improved without an immediate improvement. The right grip strength was repetitively examined before and after the salbutamol treatment about two month intervals (Figure 1). Despite the reduction in the dosage of steroids, the average value of her right grip strength in the latter half of the observation period (average 23.2 kg, SD: 1.3 kg) significantly increased by about 10% compared with the average grip strength value in the first half of the observation period (average 21.1 kg, SD: 1.8 kg). The titers of anti-MuSK antibodies decreased before the reduction of the steroid dosage and almost unchanged during the latter half of the observation period (Figure 1).

Discussion

ChE-Is may deteriorate hypersensitivity symptoms and temporary myasthenic symptoms [1] as well as reduce AChR numbers at the neuromuscular junctions in MuSK-MG model animals [11]. The sympathetic neurons made close contact with neuromuscular junctions and sympathetic agonists increased ACh release from the motor nerve terminals [6]. In CMS with abnormality in the MuSK gene, salbutamol but not ChE-Is improved myasthenic symptoms [7-9]. Also salbutamol improved

![Figure 1: Serial changes of the right grip strength, the titer of anti-MuSK antibodies and the dosage of salbutamol and prednisolone. The salbutamol treatment started in January 2014 (arrow). The star indicates the time, when the dose of prednisolone was decreased in June 2015. Within two years after the salbutamol treatment, her grip strength gradually increased in spite of the decrease in the dose of prednisolone. The mean value of the grip strength after the reduction of the dosage of prednisolone (round points) significantly increased to about 110% of the mean value before the reduction of the steroid dosage (triangle points).](image)
weakness and weight loss of MuSK-MG model animals [10]. In this MuSK-MG patient, the salbutamol treatment gradually improved myasthenic symptoms and grip strength in a slow time course over 1-2 years from the start of salbutamol medication without apparent immediate improving effects such as immediate amelioration of the neuromuscular transmission observed by ChE-Is. Similar slow clinical improvement over 6 months was observed in the treatment outcome of ephedrine or salbutamol in CMS of various kinds of gene abnormalities [12]. This slow improvement effect of salbutamol might be due to the anabolic properties directly act on muscle fibers providing therapeutic potential for attenuating or potentially reversing the muscle wasting, muscle fiber atrophy, and associated muscle weakness [13].

In the future, clinical trials by a large number of MuSK-MG patients are required to determine whether salbutamol can be a therapeutic drug to alleviate myasthenic symptoms substituting for the ChE-Is.

Ethical Statement

The author states no conflict of interest (COI) to declare.

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References


