

A case of MuSK-antibody-positive myasthenia gravis with respiratory arrest was not diagnosed by either an initial edrophonium test or an electrophysiological study

Youichi Yanagawa MD. PhD., Yu Hongo MD.*,
Hiroshi Shiozaki MD. *, Keiko Kamakura MD. PhD.*,
Masahiro Sonoo MD. PhD.**
Masakatsu Motomura MD. PhD.***

Department of Traumatology and Critical Care Medicine,
National Defense Medical College (NDMC)

*Department of Internal Medicine, Division of Neurology, NDMC

**Department of Internal Medicine, University Hospital, Teikyo University
School of Medicine

***First Department of Internal Medicine, Graduate School of Biomedical
Science, Nagasaki University

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Corresponding author: Youichi Yanagawa

Department of Traumatology and Critical Care Medicine, NDMC

3-2 Namiki Tokorozawa Saitama, Japan 359-8513

Tel: 04-2995-1888, Fax: 04-2996-5221, e-mail: yanagawa@ndmc.ac.jp

Abstract

A sixty-nine-year-old male who presented in a coma due to sudden respiratory arrest was transferred to our hospital. After endotracheal intubation with manual ventilation, he became alert and his neurological findings were within the normal range, except for palsy of the respiratory muscles. Biochemical analyses of the blood and brain computed tomography failed to indicate the cause of the respiratory arrest. An edrophonium test did not improve the respiratory arrest. An urgent electromyogram at the dorsal interossei, biceps and sternocleidomastoideus muscle and a repetitive nerve stimulation test at the trapezius and deltoid muscle were also negative on the 1st hospital day. After obtaining his detail past history which revealed double vision at 57 years old, weakness of muscle strength of the neck, dysphagia and sleep apnea at 67 years old, the electrophysiological study was performed on the 16th day in the hospital. A repetitive nerve stimulation test at the levator labii superioris alaeque nasi showed a waning phenomenon. Moreover, single fiber electromyography showed an abnormal jitter at the frontal muscle. These results indicated a diagnosis of myasthenia gravis (MG). His anti-acetylcholine receptor (AChR) antibody was found to be negative, but anti-muscle-specific tyrosine kinase (MuSK) antibody was positive. After treatment with plasmapheresis and predonisolone, he regained normal respiratory function. He was discharged after 72 days with no neurological deficits.

Anti-MuSK- antibody-positive MG tends to be associated with a

lower incidence of a positive edrophonium test, a lower incidence of a positive electrophysiological study excluding the face and a higher incidence of respiratory failure in comparison to anti-AchR-antibody-positive MG. Respiratory failure is curable with treatment. Accordingly, in addition to obtaining a precise diagnosis, an emergency physician should recommend an electrophysiological study including the face to make a differential diagnosis for respiratory arrest when biochemical and radiological studies fail to indicate the cause of the respiratory arrest.

1. Introduction

This report describes a case of MuSK-MG presenting with total respiratory arrest and a coma which was initially not diagnosed by an edrophonium test and an electrophysiological study, but dramatically subsided due to the administration of appropriate treatment after making a precise diagnosis. Muscle-specific kinase (MuSK) is expressed at the postsynaptic membranes of neuromuscular junctions (NMJ) and forms complexes with acetylcholine receptors (AChR)¹. Autoantibodies to AchR are not detectable in approximately 15% of the patients with generalized myasthenia gravis (MG)². Antibodies to MuSK are found in 30-40% of the MG patients seronegative for AChR antibodies². The presence of anti-MuSK antibody appears to define a subgroup of MG patients characterized by a younger onset age, weakness predominant in the bulbar, facial and neck muscles and more frequent myasthenic crises, such as respiratory failure (22-46%) in comparison to anti-AchR-antibody-positive MG²⁻⁶. Most patients with anti-MuSK-antibody-positive MG (MuSK-MG) have a good response to simple plasma exchange and predonisolone^{3,7} and therefore a correct and timely diagnosis is important.

2. Case presentation

A sixty-nine-year-old male presenting with a coma due to sudden respiratory arrest was transferred to the hospital. His elder brother and sister had a past history of cerebral infarction and his younger brother had

died of cardiac disease. On examination, the patient was in a deep coma (Glasgow Coma Scale; E1V1M1). His pupils were equally round, measuring 2.5 mm in diameter and were reactive to light stimulation. His vital signs were: blood pressure, 130/90 mmHg; pulse rate, 96/min; and axillary temperature, 33.8 °C. The arterial blood gas analysis under a 10 L/min oxygen mask showed PH 7.115, PCO₂ 157 mmHg, PO₂ 181 mmHg, HCO₃⁻ 50.9 mmol/l, base excess 21.3 mmol/L, thus indicating respiratory acidosis. After endotracheal intubation with manual ventilation, he became alert and his neurological findings were within the normal range except for palsy of the respiratory muscles. Accordingly, a decreasing rate of manual ventilation resulted in CO₂ narcosis. The results of the biochemical analyses of the blood was as follows: white blood cells, 7600/ μ l; haemoglobin, 13.9g/dl; platelets, 10.6×10^4 / μ l; total bilirubin, 1.2 mg/dl; aspartate aminotransferase, 66 IU/L; alanine aminotransferase, 75 IU/L; total protein, 5.9 g/dl; glucose, 109 mg/dl; blood urea nitrogen, 16 mg/dl; creatinine, 0.66 mg/dl; sodium, 146 mEq/L; potassium, 4.4 mEq/L; chloride, 98 mEq/L; creatine phosphokinase, 47 IU/L; C-reactive protein, under 0.3 mg/dl; ammonia, 72 μ g/dl; lactate acid, 7.2 mg/dl; Thyroid-stimulating hormone, 1.89 uIU/ml; free thyroxin, 1.20 ng/dl. His chest X-ray, electrocardiogram and brain computed tomography were normal. An edrophonium test did not improve the palsy of the respiratory muscles. He was temporarily suspected to have amyotrophic lateral sclerosis, however, an urgent electromyogram at the dorsal interossei, biceps and sternocleidomastoideus muscles was negative. In addition, a

repetitive nerve stimulation test at the trapezius and dertoideus muscles was also negative. He was admitted and underwent mechanical ventilation without a precise diagnosis for the respiratory arrest. After obtaining his detailed past history which revealed double vision at 57 years old, weakness of muscle strength of the neck, dysphagia and sleep apnea at 67 years old, he was suspected to suffer from a neuromuscular junction abnormality. As a result, an electrophysiological study was performed after 16 days in the hospital. The repetitive nerve stimulation tests at the trapezius, deltoid, extensor digitorum minimi and abductor digiti minimi muscle were negative. However, the repetitive nerve stimulation tests at the levator labii superioris alaeque nasi showed a waning phenomenon (**Figure 1**). Moreover, single fiber electromyography showed an increasing and blocking jitter at the frontal muscle. He was thus diagnosed to have myasthenia gravis (MG). His anti-AChR antibody was found to be negative, but the anti-MuSK antibody was positive. After treatment with plasmapheresis and predonisolone, he dramatically regained normal respiratory function. He was discharged after 72 days without any neurological deficits with continued treatment with steroids and tacrolimus.

3. Discussion

The typical causes of respiratory arrest are; 1). An abnormality of the brainstem due to a congenital anomaly, vascular injury, trauma, infection, polimyelitis degenerative disease, poisoning or Ondine's curse, 2). An abnormality of the spinal cord due to trauma, poliomyelitis or motor

neuron disease, 3). peripheral nerve disease, 4). An abnormality of neuromuscular junctions, such as myasthenia gravis, and 5). A respiratory disease such as muscular dystrophy or myopathy⁸⁻¹⁷. According to the results of biochemical, radiological and electrophysiological studies, we diagnosed this case to have MuSK-MG with myasthenic crises.

In comparison to anti-AchR-antibody-positive MG (AChR-MG), MuSK-MG tends to have a lower incidence of a positive finding on an edrophonium test. Hatanaka *et al.* report the edrophonium test to be positive in 5 of 10 tested patients (50%) in the MuSK-MG, while the edrophonium test was positive in 32 of 33 tested patients (97%) in the AChR-MG¹⁸. In addition, while lacking data of AChR-MG, Lavrnica *et al.* reported the edrophonium test to be positive in only 5 of 17 tested patients (29%) in the MuSK-MG⁶. Accordingly, the edrophonium test is not considered to be a suitable test for detecting MuSK-MG.

MuSK-MG tends to have a lower incidence of a positive electrophysiological study of the extremities, excluding the face in comparison to AChR-MG. Decreased repetitive nerve stimulation and a jitter with single-fiber electromyography are characteristic of AChR-MG¹⁹. Oh *et al.* compared the electrophysiological features of 14 MuSK-MG, 73 AChR-MG and 22 anti-MuSK and AchR-antibody-negative MG patients²⁰. They found that a repetitive nerve stimulation test in the orbicularis oculi were more common and severe in MuSK-MG than in the other two groups. This emphasized the importance of including the facial muscles in repetitive nerve stimulation protocols when diagnosing MuSK-MG.

Farrugia *et al.* examined the findings from single-fiber electromyography in extensor digitorum communis and orbicularis oculi in 13 MuSK-MG and 12 AChR-MG patients with similar clinical scores²¹. More than 70% of the AChR-MG patients had an abnormal jitter in both the extensor digitorum communis and orbicularis oculi, but the majority of the MuSK-MG patients had a normal jitter in the extensor digitorum communis despite an abnormal jitter in the orbicularis oculi. Accordingly, an electrophysiological study including the face muscle is an important test for detecting the MuSK-MG. Kuwabara *et al.* reported² that two cases of MuSK-MG patients, who had negative results by both an edrophonium and repetitive nerve stimulation test at the abductor digiti minimi, were diagnosed based on an increased jitter by single-fiber electromyography, which was similar to the findings in the current patient.

4. Conclusion

In addition to determining the precise present illness, an emergency physician should recommend an electrophysiological study including the face to make a differential diagnosis for respiratory arrest when biochemical and radiological studies fail to indicate the cause of respiratory arrest.

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Figure 1

Repetitive nerve stimulation test at the levator labii superioris alaeque nasi showed a waning phenomenon.

