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【 CASE REPORT 】

Emergency Caesarean Section Saved Both an Anti-MuSK Antibody-positive Myasthenia Gravis Mother with Pregnancy-induced Hypertension and Her Premature Baby

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Abstract:
We herein report the case of a 46-year-old pregnant woman with anti-muscle specific kinase (MuSK) antibody-positive myasthenia gravis (MG) who showed pregnancy-induced hypertension and developed respiratory failure at 30 weeks and 5 days of pregnancy, and who underwent an emergency caesarean section (CS). Her MG symptoms gradually improved in the subsequent weeks. The premature baby with positive MuSK antibodies was successfully delivered, but the male baby required temporary artificial ventilation. However, his condition also gradually improved over time. The present case suggests that an emergency CS could rescue both the mother, who was in critical condition, and the prematurely born baby, even when suffering from acute respiratory insufficiency.

Key words: myasthenia gravis, anti-MuSK antibody, emergency caesarean section, pregnancy-induced hypertension, premature baby

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Introduction

Myasthenia gravis (MG) is an autoimmune disease characterized by muscle weakness and fatigability. Among the patients with MG, but without anti-acetylcholine receptor (AChR) antibodies, anti-muscle specific kinase (MuSK) antibodies are detected in 30-40% of all cases (1-3). Bulbar symptoms have been reported to be most commonly observed in anti-MuSK antibody-positive MG (MuSK-MG) individuals who cannot be medically treated (4).

MuSK-MG has a higher prevalence in females in their twenties and thirties (5, 6). In maternal MG, medical care is often difficult because the clinical course of the disease during pregnancy can be unpredictable, and such newly born infants may develop transient neonatal myasthenia gravis (NMG) (7, 8). Several cases of pregnant MuSK-MG mothers who underwent a scheduled caesarean section (CS) have been reported (9-12). We herein describe, for the first time, an emergency CS case in which both the MuSK-MG mother, who had developed respiratory failure, and her prematurely born baby, were successfully treated and survived.

Case Report

A 43-year-old woman occasionally noticed double vision and bilateral eyelid ptosis, but otherwise had no particular past medical or familial history. She was diagnosed with dysarthria and dysphagia at 44 years of age. She became pregnant for the first time when she was 46, but was admitted to her previous hospital due to a worsening of dysarthria and dysphagia at 20 weeks (w) of pregnancy. A blood ex-

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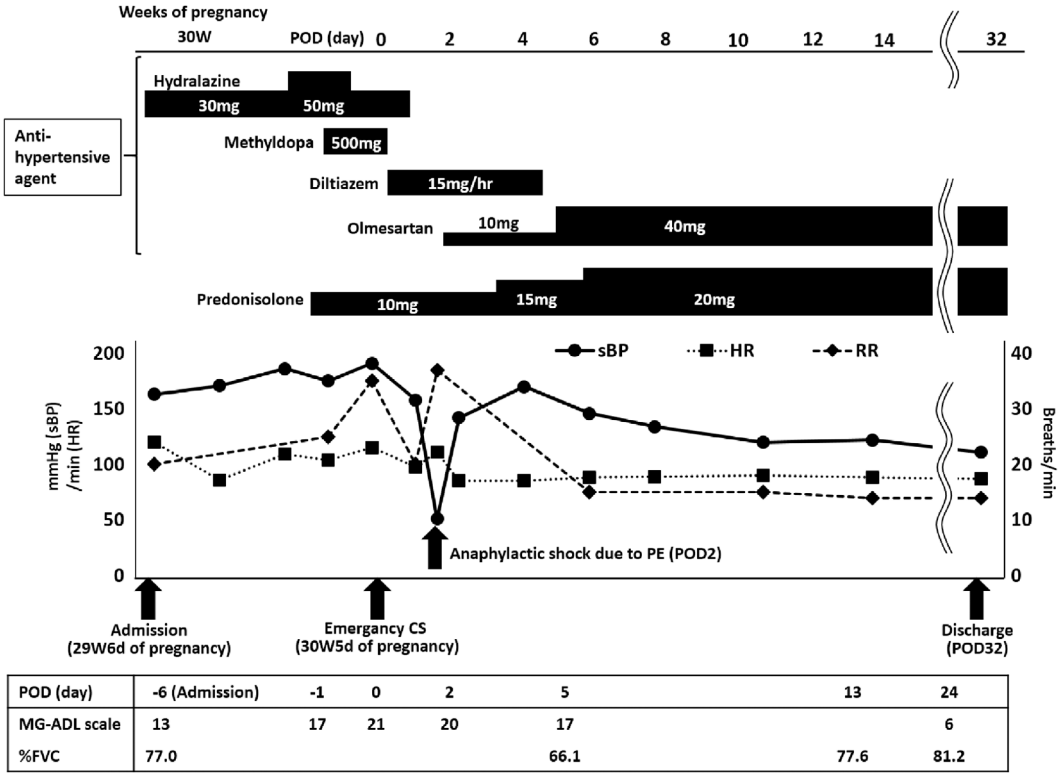

POD (day)	-6 (Admission)	-1	0	2	5	13	24
MG-ADL scale	13	17	21	20	17		6
%FVC	77.0				66.1	77.6	81.2

Figure. **Hospital course and medication of the present case. CS: caesarean section, d: days, HR: heart rate, MG: myasthenia gravis, POD: post-operative day, RR: respiratory rate, sBP: systolic blood pressure, w: weeks**

Table 1. **The Titers of Anti-MuSK Antibodies (Cut-off Value <0.02 nmol/L) of Mother and Baby.**

POD (day)		-2	0	1	8	14	26	29	43
Anti-MuSK antibodies (nmol/L)	Mother	4.88					5.32		
	Baby		1.65*	1.07	0.13	0.33		0.11	0.06

* Umbilical cord blood

amination showed her to be anti-AChR antibody-negative but anti-MuSK antibody-positive, so she was referred to our clinic with suspected MG at 23 w of pregnancy.

After undergoing neurological examinations, she presented with bilateral eyelid ptosis, bilateral upper gaze limitation, double vision in all directions, mild facial weakness, dysarthria, dysphagia and muscle weakness in neck flexion. Repetitive nerve stimulation of the facial nerve with 3 Hz showed 32 % waning. She showed a slight decrease in her vital capacity to 82 % with arterial blood gas (ABG) of pH 7.43, partial pressure oxygen (PO_2) 97.9 mmHg, carbon dioxide partial pressure (PCO_2) 35.4 mmHg, bicarbonate (HCO_3^-) 23.3 mmol/L, and alveolar-arterial oxygen difference ($AaDO_2$) 9.1, but no effort dyspnea or thymoma in the thoracic CT. An edrophonium test was not conducted to avoid a possible worsening of MG symptoms with anti-MuSK antibodies. She was diagnosed as MuSk-MG. Her dysarthria and dysphagia worsened while at home by 6 w, so she was admitted to our hospital at 29 w and 6 days (29 w 6 d) of pregnancy.

However, her myasthenic symptoms, including easy fatigability, dysarthria, and dysphagia, gradually worsened even after admission, and she developed sinus tachycardia of 100-120/min, pregnancy-induced hypertension with a systolic blood pressure (sBP) to 170-190 mmHg, and positive urine protein (4+), all of which were poorly controlled by medications, such as hydralazine and methyldopa. Oral prednisolone was started from 10 mg/d, but she required tube feeding at 30 w 4 d. Finally, she displayed respiratory insufficiency with tachypnea (35-40/min), hypercapnia, and oxygen inhalation was initiated with 2 L/min by nasal cannula at 30 w 5 d of pregnancy (ABG was pH 7.38, PO_2 135.7 mmHg, PCO_2 46.3 mmHg, HCO_3^- 26.6 mmol/L, and $AaDO_2$ 13.2), leading to an emergency CS under spinal anesthesia (Figure). At 4 minutes from the start of the surgery, the baby (boy) was safely delivered, but with a very low body weight (1,456 g) and an apgar score of 4 (at 1 minute)/7 (at 5 minutes), and moderate suspended animation, which re-

Table 2. Pregnant Patients with Anti-MuSK-mediated Myasthenia Gravis and Their Children.

Case No	Age at MG onset (years)	Age at diagnosis of MuSK-MG (years)	Age at pregnancy (years)	Past pregnancy	MG condition during pregnancy	Delivery	After delivery MG condition	Baby after birth		
								AS (1m/5m) & Weight	Anti-MuSK antibody	Symptom & course
1 (13)	13	23	24	2 miscarriage	Steady	38W1d Vaginal birth	n.m.	AS 10/10 3,190g	+	Initial dysphagia & hypotonia, normal development
2 (14)	38	39	39	2 miscarriage (Gravida 3)	Worsened at 15 & 19W	34W4d Vaginal birth with PROM	Steady	AS 9/10 2,360g	n.e.	Discharge on Day 2
3 (9)	25	32	34	First baby, CS at age 25	Steady	37W6d Scheduled CS	Steady	AS 7/9 2,558g	+	Initial dyspnea & from hypo to hypertonia of lower limbs
4 (10)	22	26	26		Polyhydramnios at 33W	38W Scheduled CS	Facial weakness & bulbar palsy for 4M	AS 8/8 2,950g	+	Ventilation for 39 d, hypotonia for 6M
5 (11)	29	30	30	Miscarriage at 10 W	Polyhydramnios & worsened state during the 2nd trimester	34W Scheduled CS	Bulbar palsy, facial weakness, limbs weakness, dyspnea	AS 3/6 n.m.	n.e.	PE on 11d, IVIg on 23 d, ventilation for 44 d, normal development
6 (12)	30	30	30		Worsened at 8M PE on 37W1d	37W6d Scheduled CS	Bulbar palsy at 2W	AS 9/9 2,482g	+	Hypotonia, tube feeding for 14 d, normal development
Present case	43	46	46		Worsened at 29 - 30W	30W5d, Emergency CS	Initial anaphylactic shock, MG symptom improved	AS 4/7 1,456g	+	Ventilator for 16 d, normal development

AS: Apgar score (at 1 min/at 5 min), CS: caesarean section, d: days, M: months, n.e.: not examined, n.m.: not mentioned, PE: plasma exchange, PROM: premature rupture of membranes, Ref: reference, W: weeks

quired the baby to receive tracheal intubation with artificial ventilation. An examination of the umbilical cord blood showed that anti-MuSK antibodies were positive (1.65 nmol/L; normal range 0-0.02 nmol/L).

The mother's dysarthria, eyelid ptosis and double vision worsened after the delivery, although her respiratory status improved as did her blood pressure (BP) and heart rate. She thus received plasma exchange (PE) with fresh frozen plasma (FFP) on post-operative day (POD) 2, but she then became acutely hypotensive (BP 51/35 mmHg) and devel-

oped tachycardia (111/min) followed by anaphylactic shock which occurred 5 minutes after FFP administration. Thus, FFP administration was immediately stopped, and she was successfully resuscitated. Oral prednisolone treatment increased from 10 to 20 mg/d after POD6 (Figure). With this steroid and antihypertensive olmesartan, her MG symptoms and hypertension gradually improved. Her baby also recovered from respiratory failure, and underwent extubation on POD16 without any trouble. The mother was able to hold her baby for the first time on POD23, and she was discharged on POD32 while her baby was discharged on POD 53. The anti-MuSK antibody levels in the serum of her baby decreased, as assessed by POD43, over the clinical course. Maternal anti-MuSK antibody titers remained high (Table 1).

Discussion

This case report shows that an emergency CS was able to save both the critical MuSK-MG mother and her prematurely born baby. There are only six cases reported thus far of pregnant MuSK-MG, four of which were delivered by CS (9-12), while two were delivered vaginally (13, 14). All six of those deliveries were performed at 34-38 w of pregnancy. In contrast, this is the first report of a successful emergency CS as early as 30 w with very low baby weight (1,456 g, Table 2).

From a total of seven MuSK-MG patients, three experienced miscarriages in the past and four showed worsened MG symptoms during pregnancy (Table 2). The present case developed tachycardia, tachypnea, easy fatigability, dysarthria, dysphagia, and pregnancy-induced hypertension, even after admission. We thought that the mother's respiratory insufficiency had probably been caused by MG symptoms, pregnancy-induced hypertension, and fetal compression to the mother's diaphragm, leading her to need an emergency CS. Only a few hours after delivery, the mother's MG symptoms temporarily improved, most likely due to the release of fetal compression from her diaphragm. Although this mother initially showed worsening bulbar symptoms and anaphylactic shock after the emergency CS, she recovered safely from these fetal problems and her MG symptoms gradually improved (Figure).

Among the seven recorded MuSK-MG-related deliveries, five babies were positive for anti-MuSK antibodies (two were not examined), five developed transient NMG, and three required artificial ventilation for 16-44 d (Table 2). Polyhydramnios is a sign of NMG (10, 11). Two babies (Cases No. 4 and 5) with polyhydramnios showed more severe symptoms than the other babies (Table 2). Although the present case showed an upper limit volume of amniotic fluid at 25 w 6 d of pregnancy, the baby did not show any fetal abnormalities. The anti-MuSK antibodies of the present case decreased within the first month (Table 1). The present baby briefly showed mild generalized hypotonia, delayed gastrointestinal transit, and respiratory distress syndrome, which required tracheal intubation with artificial ventilation for 16 d. The present baby was delivered by emergency CS at 30 w 5 d of pregnancy. From this reason, it was difficult to determine whether his symptoms were caused by NMG or premature birth with the deficiency of pulmonary surfactant. However, these symptoms gradually improved within 44 d, and he developed normally after the delivery.

The present case suggests that careful monitoring is required for MuSK-MG patients during pregnancy, and that an emergency CS can save the lives of both the mother and baby, even when suffering from acute respiratory insufficiency.

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

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