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Abnormal Responses to Muscle Relaxants in a Patient with Primary Hyperparathyroidism

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The classical features of primary hyperparathyroidism include hypercalcemia, soft tissue calcification, and osteitis fibrosa cystica. Muscle weakness and atrophy are relatively common as well, but the motor deficit seems to be neuropathic rather than myopathic in origin.[1] Neuromuscular transmission has not been well studied, so the responses to the muscle relaxants are not known.[1]

We report a case of primary hyperparathyroidism that demonstrated an abnormal responses to both succinylcholine and atracurium.

REPORT OF A CASE

A 60-yr-old man, weighing 40 kg, was referred because of hypercalcemia, weakness, polydypsia, and polyurea. There was no history of renal involvement. The patient was slightly confused on admission. He had short limbs, vitiligo all over the body, and band keratopathy in both cornea. Muscle weakness and atrophy were noted in all extremities. Muscle tone was decreased and reflexes in the limbs were slightly hyperactive, but no fasciculations were observed in the muscles. Cerebellar and sensory findings were normal. A firm mass on the left side of the neck that moved with swallowing was noted. The trachea was not deviated.

Radiologic examination disclosed osteitis fibrosa cystica with cysts of varying size in the tibia, skull, ribs, and pelvic bones and vascular calcification in the pelvic region. Bone biopsy indicated the presence of fibroblastic stroma containing osteoclast-like giant cells, areas of new bone formation with multiple cysts, and deposition of hemosiderin pigments.

Laboratory values on admission were: serum calcium 15 $mg \cdot dl^{-1}$ (normal 8.5–10.5 $mg \cdot dl^{-1}$), serum phosphorus 2.7 $mg \cdot dl^{-1}$ (normal 2.5–4.9 $mg \cdot dl^{-1}$) and serum sodium 129 $mEq \cdot l^{-1}$. Serum potassium, chloride, and magnesium were within normal limits. ECG was normal. Alkaline phosphatase was 82 $IU \cdot dl^{-1}$ (normal 5–14 $IU \cdot dl^{-1}$). Human midmolecule parathyroid hormone (PTH-MM), which is considered to be the most important marker for primary hyperparathyroid disease,[2] was more than 1,000 $pmol \cdot l^{-1}$ (normal 29–85 $pmol \cdot l^{-1}$). Thyroid and liver function tests, serum protein electophoresis, blood urea nitrogen, creatinine, and fasting blood sugar were within normal limits. Urine analysis for Bence-Jones protein was negative. Twenty-four-h urine analysis was: volume 7,400 ml, calcium 1,125 mg (normal 42.2–353.4 mg/24 h), protein 977 mg (normal 165 mg/24 h), creatinine 1,184 mg (normal 800–2,000 mg/24 h).

Computerized tomography (CT) disclosed a 2.4 × 4 cm mass in the inferior pole of the left thyroid lobe and a diagnosis of parathyroid adenoma was made. The patient was treated by diuresis with furosemide, saline infusion, and oral phosphate and magnesium for 1 week in order to restore serum electrolytes to a normal concentration.

The patient was scheduled for surgical removal of the parathyroid adenoma. He arrived in the operating room unpremedicated with a normal saline infusion running *via* a peripheral vein. The ECG and temperature were monitored continuously. Arterial blood pressure was monitored every 5 min by an electronic oscillotonometer.

Anesthesia was induced with fentanyl 2 $\mu g \cdot kg^{-1}$ and thiopental 5 $mg \cdot kg^{-1}$ iv and was maintained with 70% nitrous oxide in oxygen and halothane 0.5–1%.

Following induction of anesthesia, the ulnar nerve was stimulated percutaneously at the elbow with square wave supramaximal stimuli of 0.2 ms duration, delivered in a train-of-four (TOF) sequence at 2-Hz frequency every 10 s. The contraction of the adductor pollicis was recorded using a force displacement transducer and neuromuscular function analyzer.[3] The preload tension on the thumb was maintained at 300 g throughout the procedure. After stabilization of twitch recording for 10 min the TOF ratio was noted to be 0.86. Succinylcholine 1 $mg \cdot kg^{-1}$ was injected iv, and the trachea was intubated after complete suppression of twitch response. Ventilation was adjusted to maintain a normal end-tidal CO_2.

There was no response to peripheral nerve stimulation for 15 min following succinycholine injection. The first twitch of TOF recovered to 25% and 50% after 16.5 and 18.3 min, respectively. The TOF ratio at these times were 0.86 and 0.83, respectively. Neuromuscular blockade was subsequently maintained with atracurium 0.5 $mg \cdot kg^{-1}$ and incremental doses of either 0.1 or 0.2 $mg \cdot kg^{-1}$ whenever the first twitch of TOF stimulation (T1) had recovered to 20% of control value for at least three successive stimulations (table 1).

Forty seconds after the initial dose of atracurium, there was complete suppression of twitch response. Recovery of T1 to 20% of control took 23.3 min. The mean duration of 0.1 $mg \cdot kg^{-1}$ incremental doses was 10.3 ± 0.7 (SD) and that of 0.2 $mg \cdot kg^{-1}$ was 22.1 ± 8.0 (SD).

Arterial blood pressure, heart rate, and body temperature were stable throughout the procedure. Arterial blood gases and acid–base status were within normal limits. A 4 × 2.5 × 2 cm adenoma of the left lower parathyroid was removed. After completion of surgery, which lasted for 130 min, residual neuromuscular block was reversed with 2 mg neostigmine and 1 mg atropine iv. At the time of the reversal, T1 was 20% of control twitch tension. The response to neostigmine was rapid, and TOF ratio had recovered to 0.75 in 6.3 min. With the return of spontaneous respiration the trachea was extubated, and the patient sent to the recovery room; further progress was uneventful. The duration of anesthesia was 160 min.

A sample of venous blood taken during surgery revealed a plasma cholinesterase activity of 4.4 $U \cdot l^{-1}$ (normal 7–19 $U \cdot l^{-1}$). The enzyme activity was measured by the change in absorbance at 600 nm following

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TABLE 1. Dose, Onset, Intensity, and Duration of Atracurium Blockade

	Dose of Atracurium					
	20 mg	4 mg	4 mg	8 mg	8 mg	4 mg
T1* (% of control†) at time of injection	50	20	24	20	20	28
Onset time‡ (s)	40	43	47	40	45	56
Maximum twitch suppression following injection (% of control)	0	6	10	0	0	8
Time from beginning of injection to the return of T1 to 20% of control (min)	23.3	10	9.5	21.3	22.9	11.3

* Amplitude of the first evoked response of the train-of-four.

† Control value of T1 was quantitated under nitrous oxide–oxygen–halothane anesthesia and before the administration of succinylcholine.

‡ Time from the injection of atracurium until the first decrease of the twitch was observed.

reduction of butyrylthiocholine to thiocholine using a plasma cholinesterase pack (PchE® pack, Dupont) and the Dupont clinical analyzer. The necessary reagents for qualitative studies of plasma cholinesterase were not available.

Postoperatively the patient gradually regained his energy and strength and his serum calcium decreased to 7.1 $mg \cdot dl^{-1}$. Calcium supplement was prescribed for 8 days. The patient was discharged 2 weeks after surgery without medication; 1 month later his general condition had improved and his weight increased to 48 kg.

DISCUSSION

A patient with parathyroid adenoma rarely presents with a palpable parathyroid gland on physical examination. Arnaud[4] stated that enlarged parathyroid glands are almost never palpable clinically and, even in the presence of primary hyperparathyroidism, a nodule felt in the neck is almost certain to be a thyroid rather than a parathyroid. The clinical suspicion in this case was confirmed by both CT scan and the pathologic examination of the parathyroid adenoma. Thyroid scan and thyroid function tests were all normal.

Katz and Ryan[5] noted a marked variation in responses of patients to clinically used doses of succinylcholine. Still, a duration of 16 to 19 min is unusually long. This might be the case in this patient or it is probably due to the low level of plasma cholinesterase activity. Whittaker[6] did not include hyperparathyroidism as a cause of decreased plasma cholinesterase activity.

Patients with hyperparathyroidism seemed sensitive to all electromyographic (EMG) procedures and were unable to tolerate repetitive nerve stimulation at supramaximal intensities.[1] This may explain the low TOF ratio recorded in our patient before the administration of muscle relaxants. Halothane alone has not been reported to cause any depression in the TOF response. Miller *et al.*[7] found that all patients anesthetized with 1.25 MAC halothane and stimulated at 80 Hz could sustain tetanus. Patten *et al.*[1] also demonstrated atrophy of both type I and type II muscle fibers, with type II fibers more extensively involved. Perhaps type II atrophy is neurogenic in origin.[8,9] This suggests that the dysfunction is in the axon or in the motor neuron soma itself.[1]

This anatomic localization of the neuromuscular involvement may be the same for amyotrophic lateral sclerosis and progressive muscular atrophy as for hyperparathyroid patients.[1] Patients with amyotrophic lateral sclerosis have an increased response to nondepolarizing muscle relaxants.[10] However, patients with muscular dystrophy may have a normal[11] or increased response to nondepolarizing muscle relaxants.[12]

Foldes *et al.*[13] found that the duration of action of 0.4 and 0.5 $mg \cdot kg^{-1}$ of atracurium in normal patients was 39.1 ± 1.6 and 43.6 ± 2.2 (mean ± SEM) min, respectively. This is in agreement with our own results with atracurium in normal patients.[14] Similarly, Berman *et al.*[15] reported that following atracurium 0.5 $mg \cdot kg^{-1}$, the interval from 100% suppression of twitch height to 25% recovery was 41.1 ± 6 (mean ± SEM) min. Also, Naguib *et al.*[16] reported that duration of action of atracurium 0.5 $mg \cdot kg^{-1}$ from loss of twitch to 20% recovery was 40.1 ± 9.3 (mean ± SD) min. Using smaller doses of atracurium (0.25 and 0.4 $mg \cdot kg^{-1}$) Nguyen *et al.*[17] and Ramsey *et al.*[18] found that times to 25% recovery of twitch height in nor-mal patients were 30.7 ± 1.6 (mean ± SEM) and 42.2 ± 4.4 (mean ± SD) min, respectively. The duration of a 0.1 $mg \cdot kg^{-1}$ increment was reported to be 20.9 ± 0.9[14] and 19.2 ± 0.5[17] (mean ± SEM) min. In contrast, the duration of action of atracurium in this patient was considerably shorter: 23.3 min for the initial dose and approximately 10 min for 0.1 $mg \cdot kg^{-1}$ incremental doses (table 1).

Stirt *et al.*[19] found that prior administration of succinylcholine increases the intensity but not the duration of atracurium blockade. However, in this patient, the duration was shorter. Electrolytes and acid–base balance status were normal and, therefore, were not expected to alter the metabolism of atracurium. We would expect a patient with muscle weakness and possibly having neurogenic atrophy to have an exaggerated response to nondepolarizing muscle relaxants. We cannot explain the reduced response of this patient to atracurium.

This case demonstrates that monitoring of neuromuscular function is recommended in patients with primary hyperparathyroidism. Increased sensitivity to succinyl-

choline as observed in this patient is probably due to the reduced plasma cholinesterase activity. This may be related to hyperparathyroidism or may be a coincidental finding. The response to atracurium, however, was reduced with no apparent explanation.

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Rare Misplacements of Epidural Catheters

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Continuous epidural analgesia–anesthesia, even in skilled hands, has a failure rate as high as 8%.[1] Technical difficulties may result from abnormalities of the vertebral column and bands or sheaths within the epidural space. Furthermore, kinking, knots, and misplaced epidural catethers may cause incomplete or absent analgesia.[2–10] We describe accidental misplacement of epidural catheters into the pleural cavity and the retroperitoneal space.

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Report of Two Cases

Case 1. A 61-yr-old, 106 kg man was scheduled for right thoracotomy for suspected pulmonary carcinoma in the right lower lobe. He had been treated for low back pain and had a moderate-to-severe lumbar scoliosis with convexity to the left. Prior to induction of general anesthesia, an anesthesiologist experienced in epidural anesthesia inserted an epidural catheter at the midthoracic level, using a paravertebral approach with the "loss-of-resistance" technique for identifying the epidural space. Some technical difficulties were encountered because of poor resistance of the deeper tissue layers. However a "loss-of-resistance" feeling was evident, and the catheter inserted. General anesthesia was maintained with halothane, N_2O, and O_2. Administration of 8 ml of bupivacaine 0.5%, given 20 min after induction of general anesthesia, did not alter arterial blood pressure or heart rate. Approximately 1 h after surgery had begun, the surgeon located the epidural catheter in the right pleural cavity. The catheter was immediately withdrawn. The remainder of the anesthetic and operative procedures were smooth and uneventful.

Case 2. A 59-yr-old man was undergoing emergency aortic surgery because of severe ischemia of the lower limbs. By clinical examination