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Case Report

Journal of Critical Care Research and Emergency Medicine

A Patient with Small Cell Lung Cancer Presenting with Symptoms of Lambert-Eaton Myasthenic Syndrome Case Report

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Submitted: 04 December 2024 **Accepted:** 09 December 2024 **Published:** 15 Janauary 2025

Citation: *Yu, C.-H., Yun, Y.-T., & Chen, Y.-C. (2025). A patient with Small Cell Lung Cancer Presenting with symptoms of Lambert–Eaton myasthenic syndrome Case Report. J Cri Res & Eme Med, 4(1), 01-04.*

Abstract

Background: *Small cell lung cancer (SCLC) accounts for about 10-15% of lung cancer. Early diagnosis and treatment of lung cancer can effectively improve the quality of life. From the literature, it is known that Lambert-Eaton Myasthenic Syndrome (LEMS) is a paraneoplastic syndrome, and its symptoms may precede those of cancer. In this case, the patient was first diagnosed with LEMS and later found to have SCLC. Following appropriate treatment, the patient's muscle strength improved.*

Case Description: *A 60-year-old man with neck weakness, exertional dyspnea, proximal muscle weakness, and weight decreased from 80 kg to 60 kg in two months. First suspected diagnose was MG, patient received neurological examination (Electromyography, repetitive stimulation tests), the blood tests of anti-acetylcholine receptor antibodies (anti-AChR Ab) and anti-muscle-specific kinase antibodies (anti-MuSK Ab) were negative. LEMS was highly suspected. LEMS was frequently found with Small Cell lung cancer patients; our chest CT revealed mediastinal and right hilar lymphadenopathy, after the biopsy pathology report showed metastatic neuroendocrine carcinoma, consistent with SCLC. When Diagnosis confirmed, we started the chemotherapy. The patient's muscle strength improved to 5.*

Conclusions: *Electromyography and repetitive stimulation tests should be conducted early. While anti-voltage-gated calcium channel (anti-VGCC) antibodies test have a 90% specificity. LEMS was highly assosiated with SCLC. Tumor treatment can significantly affect the symptoms of myasthenia to have a better quality of life.*

Keywords: Lambert-Eaton Myasthenic Syndrome, Myasthenia Gravis, Paraneoplastic Neurological Syndromes, Small Cell Lung Cancer

Introduction

When a patient presents with symptoms of muscle weakness, the diagnosis can be differentiated into myasthenia gravis and Lambert-Eaton Myasthenic Syndrome (LEMS) based on changes in muscle strength, neurological reflexes, repetitive stimulation test (RST), and blood tests. LEMS is a presynaptic neuromuscular junction disorder in which acetylcholine (ACh) release is impaired. It is primarily caused by autoimmune diseases or paraneoplastic neurological syndromes (PNS) associated with malignancies, including small cell lung cancer (SCLC), thymoma, and neuroendocrine tumors [1].

LEMS is a chronic condition that cannot be completely cured and has a long-term impact on a patient's daily life. Among malignancies, small cell lung cancer tends to progress more rapidly. As a result, when a patient is diagnosed with LEMS, muscle weakness and other symptoms are often noticed before cancer symptoms appear. Early CT scans should be performed, and upon cancer diagnosis, appropriate oncological treatment should be initiated. The symptoms of LEMS improve with treatment of the underlying tumor [2].

Case Presentation

A 60-year-old male patient with a medical history of hypertension, hyperlipidemia, type 2 diabetes, hyperthyroidism, hepatitis B, coronary artery disease, and prior stroke (non-disabling with normal limb strength) presented with progressive muscle weakness. The patient had a 40-year smoking history (5 cigarettes/day) and worked as a manager in China. In September 2022, he developed neck weakness, exertional dyspnea, and progressive proximal muscle weakness, particularly in the upper limbs. Symptoms were worse in the morning and improved with activity, although fatigue frequently followed exertion. Subsequently, he experienced dysphagia, dysarthria, and hoarseness, with worsening symptoms requiring walking aids or a wheelchair within a month. Due to severe dysphagia, his weight dropped from 80 kg to 60 kg in two months, significantly impairing his daily life. He returned to Taiwan for treatment in November 2022.

At the neurology outpatient clinic, MG was initially suspected based on clinical symptoms. The patient was prescribed cholinesterase inhibitors (pyridostigmine), which provided mild improvement after 2–3 doses. He was admitted for further evaluation and treatment. During hospitalization, he received oral corticosteroids (prednisolone), immunosuppressants (azathioprine), and five sessions of double-filtration plasmapheresis (DFPP). Physical examination revealed decreased deep tendon reflexes: biceps (1+), triceps (1+), brachioradialis (1+), and patellar (1+), with absent Achilles reflexes. Muscle strength was graded at 4/5. RST at 3 Hz showed progressive decremental responses after 1, 3, and 4 minutes of rest and exercise. At 30 Hz stimulation, an incremental response was noted at rest. Compound muscle action potential (CMAP) amplitudes were significantly reduced. Serological tests for anti-acetylcholine receptor antibodies (anti-AChR Ab) and anti-muscle-specific kinase antibodies (anti-MuSK Ab) were negative. Given the clinical presentation and test results, LEMS was highly suspected. Further investigations, including autoimmune antibody screening and imaging studies, were performed. Autoimmune antibodies were negative, but CT revealed mediastinal and right hilar lymphadenopathy (Figures 1 and 2). Right cervical lymph node biopsy showed metastatic neuroendocrine carcinoma, consistent with SCLC. Additional staging studies, including magnetic resonance imaging (MRI) of the brain, showed no brain metastases. Positron emission tomography (PET) revealed malignancies in the right supraclavicular fossa, paratracheal area, and right hilar region, staging the tumor at IIIb.

The patient underwent chemotherapy with etoposide and cisplatin from December 6–8, 2022. Following treatment, muscle strength improved to 4+ to 5/5. This case highlights the importance of prompt cancer screening in LEMS patients, as timely tumor treatment can lead to symptom improvement.

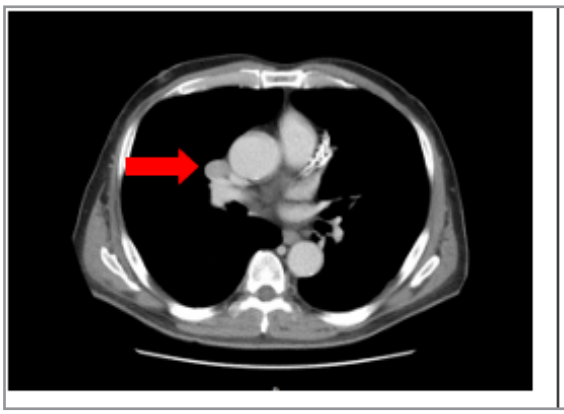

Figure : 1

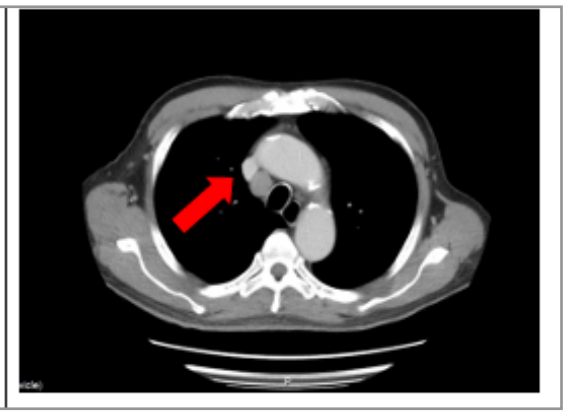

Figure: 2

Discussion

LEMS and MG are both disorders of the neuromuscular junction that result in muscle weakness. However, they exhibit distinct clinical features, electrophysiological characteristics, and associated antibodies. Careful evaluation of the patient's medical history, physical examination, and laboratory findings is essential for differentiation between these two conditions. In LEMS, distinguishing features include diminished or absent deep tendon reflexes and accompanying autonomic symptoms, which are not commonly observed in MG. The pattern of muscle weakness also differs: LEMS primarily affects proximal limb muscles, whereas MG typically presents with ocular muscle involvement. Electrophysiological studies, RST, play a crucial role in differentiation. In LEMS, RST demonstrates a decremental response to low-frequency stimulation, while high-frequency stimulation or post-exercise tests show an incremental response. Conversely, MG is characterized by a progressive decline in muscle response amplitude with low-frequency stimulation. Serological testing further aids in diagnosis. LEMS is often associated with antibodies against voltage-gated calcium channels (VGCC), whereas MG is commonly linked to antibodies against acetylcholine receptors (AChR). Additionally, the associated malignancies differ; MG is often linked to thymomas, whereas LEMS is primarily associated with SCLC [3, 4]. In this case, the patient exhibited proximal limb weakness that worsened with activity and lacked autonomic symptoms. Deep tendon reflexes were diminished or absent, initially pointing toward a diagnosis of MG. Treatment with pyridostigmine yielded improvement. However, subsequent neurological examinations and electrophysiological findings were consistent with LEMS. RST at 3 Hz showed a decremental response in muscle amplitude after rest and exercise, while stimulation at 30 Hz demonstrated an incremental

response at rest. Additionally, CMAP amplitudes were significantly reduced, which supported the possibility of LEMS.

The etiology of Lambert-Eaton myasthenic syndrome (LEMS) can be classified into two main categories: autoimmune disease and paraneoplastic syndrome caused by malignancies. LEMS is a rare neuromuscular disorder commonly associated with small cell lung cancer (SCLC) [5]. It is primarily a neuromuscular junction disorder caused by autoantibodies targeting presynaptic voltage-gated calcium channels (VGCC). These antibodies reduce calcium ion influx, impairing neurotransmitter vesicle release and subsequently decreasing acetylcholine secretion, which leads to impaired muscle contraction and muscle weakness. These autoantibodies are detected in over 90% of LEMS patients [5, 6].

Approximately 50–60% of LEMS cases are associated with SCLC, making it a paraneoplastic syndrome. Tumor cells are believed to express antigens similar to VGCC, triggering an immune response [4, 7.] The clinical manifestations of LEMS include autonomic dysfunction (dry mouth, constipation, sexual dysfunction, and orthostatic hypotension), muscle weakness predominantly affecting proximal limb and neck muscles, and diminished or absent deep tendon reflexes [7]. LEMS is diagnosed through repetitive nerve stimulation tests, electromyography (EMG), and serological tests detecting anti-VGCC antibodies. Electrophysiological findings include a decremental response in compound muscle action potentials (CMAP) with repetitive nerve stimulation (RNS). Unlike the "U-shaped" pattern seen in myasthenia gravis (MG), LEMS shows a CMAP increment of over 100%, which is a diagnostic hallmark [1]. The management of LEMS includes treating the underlying malignancy, corticosteroids, oral immunosuppressants, oral acetylcholinesterase inhibitors, intravenous immunoglobulin (IVIG, which suppresses the immune response to improve LEMS symptoms), and plasmapheresis (which removes circulating antibodies to improve symptoms) [6]. In this case, prior to a definitive diagnosis, the patient was treated with pyridostigmine (acetylcholinesterase inhibitor), prednisolone (steroid), and azathioprine (immunosuppressant). Additionally, the patient underwent five sessions of double filtration plasmapheresis (DFPP). Following further investigations, LEMS was strongly suspected. Based on literature recommendations, as LEMS is primarily associated with autoimmune disease or malignancy, serological tests for autoimmune-related antibodies were performed, all of which were negative, ruling out autoimmune etiology. Subsequent imaging revealed lymphadenopathy, and biopsy confirmed SCLC. Once the diagnosis was confirmed, anti-cancer therapy was initiated.

Paraneoplastic neurological syndromes (PNS) refer to non-metastatic effects of tumors where autoantibody responses, triggered by lymphocytes targeting cancer cells, lead to neuroendocrine abnormalities. PNS can affect multiple organ systems, including the nervous, endocrine, hematologic, dermatologic, and musculoskeletal systems. Literature indicates that approximately 50% of PNS cases are associated with SCLC [8]. Common PNS disorders include syndrome of inappropriate antidiuretic hormone secretion (SIADH), ectopic Cushing's syndrome (ECS), and Lambert-Eaton myasthenic syndrome (LEMS) [9]. Studies have identified independent risk factors for SCLC in LEMS patients, including weight loss ≥ 5%, smoking history at disease onset, and age ≥ 50 years [7]. In this case, the patient experienced a 20% weight loss over two months despite only a moderate reduction in food intake (to 50–75% of normal levels). Coupled with a long-term smoking history and an age of 60 years, as well as the clinical presentation, SCLC was strongly suspected, prompting further tumor surveys. SCLC accounts for approximately 15% of all lung cancers, with rapid progression and a high likelihood of metastasis. It is often diagnosed at advanced stages. Depending on the stage, treatment options include surgery, chemotherapy, and immunotherapy. Symptomatic improvement in LEMS often correlates with effective tumor treatment [10]. Following a confirmed diagnosis, this patient began chemotherapy for SCLC, resulting in significant clinical improvement. Muscle strength improved from 4+ to 5.

Conclusions

When the patient presented with muscle weakness, the degree of muscle strength reduction was documented. Neurological reflex tests were performed on both proximal and distal muscles, and the differences between the two muscle groups were compared. Additionally, considering the patient's history of smoking, a comprehensive assessment raised suspicion of Lambert-Eaton Myasthenic Syndrome (LEMS).

Literature review indicates a strong association between LEMS and tumors, particularly small cell lung cancer (SCLC). Therefore, early diagnosis of LEMS can lead to the early detection of SCLC. When a patient presents with symptoms of myasthenia, it is important to consider the possibility of a paraneoplastic syndrome (PNS). Typical PNS is characterized by neurological symptoms, and early tests including electromyography (EMG) and repetitive stimulation tests should be conducted. While literature suggests testing for anti-voltage-gated calcium channel (anti-VGCC) antibodies, which have a 90% specificity, this test was not performed in this case due to its high cost and limited availability. Since approximately 60% of patients with LEMS may have an underlying SCLC, it is recommended to regularly monitor suspected LEMS patients with CT scans. Tumor treatment can significantly affect the symptoms of myasthenia, and early detection of tumor involvement can facilitate appropriate oncological treatment, thereby improving the patient's condition. In this case, after the diagnosis of small cell lung cancer and the initiation of chemotherapy, the patient's muscle strength significantly improved, leading to a better quality of life.

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