

[CASE REPORT]

Myasthenia Gravis Presenting with Myasthenic Crisis Mimicking Status Asthmatics

Hitoshi Kubo¹, Tomoya Katsuta¹, Norihiko Nakanishi¹, Koji Inoue¹ and Kensho Okamoto²

Abstract:

A 23-year-old woman was transferred to our hospital due to exacerbating dyspnea with wheeze. After admission, we started mechanical ventilation immediately, and she was diagnosed with status asthmatics. On the following day, she was able to be weaned from the ventilator. However, she required re-intubation because of an unstable respiratory condition just after extubation. Detailed neurological investigations identified blepharoptosis and muscle weakness with easy fatigability. An edrophonium test was positive. Anti-acetylcholine receptor antibody was detected in her serum. She was finally diagnosed with myasthenia gravis and successfully treated with neostigmine and a low-dose corticosteroid.

Key words: myasthenia gravis, status asthmatics, acute respiratory failure

(Intern Med 60: 3953-3956, 2021)

(DOI: 10.2169/internalmedicine.7426-21)

Introduction

Bronchial asthma (BA) is a disease characterized by recurrent dyspnea due to chronic inflammation of the airways. Myasthenia gravis (MG) is an autoimmune disease characterized by weakness of both extraocular and skeletal muscles with easy fatigability due to specific autoantibodies to the molecules of the postsynaptic membrane at the neuromuscular junction. The condition wherein bulbar palsy and the respiratory condition are rapidly exacerbated, resulting in respiratory failure, in patients with MG is called myasthenic crisis.

We herein report a case of myasthenia gravis that was initially diagnosed as status asthmatics.

Case Report

In December 2016, a 23-year-old Japanese woman became aware of dyspnea at night. Two days before admission, she consulted a nearby hospital because of exacerbating dyspnea. She presented with hypoxemia and wheezing in all lung fields. Since chest radiograph showed infiltrative shadow, we diagnosed her with acute pneumonia with status

asthmatics. After hospitalization, her respiratory condition and consciousness level rapidly deteriorated and were refractory to treatment with antibiotics and oxygen therapy. She was therefore intubated and in that condition was transferred to our hospital.

On admission, she was mildly drowsy, afebrile and normotensive with mild tachycardia (116 beats/min) and tachypnea (respiratory rate 26/min). Severe wheeze was heard in the bilateral lung fields. The oxyhemoglobin saturation measured by pulse oximetry (SpO₂) was 99% under a high fraction of inspiratory concentration (FiO₂) of 0.4. She had no history of substance abuse disorder, such as heroin use. The laboratory examinations showed mild anemia, leukocytosis, and elevated C-reactive protein. An arterial blood gas analysis revealed marked respiratory acidosis related to hypercapnia (Table 1).

Computed tomography showed massive consolidations in the dorsal portion of both lower lung lobes, suggestive of aspiration (Fig. 1). Given her history of pediatric asthma and current smoking habit, we diagnosed her with status asthmatics with aspiration pneumonia. Mucus plugs were detected in the bilateral lower bronchi by bronchoscopy (Fig. 2); her wheeze disappeared immediately after their removal.

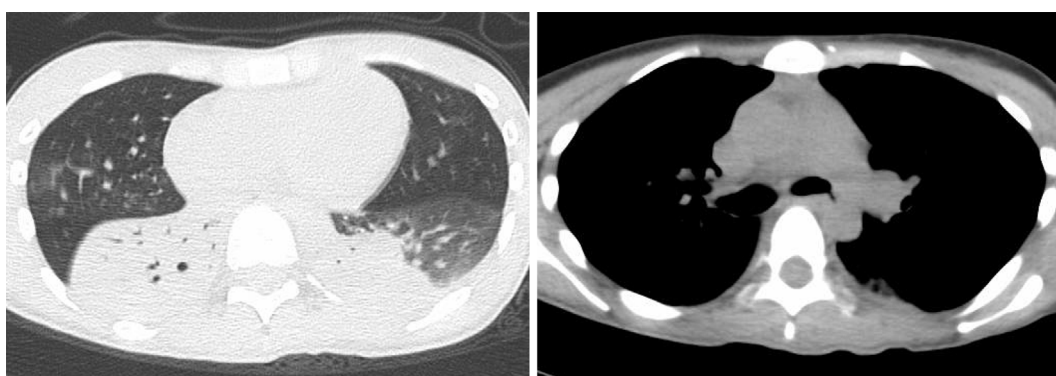
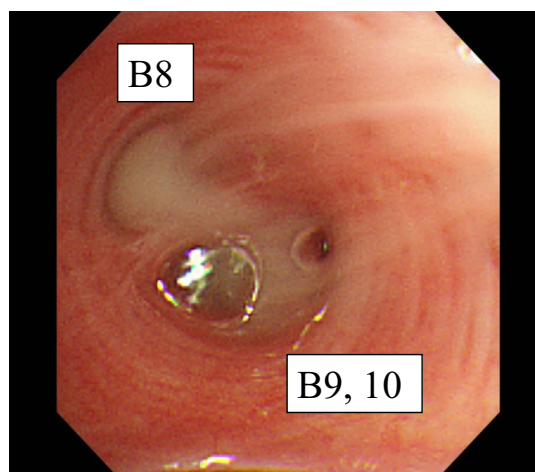
¹Department of Respiriology, Ehime Prefectural Central Hospital, Japan and ²Department of Neurology, Ehime Prefectural Central Hospital, Japan

Received: February 26, 2021; Accepted: April 18, 2021; Advance Publication by J-STAGE: June 12, 2021

Correspondence to Dr. Hitoshi Kubo, m10030hk@jichi.ac.jp

Table 1. Laboratory Findings at the Time of Transport before Mechanical Ventilation.

WBC	15,640 / μ g	TP	7.1 g/dL	pH	7.236
RBC	440 $\times 10^4/\mu$ L	ALB	4.0 g/dL	pCO ₂	70.0 mmHg
HGB	10.6 g/dL	BUN	15.0 mg/dL	pO ₂	190.0 mmHg
PLT	37.4 $\times 10^4/\mu$ L	Cre	0.42 mg/dL	Na ⁺	139.0 mmol/L
PT	89.0 %	Na	142 mEq/L	K ⁺	3.80 mmol/L
PT-INR	1.06	K	4.0 mEq/L	Cl ⁻	109 mmol/L
APTT	25.1 s	Cl	105 mEq/L	Ca ²⁺	1.12 mmol/L
D-dimer	1.0 μ g/mL	CRP	5.69 mg/dL	Glucose	186 mg/dL
AST	22 U/L	eGFR	151 mL/min/1.73m ²	Lac	1.4 mmol/L
ALT	16 U/L	TSH	0.329 μ IU/mL	HCO ₃ ⁻	28.7 mmol/L
LDH	162 U/L	FT4	0.97 ng/dL	BE	1.9 mmol/L
CK	51 U/L			AnGap	5.5 mmol/L

**Figure 1. Chest computed tomography showed massive pneumonia with atelectasis in both lower lungs. Thymoma and thymus hyperplasia were not seen.****Figure 2. Bronchoscopy showed that the bronchus of the lower lung (B8, 9, 10) was obstructed by mucus sputum.**

We started treatment with corticosteroids and antibiotics under mechanical ventilation (Fig. 3). Her oxygenation and hypercapnia improved rapidly, but the tidal volume was still low at approximately 300 mL. The spontaneous breathing trial and cuff leak test was normal. Neither consciousness disturbance nor recurrence of wheezing was observed at this time, so we attempted extubation on the second day. How-

ever, she required re-intubation due to difficulty maintaining oxygenation just after extubation.

We decided to perform extubation under assistance with noninvasive positive pressure ventilation (NPPV) on the fifth day. For a short while afterward, she had difficulty evacuating sputum on her own, despite respiratory rehabilitation. Detailed history-taking showed that she had been aware of diplopia, dysphagia, habitual nasal regurgitation and muscle weakness of limbs with diurnal fluctuation for the past three years. Neurological investigations revealed blepharoptosis, external ophthalmoparesis and muscle weakness of the face, neck and limbs. The edrophonium test was positive. The Harvey-Masland test showed waning at low frequent repetitive stimulation (Fig. 4). The anti-acetylcholine receptor antibody level was 76.4 nmol/L in her serum. Given these findings, we diagnosed her with generalized myasthenia gravis.

Treatment with neostigmine improved blepharoptosis, external ophthalmoparesis and dysphagia. Following the administration of low-dose oral prednisolone, the muscle weakness of the neck and limbs was also improved to the normal range. Initial worsening did not occur. She began walking without aid again and was discharged on day 19. Thereafter, the fractional exhaled nitric oxide (FeNO) level normalized to 9 ppb. An airway reversibility test revealed normal find-

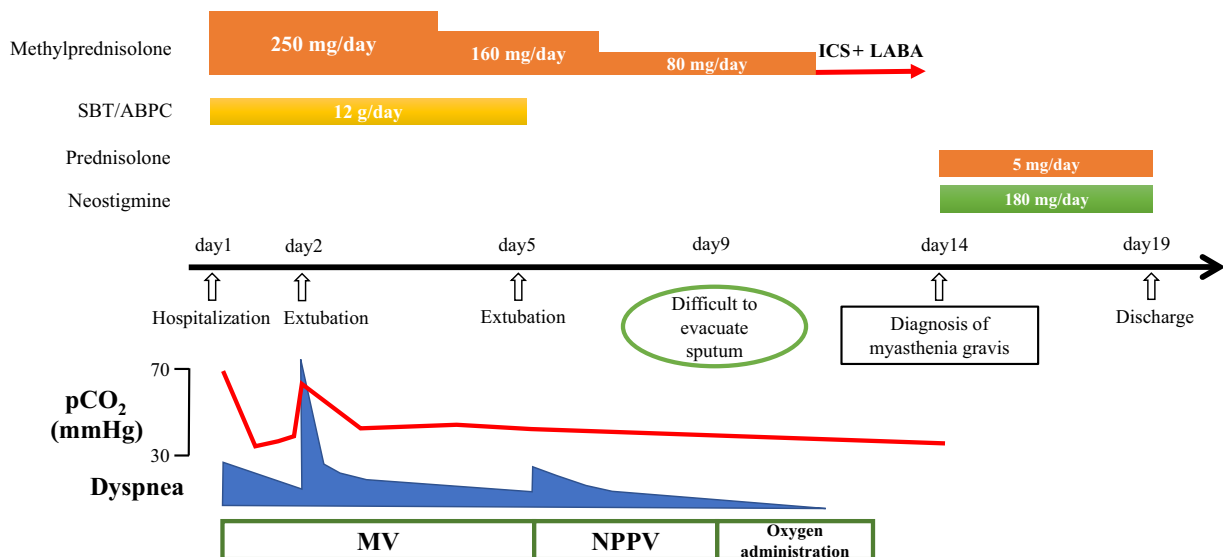


Figure 3. Treatment course during hospitalization. SBT/ABPC: sulbactam/ampicillin, ICS: inhaled corticosteroid, LABA: long-acting β -agonist, MV: mechanical ventilation, NPPV: noninvasive positive pressure ventilation

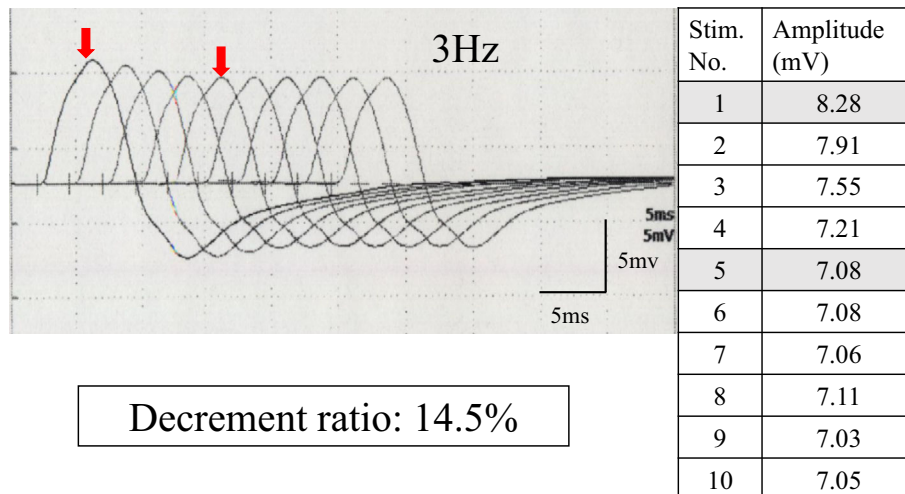


Figure 4. The waveforms delivered from the right abductor pollicis brevis elicited by the median nerve stimulation. The waveforms demonstrated the waning phenomenon at 3-Hz repetitive stimulation.

ings for airway resistance after inhalation of β -2 stimulant. She has never shown eosinophilia or asthma-like symptoms.

Discussion

This patient was initially diagnosed with acute respiratory failure due to status asthmaticus but was ultimately found to have myasthenic crisis. We mistakenly suspected she was having an asthmatic attack due to her history of pediatric asthma and current smoking habit. Despite improving her pneumonia and wheeze by removing mucus plugs, she required re-intubation because of difficulty maintaining oxygenation; this was thought to be an atypical finding of BA. Furthermore, an airway reversibility test revealed normal findings for airway resistance after inhalation of β -2 stimu-

lant. Eosinophilic inflammation was also not confirmed by the FeNO test. Based on these results, we diagnosed this patient with myasthenia crisis rather than MG coinciding with BA.

King et al. investigated the relationship between airway hyper-responsiveness and the presence of wheezing during maximal forced exhalation in patients with BA using a methacholine loading test. They reported that the sensitivity and specificity of wheezing associated with airway hyper-responsiveness were 57% and 37%, respectively (1). This result suggested that wheeze was not necessarily a specific symptom in BA. We speculated that the cause of wheeze in this case was mainly due to the lower bronchial stenosis induced by mucus plugs, not airway hyper-responsiveness associated with BA.

Table 2. Clinical Profiles of Cases with Coexisting BA and MG or MG Misdiagnosed as BA.

	Patient 1 (2)	Patient 2 (3)	Patient 3 (4)	Patient 4 (5)
Age/Sex	48/W	52/W	55/M	11/W
EO	+	+	+	-
BP	-	-	-	+
MWL	+	+	-	-
Initial treatments on admission	Not described	Prednisolone 20mg/every other day	Prednisone 30mg/day, Bronchodilator	Dexamethasone, Isoproterenol, Bronchodilator, Antibiotics

EO: external ophthalmoparesis, BP: bulbar palsy, MWL: muscle weakness of limbs

A few cases coexisting of BA and MG have been reported (2-4). There was one previous case of MG misdiagnosed as BA (5). In those cases, external ophthalmoparesis, bulbar palsy and muscle weakness of the neck and extremities were present before admission (Table 2). We were unable to obtain the detailed medical history or sufficient physical findings from the present patient, as she was intubated at admission, which resulted in a delay in making an accurate diagnosis. Qureshi et al. reported that 14% of MG patients presented with respiratory failure as an initial symptom (6). Therefore, we should keep in mind that there are some MG patients with clinical features mimicking status asthmatics, especially in emergencies.

In the present case, marked hypercapnia was observed on admission, which is considered an important finding suggesting neuromuscular disease. Furthermore, high-dose glucocorticoid, commonly used in the initial treatment of status asthmatics, may cause drug-induced worsening of the neuromuscular junction function (7). From a therapeutic perspective, the accurate differentiation of MG from BA is very important in general clinical practice. If patients with respiratory failure exhibit no response to asthma-specific treatments and are refractory to detachment from mechanical ventilation, we should consider the possibility of other underlying conditions, such as neuromuscular disorders, and check their histories and physical findings once again.

The patient described in this manuscript provided her informed consent for publication.

The authors state that they have no Conflict of Interest (COI).

References

- King DK, Thompson BT, Johnson DC. Wheezing on maximal forced exhalation in the diagnosis of atypical asthma. Lack of sensitivity and specificity. *Ann Intern Med* **110**: 451-455, 1989.
- Tanizaki Y, Takeuchi T, Nakanishi K, et al. Clinical studies on a case of bronchial asthma with myasthenia gravis. *Nihon Kyobu Shikkan Gakkai Zasshi (Jpn J Thorac Dis)* **16**: 98-102, 1978 (in Japanese, Abstract in English).
- Akiba Y, Takeuchi T, Nakanishi K, et al. Bronchial asthma complicated by myasthenia gravis. *Nihon Kyobu Shikkan Gakkai Zasshi (Jpn J Thorac Dis)* **34**: 449-453, 1996 (in Japanese, Abstract in English).
- Satkunam N, Siddiqi ZA, Vethanayagam D. Severe asthma associated with myasthenia gravis. *Can Respir J* **21**: e1-e3, 2014.
- Shigawa Y, Muramatsu R, Honma A, et al. A child with myasthenic crisis who was firstly diagnosed as bronchial asthma. *Japanese J Pediatr Pulmonol* **16**: 16-20, 2005.
- Qureshi A, Choudry M, Mohammad Y, et al. Respiratory failure as a first presentation of myasthenia gravis. *Med Sci Monit* **10**: CR684-CR689, 2004.
- Miller RG, Milner-Brown HS, Mirka A. Prednisone-induced worsening of neuromuscular function in myasthenia gravis. *Neurology* **36**: 729-732, 1986.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).