other vernitrol double-barreled vaporizer at our institution was found to exhibit a similar cross leak when tested. The cause of the trouble was apparently in the selector valve, and this required replacement of that unit by the manufacturer in each instance.

With the increasing variety and complexity of anesthetic vaporizers, it obviously becomes a routine responsibility to test the machine *and vaporizer* before each use, even if the vaporizer appears to be empty!

References

1. Safar, P., and Galla, S. J.: Overdose with Ohio halothane vaporizer, Anesthesiology 23: 715, 1962.
2. Munson, W. M.: Cardiac arrest: hazard of tipping a vaporizer, Anesthesiology 26: 235, 1965.

Sensitivity to Curare by a Patient with Undiagnosed Myasthenia Gravis Syndrome

Blossom A. Sanger, M.D., and Gilbert E. Kinyon, M.D.*

The following case report deals with a myasthenia gravis-like syndrome accompanying oat cell carcinoma of the lung.

A 53 year old white man entered the hospital with a history of weakness, weight loss, and productive cough of one year's duration. Four years prior to admission, the patient had a cervical laminectomy for "slipped disc" performed under halothane, nitrous oxide and oxygen anesthesia, with succinylcholine, 40 mg., given three times during the procedure. He received no curare at that time. Recovery was unremarkable.

On admission, physical examination revealed a thin white man, blood pressure 120/78, weight 118, temperature 101° F., normal sinus rhythm of 90. The positive findings were limited to wheezes in his chest and weakness on exertion. Admission chest roentgenogram showed a 4 cm. density in the lower lung field. Initial laboratory studies were within normal limits. Bronchoscopy and scalene node biopsy were negative; both were performed under local anesthesia.

Pulmonary function studies showed vital capacity 31 per cent of predicted normal; maximum breathing capacity was 23 per cent of predicted normal; one-second and three-second timed vital capacities were 24 per cent of predicted normals. The patient had great difficulty performing the tests and the degree of functional impairment did not correlate with the roentgen-ray findings. Arterial P_{CO_2} was 43 mm. of mercury, standard bicarbonate 27.5 mEq., oxygen saturation 92.8 per cent, P_{O_2} 68 mm. of mercury, *p*H 7.437. The patient was given intermittent positive pressure breathing therapy, and the pulmonary function tests repeated after two weeks showed vital capacity to be 55 per cent of predicted normal and a maximum breathing capacity of 32 per cent.

Forty-six days after admission, the patient was prepared for right lower lobectomy. He was given premedication of meperidine 25 mg., hydroxyzine 100 mg., and atropine 0.4 mg., 1 hour prior to induction. Anesthesia was induced with 250 mg. of 2.5 per cent thiopental, intravenously. The patient was given succinylcholine, 40 mg., intravenously and the trachea intubated. After the return of spontaneous respirations he was given meperidine, 20 mg., intravenously, and curare 3 mg., and maintained on nitrous oxide, 3.5 liters, oxygen 1.5 liters and halothane 0.5 per cent, intermittently. Two units of whole blood were administered during the 4½ hour thoracotomy. No additional relaxants nor any other medication were given. Respirations were controlled for the entire surgical procedure. Blood pressure and pulse were stable throughout the operation. After the chest

* Department of Anesthesiology, San Diego County General Hospital, San Diego, California.

TABLE 1. Summary of Laboratory Data

	HGB (g.)	FBS (mg./100 ml.)	BUN (mg./100 ml.)	TP (g./100 ml.)	A/G (g./100 ml.)	Plasma CO_2 (bicarb.) (mEq./l.)	Cl (mEq./l.)	Na^+ (mEq./l.)	K^+ (mEq./l.)	Blood and Plasma Administered and Special Tests
4–11 (preop.)	14.6	103	14	6.8	4.8/20					
4–13 (postop.)	11.6									
4–16	11.3					37	77	120	3.9	
4–17	11.1		9			43	67	130	3.9	1 unit blood
4–18						40	79	126	4.3	3 units pooled plasma
4–19	13.8	86	5			40	85	129	4.9	2 units pooled plasma Quantitative protein 892
4–20	11.7	166	5	4.9	2.4/2.5	30	93	128	4.9	4 units pooled plasma
4–21	12.6	186	7			30	89	131	4.8	2 units whole blood
4–22	13.1					31	95	133	5.0	1 unit whole blood
4–23	13.1					31	97	139	5.8	Glucose tol: 74 1/2–140– 1:170 2:139 3:139
4–26	15.4	120	15			32	89	134	5.3	
4–30							Thyroid tests: T 3:1.2 PBI-9.1			
5–17	13.9					31	85	132	4.8	T 3–1.36

was closed, return to preoperative tidal volumes did not occur. Respiration was not improved after two doses of ethamivan, given intravenously. Minimal improvement was obtained after intravenous edrophonium, 1 ml. Atropine 0.6 mg. intravenously, followed by neostigmine 1.5 mg. intravenously, in divided doses, gave greater improvement of tidal volume (100 ml.). However, respirations continued to be inadequate. One hour after operation arterial *p*H was 7.113. Tracheostomy was performed and the patient was placed on assisted positive pressure breathing.

Postoperative Course. During the five hours immediately following operation it was apparent that the patient had generalized muscle weakness, exhibited by poor hand grip, diminished ability to raise his head and diminished intercostal muscle strength. The patient was returned to the ward with his tracheostomy in place, on intermittent positive pressure breathing. Chest roentgenogram showed a small left pneumothorax, and a chest tube was inserted. The intermittent positive pressure breathing was discontinued periodically during which time the patient became very anxious. He was also less able to trip the assisting mechanism of the ventilator at night. For three days postoperatively, attempts were made to wean the patient from the intermittent positive pressure breathing. Chest roentgenogram showed improvement of his pneumothorax and fluid in his left chest. The latter, 300 ml., was removed by thoracentesis. Final pathology report was undifferentiated small cell carcinoma of the lung (oat cell carcinoma of the lung).

On the fifth postoperative day the patient was more stuporous and lethargic, had dilated pupils, respirations were minimal, blood pressure 80/40. At this time the arterial P_{CO_2} was over 100 mm. of mercury and *p*H was 7.302. He was put on continuous intermittent positive pressure breathing. Intravenous plasma was given; 750 ml. of fluid were removed from the left chest and he gradually began to improve. The next day P_{CO_2} was 52 mm. of mercury, standard bicarbonate 25.3, *p*H 7.417. He was able to breathe adequately on assisted intermittent positive pressure breathing.

Nine days postoperatively, electromyography was performed, stimulating the left ulnar nerve at the wrist and recording from the abductor digiti quinti. The response to stimuli, 2 per second to 50 per second, was without fatigue (negative Jolly test), and there was no post-tetanic facilitation. To determine the response to edrophonium, stimulation was given at 2 per second and the intensity regulated to produce a muscle response of 50 microvolts. Edrophonium, 5 mg., which was injected intravenously, potentiated the twitch response to 100 microvolts. This response lasted about four minutes. Intravenous neostigmine, 1 mg., preceded by atropine, 0.4 mg., potentiated the response to 100–125 microvolts.

The patient began to improve steadily and was placed on atropine, 3 mg., and neostigmine, 15 mg., every three hours. Intermittent positive pressure breathing was discontinued and the tracheostomy tube removed. He was discharged 31 days after operation with neostigmine discontinued. Two weeks after discharge he was seen in the Outpatient Clinic and complained of weakness in his legs and chest. His tracheostomy was completely closed. Pulmonary functions were repeated, showing improvement over the initial studies but no significant improvement 20 minutes after injection of intravenous neostigmine. However, the patient was put back on oral neostigmine and atropine and was seen one week later with definite subjective improvement in muscle strength in his legs and neck. Pertinent laboratory studies are summarized in table 1.

Discussion

Several factors may have exaggerated the patient's response to curare during operation. Immediately postoperatively the serum potassium, serum sodium and chloride were low. Abnormal potassium levels and generalized electrolyte disturbance have been reported to potentiate abnormal sensitivity to curare.[2, 3] The potassium levels, however, returned to normal limits (5.4 to 4.8) during the remainder of his hospital stay. Carbon dioxide retention has also been cited as an aggravating factor in carcinomatous neuropathy,[2] and no doubt this patient's extreme carbon dioxide retention magnified his neuropathy.

Thyroid evaluation studies revealed a protein bound iodine of 9.1 (3.5 to 8 per cent normal) and a T-3 of 1.36 (0.08 to 1.3 normal range). These tests are evidence of hyperthyroid disease which has also been reported associated with bronchogenic carcinoma.[6] Abnormalities of thyroid function are also frequently associated with myasthenia gravis (3 per cent of patients with myasthenia gravis have thyrotoxicosis).[6] It has also been reported that some cases of thyrotoxic myopathies do not exhibit dramatic improvement with neostigmine as in uncomplicated myasthenia gravis.[7] This is more typical of this patient's response.

The electromyogram performed is of particular interest. No fading was seen on repeated stimuli, nor was there demonstrated any post-tetanic facilitation (negative Jolly test). Had his condition been suspected preoperatively, it might not have been diagnosed even by myography unless he was specifically tested for neostigmine or edrophonium potentiation.[4, 8, 9] We were unable to see any potentiation of muscle response by observing the patient's fingers, but saw the increase of microvolt response in the M-wave on the oscilloscope screen.

Apart from the clinical interest of this case of association of myasthenia-like syndrome with bronchogenic malignancy, two features are to be emphasized. One is the very marked sensitivity to curare with pre-existing myasthenic disease. A total of only 3 mg. of curare was administered to this patient because of his poor pulmonary function and yet this dose completely suppressed adequate respiration for more than 24 hours which could not effectively be reversed. A second important inference from this case is the relative inaccuracy of clinical conclusions drawn by observation of finger twitch without adequate objective quantitation. No change in response of finger twitch could be seen after administration of neostigmine, yet there was significant change on the oscilloscope. In view of recent interest in the use of finger twitch response to ulnar nerve stimulation as a measurement of quality and quantity of neuromuscular blockade during and after anesthesia,[1, 5] the efficiency of the test might be greatly increased by incorporating an objective means of measuring muscle response other than naked eye observation.

References

1. Churchill-Davidson, H. C.: A portable peripheral nerve-stimulator, Anesthesiology 26: 224, 1965.
2. Craft, P. B.: Abnormal responses to muscle relaxants in carcinomatous neuropathy, Brit. Med. J. 1: 181, 1958.
3. Eckenhoff, J. E., McIntyre, A. R., and others: A symposium on muscle relaxants, Anesthesiology 20: 407, 1959.
4. Foldes, F. F., and McNall, P. G.: Myasthenia gravis: A guide for anesthesiologists, Anesthesiology 23: 837, 1962.
5. Katz, R. L.: Comparison of electrical and mechanical recording of spontaneous evoked muscle activity, Anesthesiology 26: 204, 1965.
6. Means, J. H., DeGroot, L. J., and Stanbury, J. B.: The Thyroid and its Diseases. New York, McGraw Hill, 1963.
7. Sahay, B. M., Blendis, L. M., and Greene, R.: Relation between myasthenia gravis and thyroid disease, Brit. Med. J. 1: 763, 1965.
8. Zacks, S. I.: The Motor End Plate. Philadelphia, W. B. Saunders, 1964.
9. Zacks, S. I.: Myasthenia gravis, Med. Sci. 16: 36 (April), 1965.