LAMBERT-EATON MYASTHENIC SYNDROME ASSOCIATED WITH AN ANTERIOR MEDIASTINAL SMALL CELL CARCINOMA

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Approximately 60% of patients with Lambert-Eaton myasthenic syndrome (LEMS) have small cell lung carcinoma (SCLC).¹ However, LEMS is infrequently associated with carcinomas in other sites. We present here a rare case of LEMS with an anterior mediastinal small cell carcinoma in a patient who had no pulmonary lesion detected.

Clinical summary. A 46-year-old man was admitted to a local hospital because of fatigability, muscle weakness of the extremities, and double vision. On the basis of a tentative diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy, he was treated with oral prednisolone (15 mg every other day) and 8 sessions of plasmapheresis; however, the symptoms were only temporarily relieved. Six months later, he was referred to us. On examination, bilateral ptosis, facial and bulbar paresis, proximal-dominant limb muscle atrophy, and generalized areflexia were observed. His grip was 20 kg at most. No lymph node was palpable in the patient's neck or axillae. Electrodiagnostic study demonstrated abnormally low-amplitude compound muscle action potentials and a remarkable waxing after repetitive stimulation at 50 Hz. The serum antibodies to a subtype of voltage-gated calcium channels (VGCCs), P/Q type VGCCs, markedly increased to 432.9 pmol/L (normally <20.0 pmol/L). These findings were consistent with a diagnosis of LEMS, and screening for malignant diseases was performed. Chest radiography and computed tomography (CT) revealed a solid mass on the left side of the aortic arch (Fig 1). No abnormal findings were noted in the bilateral lung fields. Bronchofiberscopy also showed no abnormalities. The serum neuron-specific enolase (NSE) and progastrin-releasing peptide were elevated to 17.1 ng/mL and 121.4 pg/mL (normally <10.0 ng/mL and 46.0 pg/mL), respectively. No metastasis was observed with brain CT, abdominal CT, or bone scintigraphy.

Through a median sternotomy, an encapsulated tumor was found on the left anterior side of the aortic arch. The tumor was adjacent to the left lobe of the thymus and did not invade surrounding structures. The tumor and the thymus were complete-

Fig 1. CT demonstrating a mass on the left side of the aortic arch.

ly resected. No intrapulmonary lesion was detected. Macroscopically, the resected tumor was solid, gray-white, and encapsulated (5 × 3.5 × 3 cm, 75 g). Microscopically, the tumor was composed of atypical small spindle cells showing dense proliferation, and it was pathologically diagnosed as small cell carcinoma. No pathologic findings were obtained to specify the origin of the carcinoma. The postoperative course was uneventful, and oral prednisolone was continued. The patient's muscle strength gradually improved, and his grip was 35 kg at 20 days after the operation. He was discharged after prophylactic adjuvant chemoradiotherapy. The value of serum NSE and progastrin-releasing peptide decreased to 8.0 ng/mL and 17.4 pg/mL 6 months after the operation. They remained at normal levels thereafter. The titer of serum anti-P/Q-type voltage-gated calcium channel antibodies (VGCCAs) was 479.1 pmol/L at 1 month and 72.6 pmol/L at 22 months after the operation. The patient is alive without recurrence at 24 months, and his muscle strength has completely recovered.

Discussion. LEMS is known to be often associated with SCLC and sometimes with other malignant diseases. However, to our knowledge, this is the first case of LEMS combined with an anterior mediastinal small cell carcinoma.

Extrapulmonary small cell carcinoma (EPSCC) is rare, and the overall 5-year survival was reported to be 13% in a recent study.² However, a patient with mediastinal EPSCC who underwent complete tumor resection with adjuvant therapy has been reported.³ Although the tumor origin in the present case was not specified, the possible origin may be lymph nodes or ectopic thymus. According to a review by Galanis and colleagues² of 81 patients with EPSCC, 5 origi-

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nated from lymph nodes and 3 from thymus. Of course, we cannot completely exclude the possibility that the tumor was a metastasis to mediastinal lymph nodes from invisible SCLC.

LEMS is an autoimmune disorder of peripheral cholinergic synapses caused by abnormal anti-VGCCAs, which inhibit the regular calcium influx through VGCCs in nerve endings.⁴ Recently, Motomura and colleagues⁵ have suggested that anti-P/Q-type VGCCAs may play a central role in the pathogenesis of LEMS. In the present case the serum anti-P/Q-type VGCCAs were markedly elevated before the operation. The titer of the antibodies remained high for at least 1 month and decreased 24 months after the operation, whereas the patient's muscle strength began to recover as early as 2 weeks after the operation. These findings suggest some discrepancy between the improvement of symptoms and the titer of anti-P/Q type-VGCCAs. Anti-P/Q-type VGCCAs show polyclonal and heterogeneous properties in its immunoreactivity. This heterogeneity would be consistent with the poor correlation between antibody titer and clinical severity. Further studies are necessary to elucidate the pathophysiologic role of the antibodies in LEMS.

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