Myasthenia Gravis Associated With Small-Cell Carcinoma of the Lung

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A 49-year-old man complained of a 3-month history of progressive generalized muscle weakness. He was diagnosed as having small-cell lung carcinoma at the same time. He received an intravenous injection of edrophonium chloride with remarkable improvement of muscle strength. Electromyographic studies revealed a compound muscle action potential that decreased after repetitive stimulation. These findings were considered representative of myasthenia gravis (MG), and inconsistent with Eaton-Lambert syndrome. The appearance of MG with small-cell lung carcinoma seems to be very rare, but possible. (Chest 1994; 105: 624-25)

Myasthenia gravis (MG) results from autoantibodies against nicotinic acetylcholine receptors (nAChRs) in the motor end plate. The disorder is characterized clinically by intermittent muscle weakness that improves after anticholinesterase medication and by decremental neuromuscular transmission during the repetitive nerve stimulation test at frequencies of 1 to 50 Hz. Although there seems to be an association between MG and thymic hyperplasia, as well as thymic tumors, such a relationship with bronchogenic carcinoma is not well established. In this report, we describe a patient who simultaneously developed MG and small-cell lung carcinoma.

CASE REPORT

A 49-year-old male cigarette smoker complained of a 3-month history of progressive generalized muscle weakness, dyspnea, and cough. He had difficulties in walking, chewing, and swallowing. He also noted an 8-kg weight loss within 3 months. On physical examination, a right supraclavicular lymph node swelling and a reduction of respiratory sound at the left lung field were noted. Neurologic examination showed evidence of ptosis and proximal muscle weakness. Results of routine laboratory examinations were all within normal ranges. Arterial blood gases showed hypoxemia (PaO₂, 61.2 mm Hg). Autoantibody against acetylcholine receptors was negative. Chest radiograph showed a dextrocardia, left hilar soft-tissue mass, and mediastinal lymph node swelling (Fig 1). Biopsy specimens of the left upper lobe lesion obtained with fiberoptic bronchoscope demonstrated an anaplastic small-cell carcinoma. Muscle biopsy specimens (sternocleidomastoid muscle and intercostal muscle) showed no remarkable change.

Because of the patient's muscle weakness, he received an intravenous injection of edrophonium chloride with remarkable though transient improvement of muscle strength. Electromyographic studies revealed normal motor and sensory nerve conduction velocities. Repeti-

References


FIGURE 1. Chest radiograph showed a dextrocardia, left hilar soft-tissue mass, and mediastinal lymph node swelling.

Eaton-Lambert syndrome.

DISCUSSION

This patient had a histologically proved small-cell anaplastic carcinoma of the lung accompanied by severe muscle weakness. Whereas the association of Eaton-Lambert syndrome with bronchogenic carcinoma is well established, such a relationship between MG and bronchogenic carcinoma has not previously been clearly demonstrated, and to our knowledge, only one case has been reported in the literature. Unlike MG, Eaton-Lambert syndrome is believed to be the result of a presynaptic abnormality of acetylcholine release, and has characteristic electromyography findings of small amplitude compound muscle action potentials, with marked facilitation at rapid stimulation rates and poor response to cholinesterase inhibitors. The repetitive stimulation test in this patient did not demonstrate these abnormalities, but rather a normal amplitude compound muscle action potential with decrement at both slow and rapid stimulation rates as seen with MG. The response to anticholinesterase agents also favored the diagnosis of MG over Eaton-Lambert syndrome.

Myasthenia gravis results from an autoimmune attack on the nAChRs of the motor end plate. There are several types of α-subunits of nAChRs. The α1-nicotinic receptor subunit is a muscle-type α-subunit, and the α2-nicotinic receptor subunit, α3-nicotinic receptor subunit, as well as the α4-nicotinic receptor subunit, are neuronal-type α-subunits. It was reported that mRNAs coding α2-nicotinic receptor subunit are expressed in the human thymus and this receptor may be involved in triggering MG. Recently, it was demonstrated that a small-cell lung cancer cell line, as well as non-small-cell lung cancer cell line and neuroblastoma cell line could express α2-nicotinic receptor subunit gene. This α2-nicotinic receptor was distinct to muscle-type α1-nicotinic receptor, which was expressed in a medulloloblastoma cell line (TE 671). In addition, the antibody against α2-nicotinic receptor subunit antibodies cross-reacted with the muscle nAChRs of TE 671 cells. Therefore, theoretically, it was possible to speculate that autoantibodies against the neuronal α2-nicotinic receptor subunit of nAChR that was expressed in some small-cell lung cancer cells can cross-react with muscle-type α1-nicotinic receptor subunit of nAChR and develop MG-like symptoms. Another possibility is that small-cell lung cancer cells in this patient may have produced muscle-type α1-nicotinic receptor subunit or neuronal-type α2-nicotinic receptor subunit.

REFERENCES

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A)

B)

FIGURE 2. Electromyographic studies revealed normal motor and sensory nerve conduction velocities. Repetitive stimulation at 3 Hz (A) and 20 Hz (B) to the left ulnar nerve with recording on the adductor dibi minimus muscle revealed a compound muscle action potential that decreased on repetitive stimulation.