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CASE REPORTS / CASE SERIES

# Monitoring of neuromuscular blockade in one muscle group alone may not reflect recovery of total muscle function in patients with ocular myasthenia gravis

# Le monitorage du bloc neuromusculaire dans un groupe de muscles peut ne pas refléter la récupération de la totalité de la fonction musculaire chez des patients souffrant de myasthénie oculaire

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**Abstract**

**Purpose** *We report on two patients with ocular myasthenia gravis who received rocuronium, followed later by sugammadex to reverse neuromuscular blockade. Recovery was monitored simultaneously at the adductor pollicis muscle (APM) and the corrugator supercilii muscle (CSM).*

**Clinical features** *Two patients with ocular myasthenia gravis (case 1: 74 yr-old female, 54 kg; case 2: 71 yr-old male, 72 kg) were scheduled for surgery under general anesthesia. Neuromuscular blockade was induced with rocuronium 0.3 mg·kg$^{-1}$ after placing two separate monitors at the APM and the CSM, respectively. Additional doses of rocuronium 0.1-0.2 mg·kg$^{-1}$ were given to maintain neuromuscular blockade at fewer than two twitches at the APM during surgery. Train-of-four response at the CSM did not show recovery of the twitch after its initial disappearance. At the end of surgery, sugammadex was administered. Twitch height at the APM recovered to the control value in 12 min (case 1) and 13 min (case 2) after sugammadex administration; however, twitch height at the CSM took 26 min (case 1) and 14 min (case 2) to recover to the control value.*

**Conclusion** *After rocuronium-induced paralysis in both patients with ocular myasthenia, spontaneous recovery and sugammadex-assisted recovery were slower at the CSM than at the APM. In patients without the disorder, CSM recovery is faster than APM recovery. Thus, in ocular myasthenia gravis, neuromuscular recovery at the APM may not reflect recovery of all muscles.*

**Résumé**

**Objectif** *Nous présentons le cas de deux patients souffrant de myasthénie oculaire qui ont reçu du rocuronium, suivi ultérieurement de sugammadex pour antagoniser le blocage neuromusculaire. La récupération a été suivie simultanément au niveau de l'adducteur du pouce et du sourcilier.*

**Caractéristiques cliniques** *Deux patients souffrant de myasthénie oculaire (cas 1: femme de 74 ans, 54 kg; cas 2: homme de 71 ans, 72 kg) devaient subir une intervention chirurgicale sous anesthésie générale. Le relâchement musculaire a été induit avec du rocuronium 0,3 mg·kg$^{-1}$ après avoir placé deux neurostimulateurs, l'un sur l'adducteur du pouce et l'autre sur le sourcilier. Des doses supplémentaires de rocuronium 0,1 à 0,2 mg·kg$^{-1}$*

**Author contributions** *Hajime Iwasaki*, *Kenichi Takahoko*, *Shigeaki Otomo,* and *Tomoki Sasakawa* were involved in the conception and design of the study. *Hajime Iwasaki*, *Kenichi Takahoko,* and *Shigeaki Otomo* were involved in the acquisition of data and in drafting the manuscript. *Hajime Iwasaki*, *Takayuki Kunisawa,* and *Hiroshi Iwasaki* were involved in the analysis and interpretation of the data. *Tomoki Sasakawa*, *Takayuki Kunisawa,* and *Hiroshi Iwasaki* were involved in manuscript revision.

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*ont été administrées pour maintenir le bloc neuromusculaire à moins de deux réponses musculaires au niveau de l'adducteur du pouce pendant l'intervention. Au niveau du sourcilier, aucune récupération des réponses Td4 (train-de-quatre) n'a été observée après leur disparition initiale. Du sugammadex a été administré à la fin de l'intervention. Au niveau de l'adducteur du pouce, la première réponse est revenue à la valeur de référence 12 minutes (pour le cas 1) et 13 minutes (pour le cas 2) après l'administration de sugammadex. Cependant, le retour de la première réponse à la valeur de référence a pris 26 minutes (cas 1) et 14 minutes (cas 2) au niveau du sourcilier.*

**Conclusion** *Chez les deux patients souffrant de myasthénie oculaire, la récupération spontanée et la récupération assistée par l'administration de sugammadex a été retardée au niveau du sourcilier par rapport à l'adducteur du pouce dans le cas d'une curarisation induite par rocuronium. Chez des patients normaux, la récupération du sourcilier est plus rapide que celle de l'adducteur du pouce. Donc, en cas de myasthénie oculaire, la récupération neuromusculaire de l'adducteur du pouce peut ne pas refléter la récupération de tous les muscles.*

Postoperative residual neuromuscular blockade following the use of non-depolarizing neuromuscular blocking agents continues to be a clinical problem despite increased awareness and better monitoring methods.[1-3] Acquired or congenital muscle diseases have the potential to aggravate residual blockade. Myasthenia gravis is an autoimmune muscle disease involving circulating autoantibodies that reduce the number of nicotinic acetylcholine receptors at the neuromuscular junction.[4] Ocular and bulbar muscles are either first or most commonly affected.[5] Ocular myasthenia gravis (OMG) is a localized form of the disease and presents only with ocular symptoms, including ptosis and diplopia.[6,7]

In view of the extreme sensitivity of patients with myasthenia gravis to non-depolarizing neuromuscular blocking agents, monitoring of neuromuscular function is imperative.[8] The recommended site for monitoring neuromuscular function in normal patients is the adductor pollicis muscle (APM) because it reflects upper airway function.[9] The corrugator supercilii muscle (CSM) is a convenient monitoring site, but it is not recommended to guide management of neuromuscular recovery because it recovers faster than the APM or the upper airway muscles in patients without the disease.[10,11] In contrast, it has been previously shown that MG patients exhibit greater sensitivity at the CSM than at the APM.[12] Nevertheless, it is uncertain whether recovery is faster at the CSM than at the APM in patients with myasthenia gravis, particularly when reversal drugs are used to antagonize neuromuscular blockade.

In this report, we describe two OMG patients who received rocuronium to induce neuromuscular blockade, followed later by sugammadex to reverse the paralysis. The recovery patterns at the APM and CSM were monitored simultaneously. The patients gave written informed consent before the publication of this case report.

## Clinical features

### Case 1

A 74-yr-old female (weight 54 kg, height 157 cm) was scheduled for capsulosynovectomy of her left elbow. The patient was diagnosed with OMG (The Myasthenia Gravis Foundation of America [MGFA] clinical classification Class 1)[13] in 1998 and underwent a thymectomy in 1999. She had no symptoms of MG and was not taking medication after her thymectomy. The patient received no premedication. Anesthesia was induced by a target-controlled infusion of propofol (target plasma propofol level 3 $\mu g \cdot mL^{-1}$).

#### *Neuromuscular monitoring*

After induction of anesthesia, neuromuscular function was assessed at the APM and the CSM every 15 sec using two separate TOF-Watch® SX accelerometers (Organon, Dublin, Ireland). Separate transducers were attached to a thumb and to the internal half of the left superciliary arch. The twitch responses of the APM were stabilized and the supramaximal current was automatically calibrated using mode CAL2 of the TOF-Watch® SX during ulnar nerve stimulation. Facial nerve stimulation was applied at the temporal area at a current of 30-35 mA to avoid direct stimulation of the CSM itself or other facial muscles.[14,15] To increase the sensitivity of the transducer, the control twitch height of the CSM was set to 100% using the CAL1 mode of the TOF-Watch®. The peripheral skin temperature was maintained above 34° by using a blanket, and end-tidal $CO_2$ was maintained at 35-40 mmHg.

#### *Neuromuscular responses*

After stabilization of the twitch responses, rocuronium 0.3 $mg \cdot kg^{-1}$ was administered (Fig. 1). Two additional incremental doses (0.1 $mg \cdot kg^{-1}$ each) were needed at the APM because the twitch response did not disappear with the initial dose. After a total dose of 0.5 $mg \cdot kg^{-1}$, only one

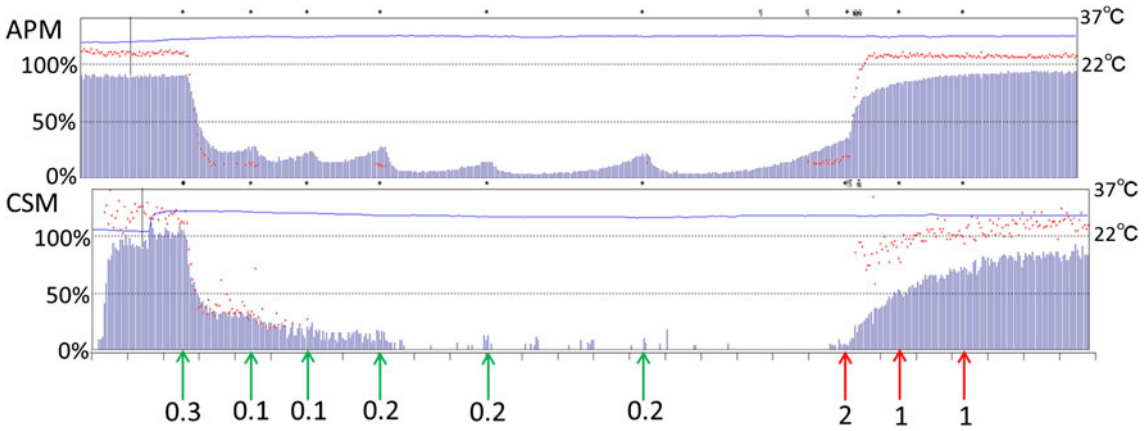


**Fig. 1** *Case 1*: Twitch height (blue bars) and TOF ratio (red dots) at the adductor pollicis muscle (APM) and the corrugator supercilii muscle (CSM) as a function of time. Blue horizontal line shows peripheral temperature. The *x*-axis shows time scale in five-minute increments. The numbers below the arrows indicate the dose ($mg \cdot kg^{-1}$) of rocuronium (green arrow) and sugammadex (red arrow)

response was observed at the APM with train-of-four (TOF) stimulation. At this point, tracheal intubation was performed. Anesthesia was maintained with propofol at a target plasma concentration of 2-3 $\mu g \cdot mL^{-1}$ and remifentanil 0.15-0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Additional doses of rocuronium 0.2 $mg \cdot kg^{-1}$ were given to maintain neuromuscular blockade at fewer than two twitches at the APM. Although twitch responses reappeared at the APM as time increased since the last dose, twitch responses at the CSM were completely absent throughout. Sugammadex 2 $mg \cdot kg^{-1}$ was administered at the end of surgery when four twitch responses were present following TOF stimulation at the APM (twitch height of the first twitch [T1 height] was 36% of baseline and the TOF ratio was 20%) (Fig. 2). The TOF ratio reached 90% within 1.5 min at the APM and within five minutes at the CSM (Table). Since the T1 height of both the APM and the CSM had not recovered to the control level, a second dose of sugammadex 1 $mg \cdot kg^{-1}$ was administered approximately seven minutes after the first dose was given. Recovery of the T1 height to control took approximately five minutes after the second sugammadex dose, while recovery of the T1 height at the CSM was only 65% of control. A third sugammadex injection (1 $mg \cdot kg^{-1}$) was given nine minutes after the second dose. Approximately ten minutes after the third dose of sugammadex, the height of the T1 at the CSM recovered almost to that of control. After tracheal extubation, the patient did not show evidence of residual paralysis, as assessed by a head lift and hand grip test.

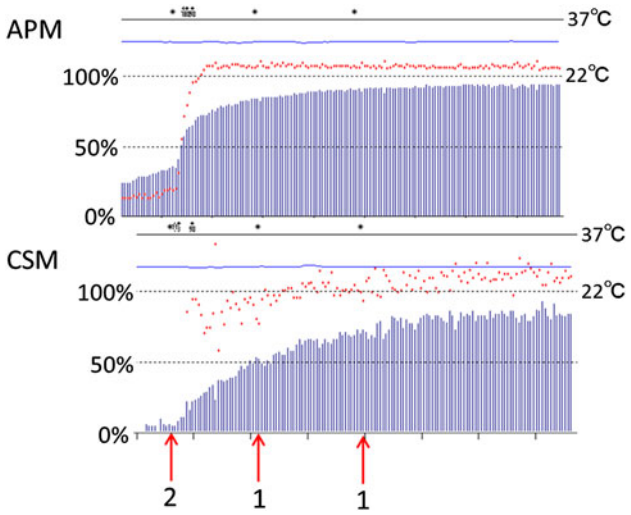


**Fig. 2** *Case 1*: Enlarged view of recovery of neuromuscular blockade at the adductor pollicis muscle (APM) and the corrugator supercilii muscle (CSM) after sugammadex administration. Blue horizontal line shows peripheral temperature. The *x*-axis shows time scale in five-minute increments. The numbers below the arrows indicate the dose ($mg \cdot kg^{-1}$) of sugammadex

## Case 2

A 71-yr-old male (weight 72 kg, height 165 cm) was scheduled for a transcervical thymectomy. He was diagnosed with OMG (MGFA clinical classification Class 1)[13] three months before the surgery. He had a slight ptosis and was taking pyridostigmine 180 $mg \cdot day^{-1}$. The patient received no premedication. After placing the epidural catheter at the T5 to T6 level, induction of anesthesia was performed with propofol 2 $mg \cdot kg^{-1}$. Neuromuscular monitoring was set up as for case 1.

### *Neuromuscular responses*

After stabilization of twitch responses, rocuronium 0.3 $mg \cdot kg^{-1}$ was administered (Fig. 3). Tracheal

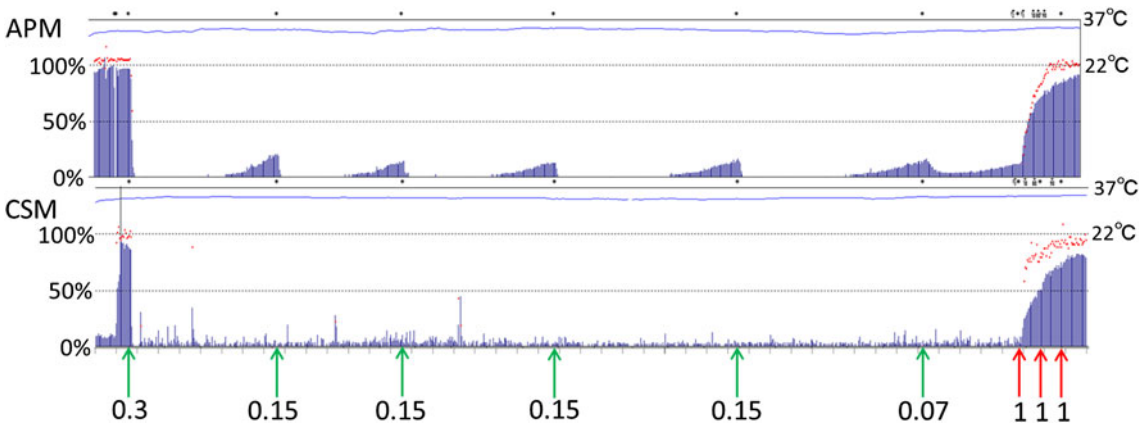


**Fig. 3** *Case 2*: Twitch height (blue bars) and TOF ratio (red dots) at the adductor pollicis muscle (APM) and the corrugator supercilii muscle (CSM) as a function of time. Blue horizontal line shows peripheral temperature. The *x*-axis shows time scale in five-minute increments. The numbers below the arrows indicate the dose ($mg \cdot kg^{-1}$) of rocuronium (green arrow) and sugammadex (red arrow)

intubation was performed after twitch responses at the APM disappeared. Anesthesia was maintained with 1.5% end-tidal sevoflurane, remifentanil 0.1-0.15 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and intermittent bolus doses (3 mL × 3) of 0.375% ropivacaine for epidural anesthesia. End-tidal sevoflurane was kept at 1.5% until full recovery of the neuromuscular blockade after surgery. Additional doses of rocuronium 0.15 $mg \cdot kg^{-1}$ were given to maintain neuromuscular blockade at fewer than two twitches at the APM during the surgery. Similar to case 1, twitch responses at the APM recovered within a short period after each rocuronium dose; however, TOF stimulation at the CSM showed no twitch response after its initial disappearance. At the end of surgery, sugammadex 1 $mg \cdot kg^{-1}$ was administered when two twitch responses were observed at the APM (Fig. 4). A second dose of sugammadex 1 $mg \cdot kg^{-1}$ was given five minutes after the first dose of sugammadex was administered because the TOF ratio was $< 90\%$ at both the APM and the CSM. Subsequently, the TOF ratio reached 90% at the APM and at the CSM in 1.5 min and 2.5 min, respectively (Table), but T1 height did not completely recover. Therefore, a third dose of sugammadex (total dose 3 $mg \cdot kg^{-1}$) was administered five minutes after the second dose. An almost complete recovery of T1 height was achieved approximately 13 and 14 min later at the APM and the CSM, respectively. After tracheal extubation, the patient showed no evidence of residual paralysis, as assessed by head lift and hand grip test.

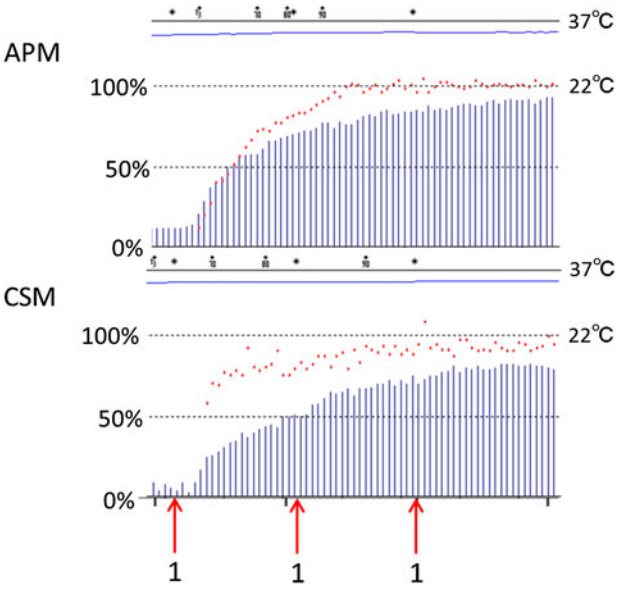


**Fig. 4** *Case 2*: Enlarged view of recovery of neuromuscular blockade at the adductor pollicis muscle (APM) and the corrugator supercilii muscle (CSM) after sugammadex administration. Blue horizontal line shows peripheral temperature. The *x*-axis shows time scale in five-minute increments. The numbers below the arrows indicate the dose ($mg \cdot kg^{-1}$) of sugammadex

## Discussion

In both patients with ocular myasthenia gravis, spontaneous recovery occurred later at the CSM than at the APM after rocuronium-induced muscle paralysis. Sugammadex-assisted recovery was also less complete and occurred later at the APM compared with the CSM. Thus, the recovery pattern of these muscles was completely opposite to that seen in patients without the disease, whose CSM recovers earlier than the APM, much like the diaphragm or the larynx.[15] In normal individuals, the CSM also shows faster recovery than the APM even when neostigmine is used to reverse rocuronium-induced neuromuscular blockade.[14] Since neuromuscular transmission in patients without the disease recovers later

**Table** Twitch height of the first twitch (T1 height), train-of-four (TOF) ratio, and recovery times after sugammadex

| | Case 1 | | Case 2 | |
|---|---|---|---|---|
| | Adductor pollicis | Corrugator supercilii | Adductor pollicis | Corrugator supercilii |
| Baseline T1 height (%) | 90 | 100 | 97 | 90 |
| Baseline TOF ratio (%) | 110 | 110 | 105 | 99 |
| T1 height (%) 3 min after rocuronium 0.3 mg·kg$^{-1}$ | 35 | 39 | 0 | 0 |
| T1 height (%) before initial sugammadex administration | 36 | 5 | 12 | 6 |
| Time (min) from initial sugammadex administration to TOF ratio = 90% | 1.5 | 5.2 | 6.5 | 7.5 |
| Time (min) from initial sugammadex administration to maximum recovery of T1 height | 12 | 26 | 13 | 14 |

at the APM than at the CSM, the APM is a better predictor of the adequacy of reversal than the CSM.[9,16] On the other hand, based on our observations, the opposite occurs in OMG patients. It therefore seems prudent to monitor both the APM and the CSM when assessing neuromuscular function in OMG patients.

The TOF ratio sometimes recovers faster than twitch height (T1) after sugammadex administration.[17,18] We observed the same phenomenon in our patients. The TOF ratio at both the CSM and the APM recovered to ≧90% before complete recovery of T1 height. Therefore, it may be more appropriate to monitor not only TOF ratio but also twitch height compared with baseline, particularly in the presence of muscle pathology.

There are several reports on the usefulness of sugammadex to reverse rocuronium-induced neuromuscular blockade in patients with myasthenia gravis.[19-22] In these studies, the doses of sugammadex administered were the same as that recommended to patients without the disease. In case 1, sugammadex 2 mg·kg$^{-1}$ was administered when four TOF responses were present at the APM (same dose as recommended in healthy patients), and the TOF ratio recovered to ≧90% in 90 sec. In case 2, sugammadex 1 mg·kg$^{-1}$ was administered at two TOF responses at the APM (half the recommended dose), and the time to a TOF ratio of ≧90% was five minutes. Also, additional doses of sugammadex (total 2 mg·kg$^{-1}$) were required to achieve complete neuromuscular recovery at the APM. Thus, it appears that at least the equivalent dose of sugammadex recommended for patients without the disease is necessary for MG patients to reverse the rocuronium-induced neuromuscular blockade, even though the total dose of rocuronium required during surgery might be less than that in healthy patients.

These cases illustrate the salient point that monitoring of the traditional muscle group, the APM, alone may not be sufficient in disease states such as OMG and may not accurately reflect the status of the muscles affected by a pathological state. In the case of OMG, recovery of the CSM might reflect the function of the bulbar muscles, which are commonly involved with the ocular muscles. The doses of sugammadex recommended for patients without the disease seem to apply to OMG patients, even if the doses of rocuronium used in OMG patients may be less than those used in patients without the disease.

**Conflict of interest** Hiroshi Iwasaki has given paid lectures for Merck (MSD), Japan and has attended MSD conferences.

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