Anesthesiology
71:779–781, 1989

Completely Absent Response to Peripheral Nerve Stimulation in an Acutely Hypothyroid Patient

LAWRENCE R. MILLER, M.D.,* JONATHAN L. BENUMOF, M.D.,† LANCELOT ALEXANDER, M.D.,‡
C. A. MILLER, M.D.,* DAVID STEIN, M.D.§

Patients with untreated severe hypothyroidism are predisposed to multiple complications when exposed to general anesthesia. These patients respond to opioids with increased central nervous system (CNS) and respiratory depression and to volatile agents with increased hypotension and myocardial depression.[1–6] In some patients with severe hypothyroidism, the upper respiratory tract is threatened by an enlarged tongue and myxedematous infiltration of the vocal cords, and the risk of pulmonary aspiration is increased due to the associated conditions of adynamic ileus, somatic obesity, and delayed gastric emptying.[1] The severely hypothyroid patient is also at risk postoperatively for respiratory failure due to respiratory muscle weakness and impaired responsiveness to hypercarbia.[6,7] The risk of postoperative respiratory failure is compounded by the fact that hypothyroid patients may be more sensitive to standard doses of nondepolarizing neuromuscular blocking drugs due to a propensity to develop hypothermia, the presence of a hypothyroid myopathy, and decreased hepatic metabolism and renal elimination of these drugs.[1,8]

We herein report a unique case of a completely absent response to peripheral nerve stimulation prior to and after the administration of neuromuscular blocking agents in a normothermic severely hypothyroid patient. Response to nerve stimulation remained absent despite clinical signs of return of adequate muscle strength, testing of multiple nerves, use of multiple nerve stimulators, and attempts to maximally increase the effective nerve stimulus intensity by reversing cathodal–anodal positions. We were therefore unable to utilize the twitch response to guide decisions when additional doses of neuromuscular blocking agents were needed and when antagonism could be expected to safely reverse the paralysis. We suggest that the acute severe hypothyroid state interfered with neuromuscular excitability.

CASE REPORT

The patient is a 34-yr-old, 115 kg, 152 cm female who had a 1-yr history of a reducible umbilical hernia, a 14-day history of nausea, vomiting, and anorexia, a 7-day history of sharp constant periumbilical pain, and a 1-day history of fever and shaking chills. On admission the hernia was tender and irreducible and the patient was scheduled for emergency laparotomy for an incarcerated umbilical hernia.

The patient had a past history of Hashimoto's thyroiditis, which was diagnosed in 1985 when she presented with weight gain, lassitude, anemia, and a "husky voice." She was receiving thyroxin 0.2 mg po bid. However, with the onset of her present illness, she had not taken her thyroid replacement therapy, and on presentation she had major complaints of marked fatigue and difficulty with memory and concentration.

Initial vital signs consisted of a blood pressure of 140/90 mmHg, pulse of 59 beats/min, a respiratory rate of 12 breaths/min, and a core temperature of 37.4° C. No orthostatic blood pressure changes were noted. Her skin was cool to touch. Her airway was remarkable for a large thick tongue. There was no palpable goiter. Deep tendon reflexes were unobtainable in all extremities. Initial laboratory findings consisted of a leukocytosis of 17.6×10^3 cells/mm^3 with a left shift. All serum electrolytes (sodium, potassium, calcium, and bicarbonate) were normal. Thyroid function tests obtained on admission revealed severe hypothyroidism with a thyroid-stimulating hormone [TSH] = 151.0 μIU/ml (0.3–7.3 μIU/ml) and a free T4 index = 0.6 μg/dl (3.4–12.7 μg/dl).

Anesthesia monitoring consisted of automated blood pressure and pulse, ECG, capnography, pulse oximetry, esophageal temperature probe, and a peripheral nerve stimulator (ACM Systems). While breathing 100% oxygen the patient received *d*-tubocurarine 3 mg iv. Four minutes later a rapid sequence induction using thiopental 350 mg iv and succinylcholine 160 mg iv was performed and while cricoid pressure was constantly applied, tracheal intubation was accomplished in 10 s. Anesthesia was maintained over the next 2 h with fentanyl 500 μg iv in five equally divided doses and isoflurane 0.5%–1.2%. Intraoperatively temperature was maintained between 37.0 and 37.5° C with the aid of a warming blanket and by passing iv fluids through a blood warmer. Throughout the case the blood pressure ranged 110–130/70–85 mmHg and pulse ranged 55–70 beats/min.

Prior to the initial surgical incision and 10 min after administration of succinylcholine, the patient had return of apparently adequate spontaneous respirations (end-tidal CO_2 = 35 mmHg). Neither single twitch nor tetanus could be elicited with a nerve stimulator despite using a maximal stimulus intensity (35 mA) with surface electrodes over bilateral facial, ulnar, median, and posterior tibial nerves. Three nerve stimulators were tried at maximal intensity over all eight nerves without eliciting any response. Each nerve stimulator was determined to be functioning properly when tested on two awake volunteers. Be-

* Resident in Anesthesiology.
† Professor of Anesthesiology.
‡ Assistant Clinical Professor of Neurosciences.
§ Resident in Neurosciences.

Received from the Department of Anesthesiology, University of California San Diego, La Jolla, California. Accepted for publication June 5, 1989. Supported by the Department of Anesthesiology, University of California San Diego.

Address reprint requests to Dr. Benumof: Anesthesia Research Lab, T-001, University of California San Diego, La Jolla, California 92093.

Key words: Hypothyroidism: Neuromuscular blockade monitoring. Peripheral nerve stimulators.

cause respirations appeared adequate, and despite the absent peripheral nerve stimulator findings, 4 mg of pancuronium was administered. After 1 h the patient was again noted to be spontaneously breathing and the surgeons thought that the abdominal muscles were inadequately relaxed. Again, no single twitch or response to tetanic stimulation could be elicited despite stimulation at maximal intensity, testing multiple nerve sites, using several different functioning nerve stimulators, and with reversing cathodal and anodal positions in an attempt to increase the nerve stimulation. Nevertheless, because of the clinical findings, a supplemental dose of 2 mg pancuronium was administered. Similarly, at the end of surgery no response could be elicited with the nerve stimulator. The pancuronium was not antagonized with an anticholinesterase because of the absence of any response to nerve stimulation. The patient was transported to the recovery room and received full mechanical ventilatory support. Thirty minutes postoperatively the patient made spontaneous movements and respirations, and she received 3.5 mg neostigmine and 0.7 mg glycopyrrolate iv. Significant reversal of neuromuscular blockade was achieved within 15 min as demonstrated by her ability to sustain head-lift for 5 s and a strong hand grasp. Arterial blood gas was drawn after another 15-min period during spontaneous ventilation and the $F_{I_{O_2}}$ = 0.4 revealed a *p*H = 7.4, Pa_{O_2} = 78 mmHg, Pa_{CO_2} = 38 mmHg, and a H_{CO_3} = 23 mEq/l. Despite this evidence of adequate clinical muscle strength, the patient continued to show no twitch or tetanic response to nerve stimulation (multiple sites, multiple stimulators). The trachea was extubated uneventfully at this time.

Twelve hours after surgery but before her first dose of replacement thyroid medication, the patient still failed to respond to nerve stimulation testing. After receiving thyroxin 0.1 mg iv qid for 2 days, gross muscle twitches were elicited with maximal facial nerve stimulation but were subjectively reduced in amplitude.

Formal nerve conduction studies were performed on the second postoperative day. All motor nerve conduction studies required very high stimulus intensities (150–300 V, 1 ms duration with TECA-42 Electromyograph®) to produce a motor response in all nerves tested. Peroneal and tibial motor responses showed normal amplitude and conduction velocities, but absent F-waves suggested some pathology of the motor neurons. Sural sensory conduction velocity was mildly reduced. Right median motor and sensory responses showed evidence of a mild carpal tunnel syndrome. The above electrophysiologic findings were interpreted (L.A. and D.S.) as being consistent with a mild demyelinating sensorimotor polyneuropathy with a superimposed right carpal tunnel syndrome.

Repeat thyroid function tests on the fifth postoperative day showed a TSH = 145 μIU/ml (0.3–7.3 μIU/m;) and an FT4I = 4.2 μg/dl (3.4–12.7 μg/dl). The patient was discharged in good condition on the seventh postoperative day receiving thyroxin 0.2 mg po qid.

Eight weeks postoperatively when the patient was clinically euthyroid with a TSH = 0.8 μIU/ml (0.3–7.3 μIU/ml) and an FT4I = 8.2 μg/dl (3.4–12.7 μg/dl), repeat peripheral nerve stimulation tests were performed using both surface and needle electrodes. Response to nerve stimulation appeared normal and equal in amplitude when using both surface and needle electrodes.

Discussion

This patient clearly had clinical and laboratory evidence of severe acute hypothyroidism. The dramatic and complete absence of response to neuromuscular stimulation made her general anesthetic course unique. In view of her clinical strength findings, management decisions based solely on the absent peripheral nerve stimulator findings would have been grossly erroneous.

In general, to properly evaluate neuromuscular function, supramaximal stimulation of the monitored nerve is mandatory.[9,10] Failure to achieve supramaximal stimulation of all the nerve fibers in a nerve may lead to erroneous overestimation of neuromuscular blockade. The ability to provide this stimulus may be influenced by such factors as stimulus current strength,[11] proper location of electrodes over the peripheral nerves,[12,13] and relative position of the polarity of the electrodes. It has been reported that when the ulnar and median nerves were stimulated with the active electrode being the cathode, the twitch response was greater than when the stimulating electrode was the anode.[9,12,13] In this patient we corrected for the possibility of an "anodal block" by interchanging the electrode connections. In practice, if the lead polarity of the stimulator is unknown, reversing the connections (red for black) will reverse the polarity and may enhance the muscle response[12] due to elimination of anodal block. In addition to interchanging the leads, we tested multiple nerves (facial, ulnar, median, and posterior tibial), adjusted the location and distance between electrodes, and used the maximum current intensity available from the peripheral nerve stimulators. Despite all these maneuvers, we were unable to elicit a response to several different functioning peripheral nerve stimulators prior to the correction of the hypothyroid state.

Aside from technical problems with the peripheral nerve stimulators, there are multiple patient conditions that can interfere with measurement of the state of neuromuscular excitability.[9] First, it has been reported that in patients with very cold extremities surface stimulation at supramaximal levels with the nerve stimulator produces a submaximal response due to decreased release of acetylcholine at the neuromuscular junction.[14] In addition, peripheral cooling may reduce blood flow to the muscles over which measurements are being made. This cold-induced vasoconstriction may result in inhibition of the diffusion of the neuromuscular blocking agents away from the neuromuscular end plates so that the reversal of the peripheral muscle may lag behind the reversal of the central respiratory muscles and peripheral monitoring would then overestimate the degree of paralysis.[14] This patient was continuously monitored with an esophageal temperature probe, and her lowest recorded temperature was 37.0° C. Although in myxedema the mean intramuscular temperature was found to be 1.0° C lower than core, this was not enough of a difference to account for the slowness of the tendon reflex,[15] nor would it be low enough here to explain the difficulty with nerve stimulator monitoring.

Second, there are chemical conditions, such as electrolyte disturbances (hypokalemia, hypercalcemia) and *p*H alterations (respiratory acidosis, metabolic alkalosis), which might interfere with the muscle response to nerve stimulation.[9,16] However, none of these chemical alterations were present in this patient.

Third, obesity[14] and enhanced tissue resistance[17] can hamper measurements of neuromuscular excitability. This patient was indeed moderately obese and perhaps had increased tissue resistance due to myxedematous changes of skin and muscle overlying the peripheral nerves that were tested. However, because of the parallel temporal changes in muscle twitch response and thyroid function, we propose that her severe hypothyroid state, rather than enhanced tissue resistance, explained the completely absent response to surface electrode nerve stimulation in the intraoperative and perioperative period prior to thyroid replacement and the partial but blunted response to surface electrode nerve stimulation testing within 48 h of initiation of iv hormonal replacement therapy. Furthermore, when the patient was clinically euthyroid 8 weeks postoperatively, despite no significant change in body weight, her response to nerve stimulation was entirely normal and equal using both surface and needle electrodes. Thus, the intraoperative absence of nerve stimulus response using surface pregelled electrodes, the requirement for unusually high stimulus intensities during formal nerve conduction studies with needle electrodes in the postoperative period, and the equal response to both surface and needle electrodes 8 weeks postoperatively when the severe hypothyroid state was fully corrected but obesity and enhanced tissue resistance persisted strongly, suggests that the unusual response to peripheral nerve stimulation was secondary to her underlying disease rather than a technical problem with the nerve stimulator–patient surface interface.

These observations have led us to propose that the acute severe hypothyroid state itself was responsible for the blunted response to nerve stimulation. We further postulate that our initial inability to produce muscle twitches with the nerve stimulator was due to a diffuse and rapidly reversible metabolic defect of acute severe hypothyroidism on nerve and/or muscle function. This contention is well supported by the parallel temporal changes in muscle twitch response and thyroid function. This effect of acute hypothyroidism on neuromuscular excitability must have been superimposed on a more sustained, less rapidly reversible, and probably chronic structural effect of hypothyroidism on peripheral nerve, as evidenced by the abnormal nerve conduction studies. Formal nerve conduction studies done 2 days after thyroid replacement therapy was begun still required high stimulus intensities and showed evidence of a mild demyelinating polyneuropathy. This is consistent with the known chronic effects of decreased thyroid function on nerve structure.[18,19]

In conclusion, acute severe hypothyroidism may interfere with both proper intraoperative monitoring of neuromuscular excitability and estimation of neuromuscular blockade. This represents yet another potential hazard for the anesthesiologist caring for the acute severely hypothyroid patient.

References

1. Murkin JM: Anesthesia and hypothyroidism: A review of thyroxine physiology, pharmacology, and anesthetic implications. Anesth Analg 61:371–383, 1982
2. Abbott TR: Anesthesia in untreated myxoedema: Report of two cases. Br J Anaesth 39:510–514, 1967
3. Roizen MF, Hensel P, Lichtor JL, Schreider BD: Patients with disorders of thyroid function. Anesthesiol Clin North Am 5: 277–286, 1987
4. White VA, Kumaga LF: Preoperative endocrine and metabolic considerations. Med Clin North Am 63:1321–1334, 1979
5. Kim JM, Hackman L: Anesthesia for untreated hypothyroidism: Report of three cases. Anesth Analg 56:299–302, 1977
6. Sherry KM, Hutchinson IL: Postoperative myxoedema. A report of coma and upper airway obstruction. Anaesthesia 39:1112–1114, 1984
7. Zwillich CW, Pierson DJ, Hofeldt FD, Lufkin EG, Weil JV: Ventilatory control in myxedema and hypothyroidism. N Engl J Med 292:662–665, 1975
8. Stoelting RK, Dierdorf SF, McCammon RL: Anesthesia and Co-Existing Disease. New York, Churchill Livingstone, 1988, pp 482–486
9. Hudes E, Lee KC: Clinical use of peripheral nerve stimulators in anesthesia. Can J Anaesth 34:525–534, 1987
10. Ali HH, Saverese JJ: Monitoring of neuromuscular function. ANESTHESIOLOGY 45:216–249, 1976
11. Kopman AF, Lawson D: Milliamperage requirements for supramaximal stimulation of the ulnar nerve with surface electrodes. ANESTHESIOLOGY 61:83–85, 1984
12. Rosenberg H, Greenhow DE: Peripheral nerve stimulator performance: The influence of output polarity and electrode placement. Can Anaesth Soc J 25:424–426, 1978
13. Berger JJ, Gravenstein JS, Munson ES: Electrode polarity and peripheral nerve stimulation. ANESTHESIOLOGY 56:402–404, 1982
14. Viby-Morgensen J: Clinical assessment of neuromuscular transmission. Br J Anaesth 54:209–223, 1982
15. Ingbar S, Braverman L: Werner's The Thyroid. Philadelphia, JB Lippincott, 1986, pp 1168–1171
16. Ali HH: Monitoring of neuromuscular function and clinical interaction. Clin Anaesthesiol 3:447–465, 1985
17. Mylrea KL, Hameroff SR, Calkins JM, Bilitt CD, Humphrey LL: Evaluation of peripheral nerve stimulators and relationship to possible errors in assessing neuromuscular blockade. ANESTHESIOLOGY 60:464–466, 1984
18. Layzer RB: Neuromuscular Manifestations of Systemic Disease. Philadelphia, FA Davis, 1985, pp 84–137
19. Dyck PJ, Lambert EH: Polyneuropathy associated with hypothyroidism. J Neuropathol Exp Neurol 29:631–658, 1970