

CASE REPORT

Lambert-Eaton myasthenic syndrome with anti-acetylcholine receptor antibody and anterior mediastinal tumor

Hideyuki Matsumoto MD, PhD | Gaku Ohtomo MD | Tsugumi Akahori MT |
Hideji Hashida MD, PhD

Department of Neurology, Japanese Red Cross Medical Center, Shibuya-ku, Tokyo, Japan

Correspondence

Hideyuki Matsumoto, Department of Neurology, Japanese Red Cross Medical Center, Shibuya-ku, Tokyo, Japan.
Email: hideyukimatsumoto.jp@gmail.com

Abstract

This report describes the case of a 65-year-old male who complained of muscular weakness of the legs with easy fatigability. Blood and imaging examinations showed positive anti-acetylcholine receptor antibody and an anterior mediastinal tumor (probably a thymic cyst), suggesting the diagnosis of myasthenia gravis (MG). However, neurological and electrophysiological examinations suggested the diagnosis of Lambert-Eaton myasthenic syndrome (LEMS). We searched repeatedly for malignant tumors. Small cell lung cancer (SCLC) was found. Chemotherapy reduced the SCLC and improved the patient's clinical symptoms. On the basis of an accurate diagnosis of LEMS, we were able to detect SCLC and administer chemotherapy at an early stage. Anti-P/Q-type voltage-gated calcium channel antibody was negative. In our case, MG and LEMS overlap syndrome in addition to MG should be differentiated. For the differentiation, the strict electrophysiological criteria of LEMS were useful.

KEYWORDS

anti-acetylcholine receptor antibody, anti-P/Q-type voltage-gated calcium channel antibody, electrophysiological examination, Lambert-Eaton myasthenic syndrome, myasthenia gravis, small cell lung cancer

1 | INTRODUCTION

Both myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) are autoimmune disorders caused by neuromuscular transmission failure; both are representative neuromuscular junctional disorders.^{1,2} In MG, anti-acetylcholine receptor (AChR) antibody is detected in approximately 80% to 85% of patients and thymic tumors are often concomitant in these patients. In LEMS, anti-P/Q-type voltage-gated calcium channel (P/Q-type VGCC) antibody is detected in approximately 80% to 90% of patients and small cell lung cancer (SCLC) is often concomitant in these patients. We experienced a patient with LEMS who had anti-AChR antibody and an anterior mediastinal tumor but did not have anti-P/Q-type VGCC antibody. In this case, in the diagnosis and treatment at the early stage, electrophysiological examination was very useful.

2 | CASE REPORT

The patient was a 65-year-old man who complained of muscular weakness of the legs with easy fatigability. Two months later, he experienced muscular weakness of the arms and speech difficulties. His symptoms gradually worsened and he eventually needed a cane to walk. One month before hospitalization, he visited another hospital. Blood examinations showed positive anti-AChR antibody (0.4 nmol/L) and chest computed topography (CT) showed an anterior mediastinal tumor with low density (Figure 1A). As the diagnosis of MG was considered, he was transferred to our hospital and hospitalized to confirm the diagnosis and to receive treatment. His past and family histories were unremarkable. He smoked 20 cigarettes per day.

On admission, his blood pressure was 150/80 Torr, pulse was 75 beats/min, and body temperature was 35.8°C. Neurological

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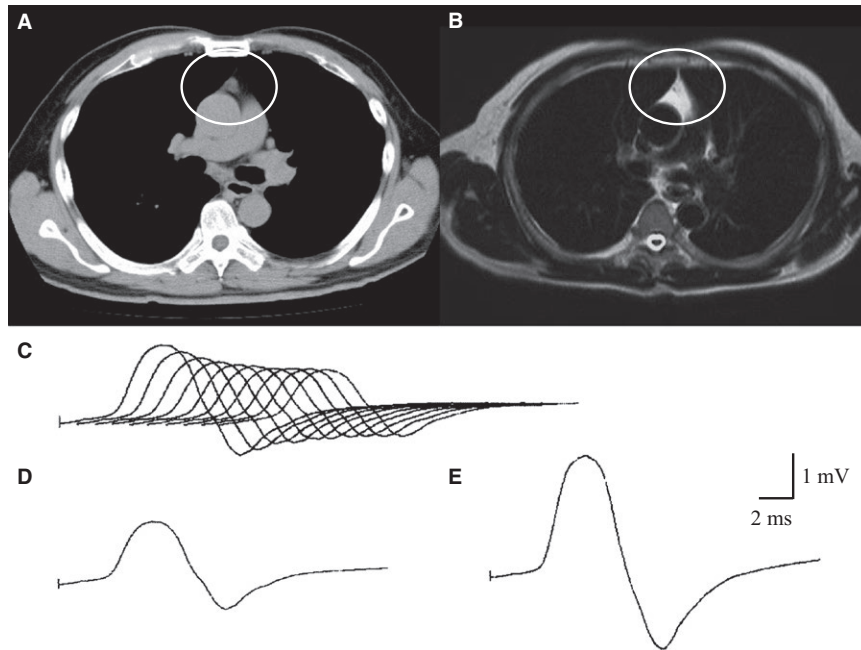


FIGURE 1 Anterior mediastinum tumor and electrophysiological examination. Chest computed topography showed a low-density tumor at the anterior mediastinum (A). Chest magnetic resonance imaging showed the anterior mediastinum tumor with homogeneously high intensity on T2-weighted image, suggesting a thymic cyst (B). Three hertz repetitive nerve stimulation test of the abductor pollicis brevis muscle showed the gradual amplitude reduction of compound muscle action potentials CMAPs (C). The amplitude of the fourth CMAP was 27% smaller than that of the first CMAP (>10%), suggesting waning. Single-pulse nerve stimulation was performed during relaxation and immediately after 10 second exercise. During relaxation (D), the CMAP amplitude was very small (1.6 mV). Immediately after 10 second exercise (E), however, the CMAP amplitude was increased to 3.9 mV. The CMAP increment was 144% (>100%). These findings fulfilled the strict electrophysiological criteria for the diagnosis of Lambert-Eaton myasthenic syndrome.⁵

examinations revealed leg-dominant muscular weakness of the proximal limbs and trunk with easy fatigability, dysarthria, diminished tendon reflexes, and autonomic dysfunctions (dry mouth and constipation). Tendon reflex is normalized by the strong contraction of the muscles relating to the tendon reflex (the duration of strong contraction was about 10 seconds). Blood reexaminations also showed positive anti-AChR antibody (0.6 nmol/L). Chest magnetic resonance imaging (MRI) showed the anterior mediastinal tumor with homogeneously high intensity on T2-weighted image (T2WI), suggesting a thymic cyst (Figure 1B). Three hertz repetitive nerve stimulation test of the right median nerve showed a gradual 27% amplitude reduction in compound muscle action potentials (CMAPs), which was so-called waning (Figure 1C). The CMAP amplitude in single-pulse nerve stimulation during relaxation was small (1.6 mV), whereas the amplitude immediately after 10 second exercise was markedly enlarged to 3.9 mV (Figure 1D,E). The CMAP increment was 144%. On the basis of the neurological and electrophysiological examinations, we made a diagnosis of LEMS, suggesting a possibility of paraneoplastic neurological syndrome. We searched repeatedly for malignant tumors. Two weeks later, follow-up chest CT showed newly appeared swollen and irregularly shaped lymph nodes at the posterior mediastinum. Bronchoscopic and cytological examinations revealed that the patient had SCLC at the early stage. Later, anti-P/Q-type VGCC antibody was found to be negative.

We administered chemotherapy for SCLC. Subsequently, the patient's clinical symptoms transiently improved in parallel with a

decrease in size of SCLC. At that time, however, follow-up electrophysiological examination again showed the typical LEMS findings: waning (23%), small CMAP (1.1 mV), and the CMAP increment after exercise (255%). Despite intensive chemotherapy, three years after the onset, he died of uncontrollable SCLC dissemination.

3 | DISCUSSION

This patient had anti-AChR antibody and an anterior mediastinal tumor, probably a thymic cyst. Because thymic cysts are sometimes observed in anti-AChR antibody-positive MG patients,³ the diagnosis of MG is strongly suspected. Actually, anti-P/Q-type VGCC antibody was negative. However, neurological and electrophysiological examinations showed clinical features suggesting LEMS rather than MG. In short, the disorder suggested by the neurological and electrophysiological examinations was not compatible with that suggested by the immunological and radiological examinations. Despite the conflicting findings, we were able to make a correct diagnosis of LEMS. For the diagnosis, neurological and electrophysiological findings were more important than the immunological and radiological findings. Furthermore, on the basis of the accurate diagnosis, we were able to detect SCLC and administer chemotherapy at an early stage. As LEMS is categorized into paraneoplastic neurological syndrome, malignant tumors should be repeatedly searched.

The specific electrophysiological findings in LEMS are waning in low-frequency repetitive nerve stimulation test, small CMAP during relaxation, and enlargement of the CMAP amplitude immediately after exercise (10 second exercise is recommended).^{1,4} It should be noted, however, that "MG and LEMS overlap syndrome," which has clinical characteristics of both MG and LEMS, has also been reported.⁵ Therefore, to differentiate LEMS from MG and "MG and LEMS overlap syndrome", strict electrophysiological criteria have been proposed.⁵ The strict criteria to make a diagnosis of LEMS are as follows: (i) CMAP amplitude is less than 5 mV in single-pulse nerve stimulation during relaxation, and (ii) the enlargement of CMAP amplitude immediately after exercise is more than 100%. Our patient fulfilled the strict criteria, leading to a diagnosis of LEMS.

In our patient, it was not easy to make a diagnosis of LEMS, although the accurate diagnosis of LEMS enabled us to detect SCLC and administer chemotherapy at the early stage. For the accurate diagnosis, electrophysiological examination was very useful. In addition, unchanged findings in follow-up electrophysiological examination may indicate that complete remission from LEMS was not achieved. Actually, chemotherapy did not consecutively improve the patient's clinical symptoms. On the other hand, it was reported that the disappearance of the LEMS patterns on the electrophysiological examination could be considered evidence of complete remission of SCLC.⁶

Recently, similar case has been reported.⁶ Lee et al. (2012) reported a case of LEMS with SCLC and anti-AChR antibody, but without any thymic tumors. The electrophysiological findings in their case also fulfilled the strict criteria of LEMS: waning (66%), small CMAP (1.1 mV < 5 mV), and the CMAP increment after exercise (121% > 100%). Therefore, as shown in both our and their cases, the strict electrophysiological criteria would be useful to distinguish LEMS from MG and "MG and LEMS overlap syndrome".

Undoubtedly, the diagnosis and treatment at the early stage must be important in any disorders. For this purpose, to differentiate LEMS from MG and "MG and LEMS overlap syndrome", the strict electrophysiological criteria of LEMS should be applied.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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