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Case Report

Discordance between Train-of-Four Response and Clinical Symptoms in a Patient with Amyotrophic Lateral Sclerosis

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A 47-year-old woman with amyotrophic lateral sclerosis was scheduled for total thyroidectomy with cervical node dissection. During anesthetic management by total intravenous anesthesia using remifentanyl, propofol, and rocuronium, train-of-four (TOF) monitoring findings were not consistent with clinical signs. Sugammadex successfully reversed shallow respiration.

Key words: amyotrophic lateral sclerosis, train-of-four, sugammadex

Amyotrophic lateral sclerosis (ALS) is motor neuron disorder, commonly called Lou Gehrig's disease. ALS is known to involve upper and lower motor neurons and to lead to death or severe disability within a few years [1]. Patient age at disease onset and the affected site are the important prognostic factors of mortality and perioperative course [2]. Response to neuromuscular blocking agents is more sensitive in patients with motor neuron disease, and monitoring of neuromuscular function is an essential part of general anesthesia in these patients [3]. However, sometimes, the results of neuromuscular monitoring are incompatible with clinical findings in ALS [3].

We report an ALS patient with train-of-four (TOF) monitoring results in distal limbs that were not consistent with respiratory status and reversed rocuronium using sugammadex after total intravenous anesthesia.

Case Report

A 47-year-old, 165-cm tall, 38-kg female was scheduled for total thyroidectomy with cervical node dissection. The patient had been diagnosed with ALS 4 years prior to this presentation, and had been taking phenytoin 2×150 mg daily on a regular basis. Her preoperative physical examination showed generalized muscle wasting without tongue atrophy, and her neurological examination revealed grade 4/5 muscle strength in upper limbs, grade 3/5 in lower limbs, grade 4/5 for neck flexion/extension, and hypoactive deep tendon reflexes without pathologic reflexes. The patient reported no slurred speech or dysphagia and was of New York Heart Association (NYHA) functional class III. Spirometry showed a forced vital capacity (FVC) of 1.831 (60% of reference), forced expiratory volume in 1 sec (FEV₁) of 1.651 (75%), and a FEV₁/FVC of 90%. Resting arterial blood gas analysis showed a pH of 7.383, PaCO₂ of 38.84 mmHg, PaO₂ of 64.1 mmHg, HCO₃⁻ of 23.3 mEq/l, and -SaO₂ of 91.8%. All other biochemistry values were within normal limits. Chest X-ray showed several calcified nodules in both upper lung fields. She was not premedicated and upon arrival at the operating the-

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atre, standard monitoring devices were applied. Vital signs were 94/64 mmHg, 59 beats/min, and SaO₂ was 92% before anesthetic induction. We applied neuromuscular monitoring devices (Innervator; Fisher & Paykel Health Care, Auckland, New Zealand) on orbicularis oculi. Anesthesia was induced and maintained with propofol (target blood concentration 1.5–3.0 µg/ml) and remifentanyl (target blood concentration 0.7–2.5 ng/ml), using a target controlled infusion device (Orchestra; Fresenius Kabi, Bad Homburg, Germany). Schnider's and Minto's pharmacokinetic models were used to calculate target effect-site concentrations for propofol and remifentanyl, respectively. Three min after administration of rocuronium 0.3 mg/kg, there was no twitching in response to TOF stimulation at 50 mA and the patient was intubated. At that time, the patient's lower limbs showed fasciculation with a bucking motion. Additional rocuronium 10 mg was administered and within 1 min, the fasciculation and bucking disappeared. Propofol and remifentanyl concentrations were adjusted to maintain a bispectral index (BIS) score between 40 and 60. Because of persistent low blood pressure, ephedrine 0.2–0.5 mg/kg/h was infused to achieve a target mean arterial pressure of over 65 mmHg, throughout the operation. At 90 min after anesthetic induction, an additional 5 mg of rocuronium was administered due to bucking during operative tracheal manipulation without TOF response. Surgery was completed without any significant sequelae and the total anesthesia time was 405 min. At the end of the operation, all 4 twitches of the TOF returned in the orbicularis oculi and the ulnar nerve TOF ratio was 0.98 (TOF -Watch SX, Organon, Dublin, Ireland). However, her tidal volume was inadequate and she was unable to open her eyes spontaneously. Accordingly, Sugammadex (1 mg/kg *iv*) was given, and about 1–2 min later, tidal volume was sufficient and eye opening was possible. Following extubation, she was monitored closely in the post-anesthetic care unit for 60 min and then transferred to an intensive care unit. Arterial blood gases and other biochemistry values were within normal limits following extubation. The patient remained in the intensive care unit for a day and was discharged from the hospital on the 4th postoperative day.

Discussion

In our patient with ALS, findings from neuromuscular monitoring of the extremities were incompatible with clinical findings. During anesthetic induction, 0.3 mg/kg of rocuronium was sufficient to prevent a TOF response, but was not sufficient for tracheal intubation. During anesthetic emergence, TOF response was > 0.9, but spontaneous respiration was not enough to allow extubation.

ALS is the most common motor neuron disease and has a slowly progressive nature with a mean survival of approximately 3 year [2], but disease progression is highly variable. Age and site a onset are known to be the most important prognostic factors [1, 2]. In our patient, onset was before the fifth decade and with no evident signs of bulbar involvement, such as slurring of speech, which leads to impaired airway protection and is known as a poor prognostic factor. Weakness of respiratory muscles can also lead to respiratory failure and death [4]. Although, our patient had a young onset mainly in her limbs, she had advanced muscle weakness and complained of dyspnea, and was evaluated as NYHA functional class III. Considering the relatively low PaO₂ result in the preoperative arterial blood gas analysis (64.1 mmHg), we concluded that ALS was aggravated enough to involve the respiratory muscles.

We chose to use total intravenous anesthesia (TIVA) with propofol and remifentanyl in this case. A previous clinical study reported that ideal intubating conditions without muscle relaxants can be achieved with propofol 3 mg/kg, fentanyl 2 µg/kg, and lidocaine 1.5 mg/kg without significant hemodynamic changes [5]. Lee *et al.* [6] reported a case of TIVA without muscle relaxant in ALS patients and determined effect site concentrations of remifentanyl and propofol of 5.5 and 5.0 ng/ml for tracheal intubation. However, in our patient blood pressures were subnormal even after the administration of ephedrine, and we could not use high doses of propofol or remifentanyl to avoid neuromuscular blocking agents.

Our patient had been taking phenytoin to stabilize nonspecific muscle cramps for several years. Chronic phenytoin therapy increases the clearance of neuromuscular blocking agents and reduces patient sensitivity to the circulating concentration of neuromuscular blocking agent (NMBA), which leads to rapid recovery

from paralysis [7–9]. However, in ALS patients, vulnerability to NMBA and to medications used to control abnormal neuromuscular movements should be considered.

Previous cases reports on ALS patients have shown that monitoring of neuromuscular function during general anesthesia is vital for proper titration of anesthetic agents, including NMBA [3, 6, 10]. However, because the site of onset, rate of disease progression, and involvement sites vary considerably in ALS patients, clinicians must interpret neuromuscular monitoring results very carefully. Kelsaka *et al.* [3] reported a case in which the TOF ratio was incompatible with clinical findings in an ALS patient. More specifically, when the TOF ratio exceeded 0.90, the depth of respiration was insufficient and the patient was unable to open his eyes [3]. In our case, we also experienced discordance between the TOF response and clinical findings during anesthetic induction and emergence.

Cholinesterase inhibitors are commonly used to reverse residual NMBA effects. This agent inactivates acetylcholinesterase (AChE), which is responsible for the breakdown of Ach, and for displacing NMBA molecules to Ach from the nicotinic receptors. Because the NMBA has longer duration of action than cholinesterase inhibitors, there is a risk of re-occurarization. Sugammadex is a new selective relaxant binding agent that directly encapsulates and inactivates NMBA, and thus, prevents re-occurarization without cholinergic side effects [11]. In our patient, we could not differentiate remnant NMBA from disease progression, but excluding the risk of re-occurarization or remnant NMBA function by administering a smaller than recommended dose (2–4 mg/kg) of sugammadex proved helpful.

In conclusion, careful consideration of disease progression and drug interactions are important for

the anesthetic management of ALS. Clinical symptoms and signs must be given preference over data from monitoring devices.

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