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Lambert-Eaton Myasthenic Syndrome: A Review of Rare Neuromuscular Disease Related to Paraneoplastic and Autoimmune

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ABSTRACT

A rare condition known as Lambert-Eaton myasthenic syndrome (LEMS) affects the neuromuscular junctions, which are the connections between muscles and nerves. Tumor-associated or autoimmune causes trigger this condition. This mechanism depends on the presence of antibodies that directly attach to voltage-gated calcium channels located on the presynaptic nerve terminals. LEMS disease is divided into non-paraneoplastic or non-tumor LEMS (NT-LEMS) and paraneoplastic LEMS (P-LEMS). NT-LEMS is believed to be caused by an autoimmune process. On the other hand, P-LEMS has an underlying tumor, and LEMS symptoms are paraneoplastic manifestations of the tumor. Clinical signs of LEMS include proximal muscle weakness, autonomic dysfunction, and decreased deep tendon reflexes. The predominant sign of LEMS is weakness of the lower extremities. The defining characteristic of LEMS is a weakness that spreads from caudal to cranial, causing oculobulbar manifestations, and from proximal to distal, potentially involving the feet and hands. The diagnosis of LEMS depends on clinical, electromyographic, and serological findings of anti-VGCC antibodies. Therefore, comprehensive oncologic screening and monitoring should promptly follow a diagnosis of LEMS. The standard approach to treating LEMS symptoms is administering drugs that improve neurotransmission, such as potassium channel blockers and amifampridine. In refractory cases, immunosuppressants or immunomodulator agents, such as a combination of prednisone and azathioprine, are used. If a tumor is detected, oncological therapy should be a priority.

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INTRODUCTION

The rare disorder, Lambert-Eaton Myasthenic Syndrome (LEMS), affects the neuromuscular junction (NMJ), which connects the muscles and nerves. A cohort study in the Netherlands and the United States estimated the prevalence at approximately 3.3-3.4 cases per million individuals. Symptoms typically appear between the ages of 55 and 60.[1] Up to 50% of cases are classified as P-LEMS, a paraneoplastic form associated with malignant tumors originating from small cell lung cancer (SCLC). Other cases are autoimmune (NT-LEMS) and commonly coexist with other disorders.[2]

In order to find LEMS, antibodies bind directly to voltage-gated calcium channels (VGCC) in the presynaptic nerve terminal. VGCC facilitates calcium entrance to nerve terminals. This increased number of incoming signals triggers presynaptic signaling pathways. Acetylcholine (ACh) is released when VGCC antibodies prevent calcium from entering the cell. Presynaptic compensatory mechanisms initiate this process. Less ACh release in the synaptic gap manifests as Mmuscle weakness in the proximal extremities and problems with the autonomic nervous system.[3]

The clinical triad usually includes proximal muscular weakness, autonomic abnormalities, and areflexia. Though subacute episodes occur infrequently, the onset is usually subtle and gradual. Initial symptoms included leg weakness (60%), general weakness (18%), muscle discomfort or stiffness (5%), dry mouth (5%), arm weakness (4%), diplopia (4%), and dysarthria (2%). Muscle weakness was found in 96% of the 227 patients with LEMS, especially in the legs. Oculobulbar symptoms were reported in 51% of patients, while 49% reported autonomic symptoms. Respiratory symptoms were seen in 16% of the patients, while 15 reported sensory symptoms.[4]

Until now, there has been no specific treatment for LEMS patients. Patients with LEMS are treated based on their symptomatic symptoms, and if LEMS manifests as a paraneoplastic syndrome, they receive oncological treatment.[5] Establishing a diagnosis of LEMS is crucial for providing appropriate therapy and detecting the risk of malignancy in LEMS. Given that LEMS is a rare neurological disease with fluctuating symptoms, delays and errors in diagnosis often occur.[6–8] Neuromuscular diseases, including myasthenia gravis, often misdiagnose LEMS. LEMS can appear idiopathically, although it is most often the result of a paraneoplastic syndrome with SCLC.[9] This review aimed to help medical doctors recognize pathophysiology, clinical features, and diagnostic procedures, as well as provide an overview of treatment options based on current treatment findings.

REVIEW

Eligibility criteria

LEMS has a global prevalence of 5 per 1,000,000 people, which is 46 times lower than myasthenia gravis. In the last ten years, there have been two published epidemiological studies on this condition.[10,11] According to a survey by Ebenroth et al. on United States Army War Veterans (USA VA), the point prevalence of LEMS was estimated at 2.6-3.3 per 1,000,000 population.[10] Meanwhile, an epidemiological study in Japan by Yoshikawa et al. found that the prevalence of LEMS was 2.7 (95% CI 1.9-3.5) in a population of 1,000,000. SCLC is commonly associated with LEMS; around 50% of LEMS patients are also diagnosed with SCLC-type lung cancer.[11]

Etiology

Lambert-Eaton Myasthenic Syndrome is divided into two categories: paraneoplastic and non-paraneoplastic. An autoimmune mechanism is believed to cause the non-paraneoplastic category, also known as NT-LEMS (non-tumor LEMS). In contrast, paraneoplastic LEMS (P-LEMS) is associated with malignant disease.[12] A tumor is the main cause of LEMS in about 60% of cases, and the paraneoplastic type of LEMS is mostly linked to SCLC. Several types of cancer, such as mixed-type lung carcinoma, non-SCLC, thymoma, prostate cancer, and lymphoproliferative disease, can happen at the same time as this illness.[8,12] The development of LEMS is helped by the fact that cancer patients make too many antibodies against voltage-gated calcium channels (VGCC). Approximately 85% to 90% of LEMS patients tested positive for anti-VGCC. In LEMS patients with SCLC, this number was closer to 100%. All patients with LEMS linked to SCLC had a prolonged smoking history, but only half of LEMS-related patients did. [13,14]

Several gene loci, though to be associated with disease emergence, link to non-paraneoplastic LEMS disease. On antibody examination, around 65% of autoimmune-related LEMS patients had the HLA-B8 gene locus. LEMS patients have other gene loci, including HLA-DR3, HLA-DQ2, and HLA-A1. Apart from these antibodies, non-paraneoplastic LEMS patients also suffer from immune-related diseases, like thyroid disease and type 1 diabetes mellitus.[15,16]

Pathophysiology

The neuromuscular junction is the leading site of disruption in LEMS disease, where calcium ions play an essential role. Physiologically, a neuromuscular junction is a connection, or synapse, that lets action

potentials from motor neurons reach motor end plates and cause muscles to contract.[17] When there is a depolarization in the presynaptic nerve membrane, an action potential starts. This makes presynaptic transmission possible.[18] The depolarization process opens up the VGCC, which makes it easier for calcium ions to reach the motor nerve terminals. This causes a lot of the neurotransmitter acetylcholine (Ach) to be released into the neuromuscular junction. Then, the ACh molecule binds to its receptor on the postsynaptic membrane of the motor end plate. This process causes the opening of sodium and potassium channels at the postsynapse. Finally, cations can enter through these channels and cause depolarization of the motor end plate. This depolarization, in turn, causes the emergence of an action potential and results in muscle contraction.[17,18]

LEMS disease has two main pathways, which are divided based on their etiologies: paraneoplastic and autoimmune.[19] In paraneoplastic etiology, the occurrence of LEMS is closely related to the presence of malignant disease. The function of the VGCC is impaired by antibodies generated by the body in response to tumor cells that express antigens against this pathway. Anti-Sry-like high-mobility group box 1 (SOX1) antibodies or anti-glial nuclear antibodies (AGNA) are immunogenic antigens that are mostly produced by malignant cells. As a result, these antigens can act like each other, which lets IgG antibodies cross-link the surface of VGCC channels.[8] More specifically, this antibody explicitly targets the P/Q subtype of VGCC. Approximately 85% of LEMS patients show positive test results for type P/Q VGCC antibodies. These antibodies may also target N- and L-type VGCC channels, M1 muscarinic acetylcholine receptors, and synaptotagmin, which has been seen sometimes in LEMS disease.[8,14,20] Autonomic symptoms in LEMS disease are caused by antibodies that target VGCC channels other than the P/Q type.[5] It is estimated that approximately 60% of LEMS patients also suffer from malignancy, the majority being SCLC. LEMS is also sometimes found in other types of cancer, like mixed-type lung carcinoma, non-SCLC, thymoma, prostate cancer, and lymphoproliferative disorders.[8]

The autoimmune pathway is believed to be the second mechanism underlying the development of LEMS. It is believed that Individuals without cancer exhibit a genetic tendency toward HLA and LEMS genotypes. HLA (human leukocyte antigen), a cell surface protein, regulates the human immune system. However, the mechanism behind the degradation of these proteins and subsequent antibody generation remains unknown.[21] Approximately 65% of NT-LEMS patients are estimated to have HLA-B8 positivity, while 50% test positive for HLA-A1. The same frequency is observed for HLA-DQ2 and HLA-DR3.[13,22]

Clinical manifestations

Proximal muscle weakness, autonomic dysfunction, and decreased deep tendon reflexes are the three main signs of LEMS disease.[8] The most common symptom of LEMS disease is weakness in the lower extremities. LEMS disease is characterized by weakness that spreads from caudal to cranial, causing oculobulbar manifestations, and from proximal to distal, affecting the feet and hands. Usually, the weakness is symmetrical. In contrast, myasthenia gravis (MG), a neuromuscular junction disorder, is common, with weakness starting in the craniobulbar area and progressing caudally. The weakness in LEMS patients comes gradually, but in some cases, it can appear more quickly.[4,17] Symptoms of weakness in the extremities develop more clearly and quickly in P-LEMS patients than in NT-LEMS. P-LEMS patients experience weakness in their proximal legs and arms three months following symptoms. In contrast, most NT-LEMS patients only experience weakness in their proximal legs.[15]

Other symptoms of LEMS include muscle pain or stiffness, dry mouth, postural hypotension, erectile dysfunction, constipation, palpitations, diplopia, dysphagia, and dysarthria.[4] Young and Leavit did a study that looked back at medical records from LEMS patients. They found that ptosis (23%) and diplopia (23.5%) are the most common signs of oculobulbar weakness in LEMS patients who also have cranial nerve disorders. Oculobulbar symptoms usually do not appear at first but occur when the patient has experienced severe limb muscle weakness.[4,23]

In autonomic disorders, the most common complaint is dry mouth. Other disorders that can arise are difficulty urinating, erectile dysfunction, constipation, and dry eyes. Autonomic disorders appear in approximately 80–96% of patients.[13]

Decreased tendon reflexes, or areflexia, are signs often found during physical examination in LEMS patients. When LEMS patients go through post-exercise facilitation, muscle strength and tendon reflexes return to normal because of muscle contractions. This can lead to a wrong interpretation when looking at tendon reflexes. Approximately 40% of LEMS patients may experience these symptoms, so tendon reflex examination should be done after rest.[17,24] Sensory disturbances, limbic encephalitis, and cerebellar ataxia are among the less common symptoms. The appearance of these findings indicates a link with paraneoplastic incidents.[4,24]

Differential diagnosis

Despite its rarity, LEMS is an important differential diagnosis to consider when diagnosing

neuromuscular junction disease in neurological clinical practice. LEMS' clinical manifestations frequently overlap with those of other myasthenic syndromes. A cohor study found that 58% of 241 patients with LEMS from the Netherlands or England initially received a misdiagnosed. Myasthenia gravis was the most common diagnosis (21%), followed by unspecified myopathy (11%), polyradiculopathy or polyneuropathy (3%), and psychosomatic depression (4%). In some existing literature, LEMS and MG can appear simultaneously, making diagnosis more difficult.[4,6] Symptoms of LEMS are similar to those of neuropathies such as amyotrophic lateral sclerosis (ALS) and Guillain-Barre syndrome (GBS). In LEMS, symptoms that can help confirm the diagnosis include the disease getting worse, muscles getting weaker from proximal to distal and caudocranial areas, symmetrical weakness symptoms, and fluctuating levels of symptom severity. Patients may also experience prominent autonomic problems and cerebellar ataxia. Prominent pain and sensory symptoms are rare.[6,9]

Table 1. Comparison of characteristics of LEMS with MG and GBS[13,17,25]

	LEMS	MG	GBS
Defect location	Presynaptic	Postsynaptic	Peripheral nerves
Motor symptoms	Weakness spreads from caudal to cranial and from proximal to distal. Weakness can improve with repetition	Weakness occurs due to fatigue and exercise. Weakness mainly occurs in the extraocular muscles. Weakness improves if the patient rests	Ascending muscle weakness and usually symmetrical
Autonomic symptoms	Dry mouth	No symptoms	Fluctuating blood pressure and pulse (labile)
Sensory symptoms	Not found	Not found	Found in 50% of patients as a sensation of paresthesia
Deep tendon reflexes	Normal	Normal	Hyporeflexia to areflexia
Antibody	AntiVGCC at the presynaptic	AntiAch at postsynaptic	Anti-GM1, Anti-GD1a, Anti-GQ1B
RNS			
- CMAP at rest	Low	Normal	Normal or slightly decreased
- CMAP after brief exercise	Increase response	No change	Significant increase response
- LRS	Decrease response	Decrease response	No decrease response or stable
- HRS	Increase response	Decrease response or normal	Increase response
EMG(fasciculations/fibrillations)	Not found	Not found	Found
Tumor	SCLC (50%)	Thymoma (16%)	No tumor

Diagnosis

Look at the patient's symptoms and use the LEMS disease triad to figure out if they have LEMS. This triad includes weak proximal muscles, problems with autonomic function, and decreased tendon reflexes. People who are clinically thought to have LEMS can get more tests to confirm the diagnosis, such as repetitive nerve stimulation (RNS), electromyography (EMG), and an autoantibody serological examination (anti-VGCC antibodies). These tests help establish the diagnosis.[6,22]

1. Repetitive Nerve Stimulation (RNS)

Lambert and Eaton found symptoms that are typical of LEMS during the RNS exam. These symptoms have since become pathognomonic signs that help find the patient with LEMS. There are three classic findings typical of LEMS on RNS examinations, including: (1) On motor nerve conduction studies, there is a significant reduction in the amplitude of the compound muscle action potential (CMAP) (< 50%). It is common for this to happen, and it does in 96% of cases of LEMS and all presynaptic neuromuscular junction disorders; (2)

When the RNS is stimulated with a low frequency (2-5 Hz), the CMAP response shows down, and the CMAP amplitude also gradually decreases. A decrease of more than 10% can be suspected as LEMS. Approximately 94-98% of those diagnosed with LEMS exhibit this finding; (3) In conditions after voluntary muscle contraction for 10-30 seconds, there is an increase in the CMAP response of up to 100%. This condition is also known as post-exercise facilitation. A very high increase in response also occurs during RNS stimulation with a frequency of 20-50 Hz.[9,25,26]

The CMAP response to low-frequency RNS stimulation goes down because of the neurotransmitter ACh levels drop in the synaptic cleft. Sanders et al. found that with repeated stimulation in LEMS, the pattern of CMAP decreasing with low-frequency RNS stimulation was more obvious. However, it was less evident in myasthenia gravis how repetitive low-frequency stimulation led to a decrease in CMAP.[26] Increase calcium ions cause a CMAP response that is up to 100% higher after short periods of voluntary exercise compared to rest. As a result, the release of the neurotransmitter ACh into the synaptic cleft also increases. The difference in training duration of 10 seconds compared to 30 seconds affects the sensitivity and specificity of the RNS examination. The sensitivity and specificity of the 10-second training are 97% and 99%, respectively, while the 30-second training has a lower level.[9,27]

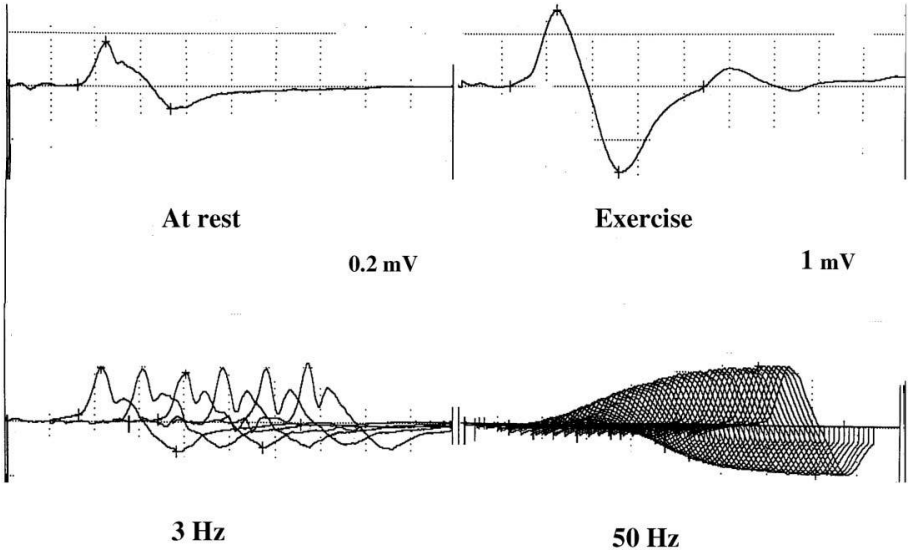

Figure 1. Classic triad pattern of RNS in LEMS. With a low CMAP of 0.28 mV at rest and a 217% decrease in low-rate stimulation (LRS) at 3 Hz. There is significant facilitation, with post-exercise facilitation (PEF) at +1030% and high-rate stimulation (HRS) at +1043%.[25]

2. Electromyography (EMG)

On the RNS exam, there may also be abnormal findings in other neuromuscular diseases. To help rule out diseases that cause other proximal muscle weaknesses, like myopathy and radiculopathy, a conventional needle electromyography (EMG) test can be used. On the RNS exam, there may also be abnormal findings in other neuromuscular diseases. To help rule out diseases that cause other proximal muscle weaknesses, like myopathy and radiculopathy, a conventional needle electromyography (EMG) test can be used. The single-fiber EMG examination reveals increased jitter and resistance to transmission. An increase in jitter indicates an obstacle in transmitting action potentials from the neuromuscular junction to the end of the motor plate so that muscle contraction is hampered. Barriers to transmission are thought to be related to the severity of LEMS disease.[4,27]

3. Serological Examination

P/Q type anti-VGCC antibodies are one part that is strongly suspected to be involved in the pathophysiology of LEMS. The presence of antibodies that cause damage to VGCC supports the diagnosis of LEMS. P/Q type anti-VGCC antibodies have a high level of sensitivity; it is reported that 90% of patients with paraneoplastic and autoimmune types of LEMS have these antibodies, and the number increases to 100% in paraneoplastic types of LEMS. This antibody examination has a weakness, namely low specificity (36%). Antibodies to VGCC have also been detected sporadically in healthy individuals and some patients with autoimmune and other paraneoplastic disorders.[4,20]

VGCC type N antibodies are also the second most common antibodies found in patients with LEMS (33-49%), especially those associated with primary lung malignancies. Particularly those associated with primary lung malignancies. If N-type antibodies are discovered, an additional underlying malignancy may

become more likely. These antibodies can also be found together with P/Q-type anti-VGCC antibodies; this event is called cross-reactivity.[20] Another antibody found in patients with LEMS is the SOX1 antibody. It is reported that around 64% of LEMS patients with SCLC are positive for this antibody. Anti-SOX1 antibodies are immunogenic tumor antigens in SCLC. Positive findings for these antibodies suggest that patients with SCLC will have LEMS in the future. The level of specificity for the anti-SOX1 antibody for LEMS with SCLC is 95%. However, the sensitivity is only 65% because this antibody is also found in most patients with other paraneoplastic neurological disorders and SCLC patients without LEMS.[28]

Management

It is important to treat the underlying malignancy in cases of LEMS associated with malignancy, such as SCLC. Until now, no treatment can cure LEMS. Therefore, the main focus of managing LEMS patients is to reduce or eliminate symptoms. However, the most effective and theoretically sound interventions focus on increasing presynaptic ACh release.[4,8]

1. Amifampridine or 3,4-diaminopyridine (3,4-DAP)

Currently, the first line of therapy to treat LEMS symptoms is amifampridine. In late 2018, amifampridine phosphate (Firdapse) tablets were the first drug authorized by the U.S. Food and Drug Administration (FDA) for the management of LEMS in adults over 17 years. Amifampridine phosphate is a salt form of 3,4-DAP that works by blocking voltage-gated potassium channels in motor nerve terminals, resulting in prolonged depolarization, allowing damaged VGCCs to remain open and causing an influx of calcium ions. Increased intracellular calcium further increases exocytosis of acetylcholine-containing vesicles and enhances impulse transmission at central, autonomic, and neuromuscular synapses.[29–31]

One recent phase 3 clinical trial conducted by Shieh *et al*. in 2019 assessed the safety and efficacy of amifampridine phosphate in the management of LEMS symptoms. This research was conducted with a randomized, double-blind, withdrawal, controlled trial study design conducted in 3 locations in the United States. Before the study, all participants had received amifampridine at a dose (divided into three or four doses per day, 30-80 mg) and a stable frequency for one week before randomization. Next, 26 participants who met the criteria were randomized to receive amifampridine phosphate (according to the optimal dose) or placebo in a 1:1 ratio. The results showed that on day 4, the amifampridine phosphate group had subject global impression (SGI) and quantitative myasthenia gravis (QMG) scores significantly better than the controls. In addition, in this study, other efficacy measures, including clinical global impression–improvement (CGI-I), triple timed up and go (3TUG), and QMG extremity domain scores were also significantly improved in the amifampridine phosphate group. During the four days of the study, only three patients (23.08%) in the amifampridine phosphate group reported side effects in the form of back pain, pain in the extremities, and mild headache, one incident each.[32]

The recommended initial daily dose of amifampridine (in adults) is 15-30 mg orally every day in divided doses given 3-4 times a day. Generally, the dose can be increased by 5 mg daily every 3-4 days until optimal response is achieved. The maximum dose based on FDA approval is 20 mg per single dose and 80 mg daily.[23]

2. Acetylcholinesterase inhibitors

AChE inhibitors usually do not significantly improve LEMS, although they may improve dry mouth. Pyridostigmine is an acetylcholinesterase inhibitor that can be an adjunctive therapy in patients with LEMS, but its effect is usually less significant than in patients with myasthenia gravis. However, its limited benefits, rapid action, favorable safety profile, wide accessibility, and cost-effectiveness make it a viable option for certain individuals. The recommended dose of pyridostigmine for LEMS patients is 30-60 mg 3-4 times daily. Side effects associated with pyridostigmine are mild, such as nausea, abdominal cramps, and diarrhea.[4,22,30]

3. Guanidine

Guanidine is approved as a first-line treatment for LEMS, but its use is minimal due to high toxicity. Guanidine increases the secretion of acetylcholine after nerve stimulation. In addition, this drug can slow down the depolarization and repolarization of the plasma membrane in muscle cells. Assume that amifampridine is not available or cannot be tolerated. In this case, administration of guanidine either alone or in combination with pyridostigmine at moderate doses (1000 mg/day) may be recommended due to its toxicity profile. Common side effects include nephrotoxicity and gastrointestinal problems, including anorexia, diarrhea, gastric irritation, and bone marrow failure.[2,22]

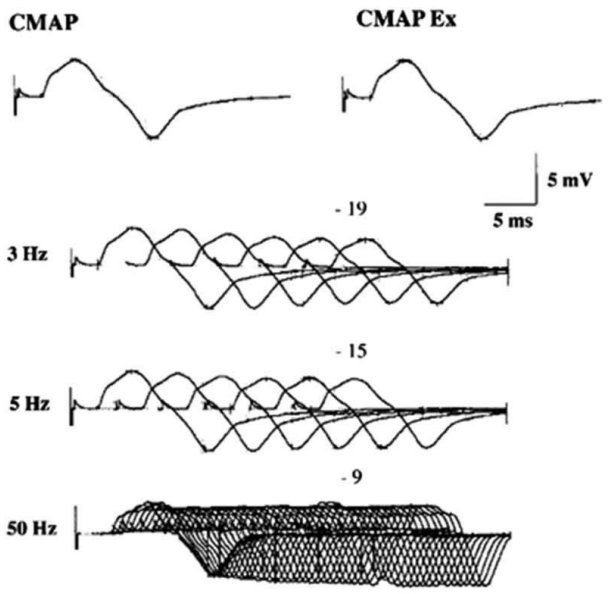

Figure 2. The most common abnormal pattern of RNS in MG.
Shows an abnormal RNS pattern with a normal CMAP of 0.4 mV at rest and no increase after exercise. LRS decreases by 215-219% at 3 and 5 Hz while remaining stable at HRS (50Hz)

4. Immunomodulator

In patients with refractory weakness to acetylcholine-elevating agents, immunomodulators may be able to target the immune system. This is because the immune system has played an important role in showing resistance to treatment.[33]

5. Intravenous immunoglobulin (IVIG)

IVIG is a first-line treatment option for those who do not respond to other therapies. Although the exact mechanism of action remains unclear, it is widely hypothesized that its mechanism of action involves the neutralization of autoantibodies and the regulation of autoreactive B cells. IVIG in a general regimen (total dose of 2 g/kg for 2-5 days) has been successfully used in the treatment of several immune-mediated neurological diseases. A 4 to 12-week maintenance regimen with repeated infusions is also valuable for patients who initially respond to IVIG therapy. This treatment is associated with problems and mild side effects such as laboratory abnormalities, rash, headache, and rarely deep vein thrombosis.[2,8,16,23]

6. Steroids and Immunosuppressive Agents

Long-term oral immunosuppression with prednisolone and azathioprine is usually recommended for patients whose LEMS symptoms do not respond well to symptomatic therapy. The recommended dose of prednisone is 1-1.5 mg/kg daily. After recovery, the dose may be reduced according to the patient's clinical condition. At the same time, the dose of azathioprine can be started at 50 mg twice a day and increased to a total dose of 2-3 mg/kg/day.[2,8,29]

7. Rituximab

Rituximab is an anti-CD20 monoclonal antibody used to manage lymphoproliferative and autoimmune conditions. Rituximab works by inducing cytotoxicity in B cells. As a result, this process effectively blocks the immune response mediated by this specific pathway. This drug is recommended when other immunosuppressive agents do not provide adequate clinical response. The standard dose for LEMS patients is 375 mg/m2 body surface once a week for four weeks and then monthly for the next two months. However, data to support its broader use still needs to be provided.[2,8,34]

8. Plasma Exchange

Therapeutic plasma exchange (TPE) has traditionally been used to selectively remove pathological contents in plasma, including autoantibodies, abnormal proteins, immune complexes, or toxins from patient plasma.[35] This drug has limited benefit in patients with LEMS, but its concomitant use with other immunosuppressive drugs may benefit some patients. Five plasma exchanges within 7-14 days are recommended in patients with myasthenia gravis (MG). However, no recommendation is currently available for LEMS. Therefore, it is recommended to use the same procedure in LEMS due to the similar pathophysiology of both diseases.[2,8,16,29]

Risk of Malignancy

The strong association between LEMS and malignancy means screening for malignant conditions should be performed immediately after diagnosing LEMS. LEMS malignancy screening consists of two steps; the first step is a study using chest computed tomography (CT) or magnetic resonance imaging (MRI) as the initial imaging screening to find the malignant part of the LEMS. If the results of the first step are negative, we go to the second step, using positron emission tomography (PET) as an additional screening test. If a negative result is detected during the first examination, the examination must be continued and repeated every 3-6 months for at least two years. High-risk patients, i.e., a positive anti-SOX1 antibody test or a Dutch-English LEMS Tumor Association Prediction (DELTA-P) score greater than two, are required quarterly.[16]

DELTA-P is a simple clinical assessment based

on age, weight loss, smoking history, bulbar symptoms, erectile dysfunction, and Karnofsky activity. The interpretation of this score is 0.2-6% for DELTA-P 0-1 and 83.9-100% for DELTA-P 3-6. This scoring system may help clinicians identify and monitor patients with LEMS at high risk for malignancy, particularly SCLC.[8,35]

Prognosis

Patients diagnosed with LEMS often have a lower quality of life due to autonomic nerve weakening and drug side effects. However, a LEMS prognosis with supportive and immunosuppressive therapy can enhance quality of life. After a year of treatment, LEMS patients' quality of life increased by 85%. The prognosis for paraneoplastic LEMS is determined by the underlying cancer. Meanwhile, the prognosis for non-paraneoplastic LEMS is similar to that of the general population.[8]

Complications

LEMS complications can be grouped into two: those related to pathophysiology and those relaed to therapy. Complications of LEMS include weakness, such as falls, broken bones, and aspiration pneumonia. Furthermore, autonomic nerve involvement causes symptoms such as dry mouth, constipation, dysphagia, and erectile dysfunction, which ultimately leads to weight loss and emaciation. LEMS therapeutic complications are associated with drug side effects. Immunosuppressive medications can result in cytopenias and infections. 3,4-DAP is associated with symptoms of tingling and numbness.[8]

CONCLUSION

Lambert Eaton's myasthenic syndrome, a rare autoimmune or paraneoplastic etiology, is caused by a decrease in in the neurotransmitter AcH in the presynaptic cleft. Despite its rarity, LEMS is the major differential diagnosis of neuromuscular disease. Clinical symptoms of LEMS include proximal muscle weakness, autonomic dysfunction, and decreased deep tendon reflexes. Lower limb weakness is a significant symptom of LEMS, as is caudal weakness radiating to the skull. LEMS is diagnosed using clinical, electromyographic, and serological manifestations of anti-VGCC antibodies. The standard approach to treating LEMS symptoms is to deliver neurotransmission-enhancing medications such as potassium channel blockers and amifampridine. In immune cases, immunosuppressants or immunomodulators can be used. When tumors are detected in LEMS patients, oncology therapy is the first priority.

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IMF prepared the abstract, introduction and correction of the article. CG and MIRR helped collect data for the article review.

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