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Case Study

Independence in activities of daily living was achieved using aerobic exercise without overwork weakness during rehabilitation: a case report of Lambert–Eaton myasthenic syndrome

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Abstract. [Purpose] Lambert–Eaton myasthenic syndrome (LEMS) is an autoimmune disease characterized by decreased transmitter secretion from neuromuscular junctions and nerve terminals. Such cases require physical therapy for independently performing daily activities; however, care must be taken to avoid overwork weakness. This study aimed to investigate the effects of aerobic exercise-based physical therapy in patients with LEMS. [Participants and Methods] We report a case of LEMS with decreased muscle endurance due to inactivity. The participant was subjected to physical therapy with an exercise modality-improved muscle endurance with low-intensity repetitions, while monitoring subjective exercise intensity over time. [Results] The participant achieved independence activities of daily living without developing overwork weakness. [Conclusion] Appropriate physical therapy is an important aspect in treating LEMS.

Key words: Lambert–Eaton myasthenic syndrome, Physical therapy, Overwork weakness

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INTRODUCTION

Lambert–Eaton myasthenic syndrome (LEMS) is an autoimmune disease in which acetylcholine secretion from neuromuscular junctions and nerve terminals are reduced, causing muscle weakness and autonomic symptoms[1, 2]. Cases of ataxia symptoms[3] due to paraneoplastic cerebellar degeneration (PCD) have also been reported. Generally, muscle strength and autonomic nervous symptoms of LEMS patients improve during medical treatment. However, if it is combined with disuse muscle weakness, due to inactivity, it is difficult to achieve independent activities of daily living (ADL) because of issues with muscle strength. Therefore, physical therapy is essential. Disuse muscle weakness requires intervention to improve muscle strength, but this needs to be managed carefully in a neuromuscular disease such as LEMS.

In physical therapy for patients with neuromuscular diseases, exercise with an appropriate load does not lead to adverse events. Aerobic exercise appears to be effective, although little evidence is available[4]. Moreover, in LEMS, it is necessary to pay attention to overwork weakness. Overwork weakness is a general term for muscle weakness caused by excessive physical activity, as observed in neuromuscular diseases[4–6]. The definition of overload varies among cases. Overwork weakness differs from disuse muscle weakness: overwork weakness persists for at least a period of time and does not improve with strength exercises.

Case reports of LEMS examine the therapeutic effects of medications with resulting improvements in muscle strength[7, 8]. However, there are no reports that have verified the usefulness of physical therapy for LEMS. Therefore, in this study, we hypothesized that appropriate physical therapy intervention would not result in overwork weakness in LEMS case. Physical

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therapy intervention for LEMS, participant was able to achieve ADL independence without overwork weakness. We report the case of LEMS who underwent muscular endurance training focused on multiple low-intensity aerobic and ADL exercises with graded exercise loads.

PARTICIPANT AND METHODS

This study included LEMS cases admitted to Steel Memorial Yawata Hospital in October 2020. The clinical diagnosis[14] was reported in previous studies and participant was diagnosed by physicians. The participant received medical treatment.

The physical therapy intervention consisted of a 40-minutes session per day, five days per week. The physical therapy program consisted mainly of aerobic exercises performed in the following order: low-load lower limb muscle strengthening, chair-stand exercise, cycle ergometer, and walking exercise. The cycle ergometer exercise program started with a fixed load of 10 watts, with a target rotation speed of 40 revolution per minute, for 10 minutes. If extreme fatigue occurred during the exercises, they were interrupted. Walking exercises were performed according to the maximum distance the patient could walk. The mBS setting during the exercise was adjusted such that the load corresponded to 4. Improved endurance has made it possible to incorporate balance exercises and ADL exercises. This study was conducted with the approval of the Ethics Committees at Steel Memorial Yawata Hospital, Japan on November 20, 2022. In accordance with the Declaration of Helsinki, the purpose of this study was explained to the participant, and her consent was obtained in writing.

The clinical symptoms of LEMS[14, 17] are as follows; main symptoms are symmetrical proximal muscle weakness, especially involving the lower extremities, with fatigue, muscle pain, and stiffness of the lower extremity and back muscles. Participant may also complain of drooping eyelids and double vision. Participant may complain of autonomic nervous symptoms such as dry mouth and constipation. Other symptoms such as PCD[3] have also been reported.

Physical therapy was initiated on the day of admission. At the physical therapy assessment for LEMS, the following outcome measures were used: the Clinical Frailty Scale (CFS)[9] was used to assess the participant's life before admission; hand grip strength, and Medical Research Council (MRC) muscle scale[10] was used for the assessment of muscle strength; Scale for the Assessment and Rating of Ataxia (SARA)[11] was used to assess ataxia due to PCD; Timed Up and Go Test (TUG)[12] was used for the assessment of gait stability and risk of falling; Berg Balance Scale (BBS)[13] was used to evaluate balance; and Barthel Index (BI) was used to assess ADL ability. Overwork weakness was carefully monitored during exercise, and myalgia or muscle weakness was assessed immediately after the intervention. Fatigue was assessed on the following day. The modified Borg Scale (mBS) was used to assess the degree of fatigue during exercise, including subjective exercise intensity (Fig. 1). The outcome measures (MRC, SARA, TUG, BBS, and BI) were assessed at admission (T1), after PE (T2), 3 days after 3,4-DAP treatment (T3), and at discharge (T4).

RESULTS

Table 1 summarizes the patient's characteristics, and Fig. 2 shows the clinical course. This is a case of a 75-year-old woman with LEMS who had a history of atrial fibrillation, hypertension, diabetes, and dyslipidemia.

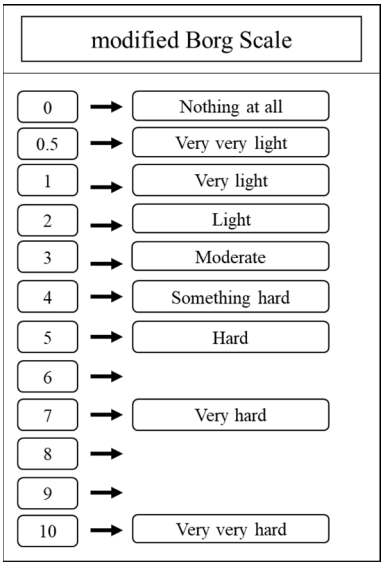

Fig. 1. The modified Borg Scale score used during aerobic exercise to evaluate subjective exercise intensity. Evaluate from 0 (No difficulty) to 10 (Very, very difficult), to monitor for overwork weakness.

Table 1. Review of LEMS patient's progress

	T1	T2	T3	T4
Days from onset (days)	5	21	43	64
Meaning of times	Admission	After PE	3 days after 3,4-DAP	Discharge
Muscle strength	50	56	58	58
MRC (sum scores)	11.3/12.6	-	-	13.8/12.3
Grip (kgf: R/L)				
SARA scale (points)	12	9	6	5
TUG (sec)	33.2	23.8	13.1	12.5
BBS (points)	25	31	33	35
BI (points)	40	55	80	100

LEMS: Lambert–Eaton myasthenic syndrome; MRC: Medical Research Council; SARA: Scale for the Assessment and Rating of Ataxia; TUG: Timed Up and Go Test; BBS: Berg Balance Scale; BI: Barthel Index; PE: plasma exchange; DAP: diaminopyridine; R: right; L: Left.

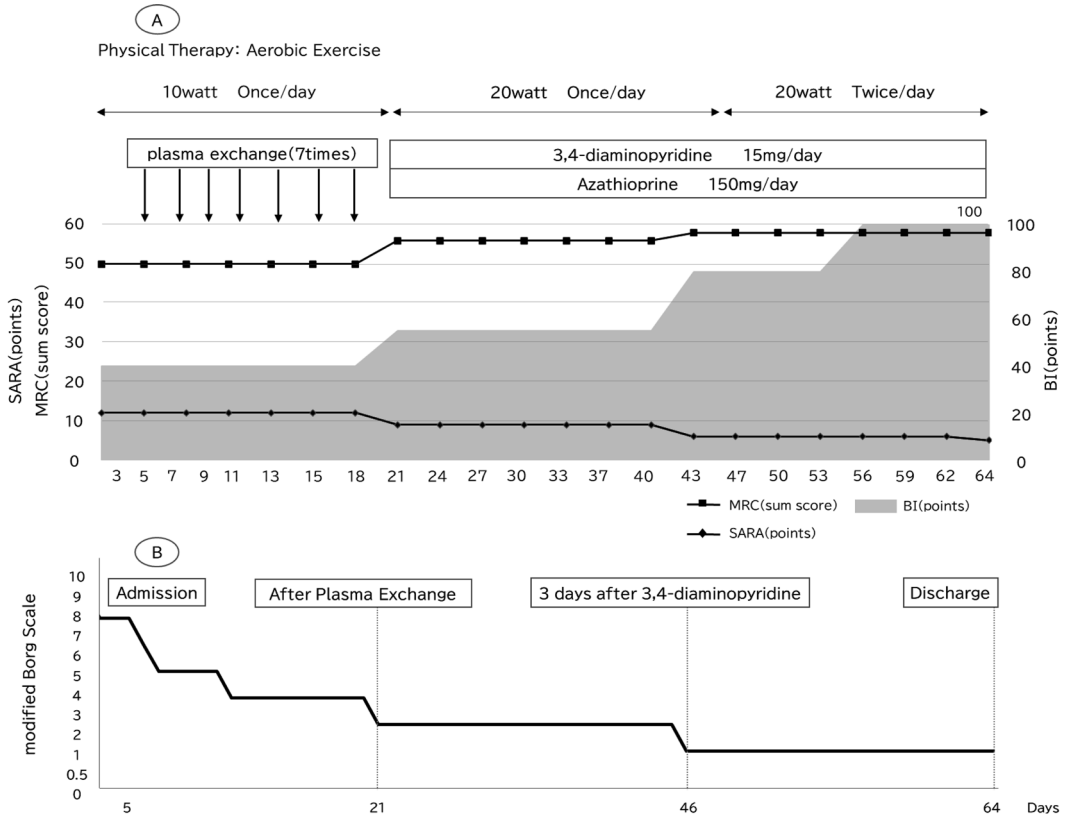

Fig. 2. [A] Chart of treatment and physical therapy. [B] Assessment of the effect of aerobic exercise on the modified Borg Scale score over time.

The participant had been prone to falls in the past 8 years and had a history of bruises and fractures. During this period, none of these were related to abnormalities in head imaging. Five months before diagnosis, the participant was urgently admitted to the hospital because of participant's right lower extremity.

Neurologically, the proximal muscles of the right upper and lower limbs showed weakness and fatigued easily upon repetitive motions. Serologically, anti-AChR, anti-MuSK, and anti-LRP4 antibodies tested negative, but the repeated stimulation test was positive for waning, while needle electromyography was normal. In the repetitive stimulation test, Waning (26% attenuation) was observed upon low-frequency stimulation at 3 Hz, but no waxing was observed with high-frequency stimulation at 30 Hz. Therefore, we made a clinical diagnosis of seronegative MG and began treatment. Participant was treated with a cholinesterase inhibitor, intravenous immunoglobulin (IVIg), and plasma exchange (PE). Treatment consisted

of prednisolone (PSL) 5 mg/day and tacrolimus. Participants had been transferred to a rehabilitation hospital 3 months prior to diagnosis.

One month before the current hospitalization, symptoms flared and PSL increased to 10 mg/day. During this period, P/Q-type VGCC antibody test (29.3 pmol/L, upper limit of normal: 20.0 pmol/L) was positive. Clinical and electrophysiological findings were suggestive of LEMS, and the diagnosis was made. This time, the participant was unable to walk without assistance and was readmitted to the hospital. Before admission, the participant was unable to perform ADL without assistance. So, CFS was 5.

In neurological examination, the participant demonstrated bilateral ptosis and mild weakness of the orbicularis oris muscle at admission (T1). Speech was normal, and she had no dysphagia. Weakness of the proximal muscles of the extremities and unsteady gait were observed. Ataxia symptoms included trunk ataxia, but not limb ataxia. The deep tendon reflexes were normal. Autonomic symptoms included frequent urination, urinary incontinence, constipation, and dry mouth. In the electrophysiological examination, the repetitive stimulation test was negative. The participant's ulner nerve and abductor digiti minimi were evaluated, but no abnormality was found. The high-frequency stimulation test was not conducted due to a lack of cooperation with this test because of the intense pain it caused. In physical therapy assessment, grip strength (right/left) was 11.3 kgf/12.6 kgf and MRC was 50. The proximal muscles of the extremities (shoulder joint and hip joint muscles) were weak. SARA was 12 points, and trunk ataxia was observed. Timed Up and Go Test was 33.2 seconds, and fall risk was high. BBS was 25 points, indicating balance impairments. Barthel Index was 40 points, and the participant needed help in performing ADL. In the early phase of the intervention, the participant was easily fatigued and had an mBS of 8, despite taking more rest periods between exercises. In addition to disease-specific muscle weakness, muscle endurance was the main problem affecting the outcome measures. In treatment, PE was implemented seven times after admission.

After PE (T2), MRC was 56, SARA was 9, TUG was 23.8 seconds, and BBS was 31. The participant showed significant improvements in muscle strength and walking ability. Weakness was observed in the proximal muscles of the extremities. The mBS gradually decreased, and overwork weakness did not arise. Therefore, the exercise load was changed to 20 watts, at 40 revolution per minute for 15-minutes. The patient was able to walk 50 meters continuously. However, participant's BI was 55 points, and assistance in ADL was still needed.

3,4-diaminopyridine (3,4-DAP) was initiated to improve the participant muscle strength and ADL ability further (Fig. 1A). Three days after 3,4-DAP treatment (T3), MRC was 58, SARA was 6, TUG was 13.1 seconds, Berg Balance Scale was 33 points, and BI was 80 points. Although the participant's walking ability and ADL abilities had improved, trunk ataxia persisted. The mBS did not exceed the target value of 4 (Fig. 1B), and overwork weakness did not occur. Therefore, physical therapy was added twice daily, without changing the exercise load, and ADL exercises were added. The participant could walk 100 meters continuously without assistance.

At the time of discharge (T4), MRC remained unchanged, and muscle strength was maintained. Scale for the Assessment and Rating of Ataxia was 5, and trunk ataxia persisted. Timed Up and Go Test was 12.5 seconds and walking ability had improved. Berg Balance Scale was 35, and balance impairment persisted. Barthel Index was 100 points: the participant was able to achieve independence in ADL, and the participant was discharged home.

Summary from T1 to T4 showed that medical treatment and physical therapy improved muscle strength (MRC improved from 50 to 58), walking ability (TUG improved from 33.2 seconds to 12.5 seconds), and achieve ADL independent (BI improved from 40 points to 100 points). However, trunk ataxia remains (SARA score is 5 points instead of 12 points) and balance disorder remains (BBS score is 35 points instead of 25 points).

DISCUSSION

The participant were LEMS cases characterized by proximal muscle weakness in the upper and lower limbs, trunk ataxia, and autonomic symptoms. After received medical treatment, the participant muscle strength was improved. However, physical therapy was necessary to maintain muscle strength and achieve independence ADL, so we implemented an intervention centered on aerobic exercise. The participant achieved independence ADL without overwork weakness and was discharged home.

In general, LEMS patients have lower extremity muscle weakness and autonomic symptoms[3, 14–17]. In this participant, muscle weakness was caused by LEMS. In addition, the CFS score before admission was 5, indicating that participant's muscle weakness was influenced by disuse. Treatment with 3,4-DAP, IVIg, PE, and other therapies can alleviate these symptoms[14–17]. This case was characterized by proximal muscle weakness in both upper and lower limbs, trunk ataxia, and autonomic symptoms. Muscle strength improved (MRC score improved from 50 to 58 points; strength improvement of proximal muscles of upper and lower limbs) after treatment with PE and 3,4-DAP. However, physical therapy was required to improve muscle strength during hospitalization. Muscle strength is the maximum force that can be exerted during a single contraction, whereas muscle endurance is the ability to continue to contract repeatedly. Skeletal muscles are roughly classified into red muscle fibers (type I) and white muscle fibers (type II); type II is involved in muscle strength, whereas type I is involved in muscle endurance. Previous research[18] has shown that type I is active during relatively low ADL. The participants achieved a certain level of muscle strength improvement through medical treatment. However, the participant continued to have low muscular endurance, and it was necessary to approach disuse muscle weakness (involving type I

fibers). Therefore, the intervention applied consisted mainly of aerobic and low-intensity muscle strength exercises. Previous research[19] has reported that low-intensity muscle strength shows the same level of improvement in physical function as high-intensity muscle strength. In addition, in this case, there was greater potential for improving muscle power, which is expressed as the product of muscle strength and contraction rate, than muscle strength. Muscle power declines more rapidly with age than does muscle strength[19] and is inversely related to ADL abilities[20]. Therefore, continuous aerobic exercise and low-intensity muscle strength make it possible to perform low-intensity activities, such as ADL, for longer periods. We thought that these interventions contributed to the improvement of disuse muscle weakness (type I fiber dysfunction).

We need to pay attention to overwork weakness[4–6], which can lead to clinical muscle pain and progressive muscle weakness due to high-intensity exercise in physical therapy for neuromuscular diseases. The definition of overload is not clear. Previous research[4–6] suggests that with the right amount of load, overwork weakness will not cause. Therefore, in this case, physical therapy was mainly performed using a cycle ergometer, according to the patient's fatigue level based on the mBS. Although mBS scores were high (when at the beginning of the intervention), but overwork weakness was not observed the following day. We concluded that muscle weakness was the result of disuse muscle weakness and not due to overwork weakness. The participants' CFS was 5 points, which means pre-symptomatic activity decline. During the subsequent period, up to discharge, no overwork weakness arose, either. We consider that participant's fatigue level was appropriately monitored, which was a factor in avoiding overwork weakness.

Finally, the participant's walking ability improved and the participant could achieve independence in ADL, which we believe was due to the effect of treatment of internal medicine and physical therapy. Treatment and physical therapy for LEMS improved muscle strength and had a positive effect on motor function and ADL. Although the participant had a good outcome during hospitalization, the symptoms of ataxia persisted. The SARA score showed improvement over time, but trunk ataxia symptoms due to PCD[3] remained. Therefore, trunk ataxia symptoms affected participants' walking ability. The clinical symptoms were characterized only by trunk ataxia. Paraneoplastic cerebellar degeneration likely affects symptoms of trunk ataxia. Therefore, the BBS, a measure of balance disturbance, could not be significantly improved.

We reported a case of LEMS in which good outcomes were achieved with medical treatment and physical therapy. We should pay attention to overwork weakness in physical therapy for LEMS. Aerobic exercise intervention can maintain muscle strength without overwork weakness, if the participant's exercise intensity is monitored over time. This case is the first report to mention physical therapy for LEMS. In general, treatment methods for LEMS vary from case to case, but physical therapy has been helpful. Therefore, physical therapy with risk management is recommended in LEMS cases.

Limitation of this study is that the electrophysiological examination during the diagnostic process of LEMS showed a negative repetitive stimulation test. However, LEMS cases showing negative repetitive stimulation tests have also been confirmed[7, 14]. Therefore, it is likely to fall under LEMS, which indicates a negative repetitive stimulation test. Furthermore, it has not been possible to evaluate sarcopenia, which may affect muscle strength improvement. Further verification and research are required in the future.

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The authors declare that no funding was obtained for this study and no conflict of interest relevant to this article.

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