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Aims and Scope

Journal of Electrodiagnosis and Neuromuscular Diseases (*J Electrodiagn Neuromuscul Dis*, JEND) is a peer-reviewed journal concerning both normal and abnormal functioning of the muscle, the neuromuscular junction, and the peripheral motor, sensory and autonomic nerves. The journal publishes clinical studies, reviews, and case reports in the fields of electrophysiology, electrodiagnosis, imaging studies including ultrasonography, and management, about neuromuscular diseases. The journal is aimed to provide an open forum for original research in basic science and clinical research that will improve our fundamental understanding and lead to effective treatments of neuromuscular diseases.
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Relationship between Chronic Obstructive Pulmonary Disease Severity and Surface Electromyography Parameters during Fatigue Caused by Knee Extensor Contractions

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Objective: Skeletal muscle dysfunction, which is characterized by decreased muscle strength and endurance, contributes to dyspnea during exercise in patients with chronic obstructive pulmonary disease (COPD), regardless of pulmonary function. This study analyzed skeletal muscle function in patients with COPD through surface electromyography (sEMG) evaluations and signal processing and attempted to determine whether sEMG parameters for muscle fatigue reflect the course of the disease.

Methods: In 24 patients with COPD, maximal voluntary isometric contraction and ramp contraction were performed during isometric knee extension, and the sEMG activity of the rectus femoris muscle was measured. The patients were divided into three groups according to their modified Medical Research Council (mMRC) grade and Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage. Patients with mMRC grades 0 and 1 were classified into group A, grade 2 into group B, and grades 3 and 4 into group C. Patients with GOLD stage 1 were classified into group I, stage 2 into group II, and stages 3 and 4 into group III. sEMG parameters were compared between groups using one-way analysis of variance.

Results: There were significant differences in the minimum median frequency and fatigue index between the mMRC groups. However, the sEMG parameters did not differ significantly among the GOLD groups.

Conclusion: Muscle fatigue differs according to the severity of subjective dyspnea in COPD. sEMG evaluations and signal processing can play supplementary roles in evaluating muscle endurance and predicting functional capacity in COPD.

Keywords: Pulmonary disease, chronic obstructive; Dyspnea; Muscle fatigue; Physical endurance; Electromyography

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Introduction

Skeletal muscle dysfunction is a common occurrence in patients with chronic obstructive pulmonary disease (COPD). Limb muscle dysfunction not only contributes to exercise intolerance, but also contributes to COPD morbidity and adversely affects life expectancy [1]. Several studies have reported that decreased muscle mass or strength is associated with increased

mortality, suggesting the importance of monitoring changes in these parameters in patients with COPD [2].

In patients with COPD, upper extremity muscle strength is relatively maintained, whereas lower extremity muscle strength is reduced [3,4]. Similar to the general population, muscle weakness in the quadriceps is associated with mortality in patients with COPD [5,6]. Muscle endurance refers to the ability to sustain a specific task and is determined by complex processes such as adequate muscle oxygen supply and oxygen extraction from the muscles. The reduction in exercise endurance in patients with COPD is due to changes in the distribution of muscle fiber types, with a decreased proportion of type I fibers and an increased proportion of type IIb fibers, as well as a decrease in muscle oxidative capacity [7,8].

During the course of the disease, muscle changes may occur before the deterioration of respiratory function [9]. Therefore, examining changes in muscle quality according to the severity of COPD is important for predicting the deterioration of physical function. Surface electromyography (sEMG) is a noninvasive method that can be used to evaluate muscle condition during activity. The assessment of neuromuscular fatigue using sEMG during dynamic exercise in patients with COPD has already been investigated [10]. The purpose of our study was to examine differences in the severity of COPD based on sEMG and to clarify its relationship with physical function. In particular, we aimed to determine whether sEMG signals for muscle fatigue can better reflect the course of the disease.

Materials and Methods

1) Subjects

This prospective study included patients diagnosed with COPD at a single center between April 2019 and 2020. Overall, 24 patients diagnosed with COPD were recruited for the study. The diagnostic criteria for COPD were based on the 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and included patients with a post-bronchodilation ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) <0.7. The inclusion criteria were patients >40 years old and had symptoms such as difficulty in breathing or difficulty performing activities of daily living. Patients with cancer, heart failure, coronary artery disease, cerebrovascular disease, heart failure, diabetes with severe complications, or uncontrolled hypertension were excluded. Patients who were unable to walk independently at the time of enrollment were also excluded. Patients were categorized according to the modified Medical Research Council (mMRC) scale and GOLD stage.

2) Experimental design

(1) sEMG

Subjects performed maximum voluntary isometric contraction (MVIC) and ramp contraction during unilateral isometric knee extension (60° knee angle). During the assessments, the physiotherapist (H.J.S.) gave verbal cues to the patient to perform the movements and assume the correct posture. The rectus femoris (RF) muscle of the dominant leg was measured [11]. A self-designed chair-type equipment was used to fix the parts other than the moving joints during RF muscle contraction. (Fig. 1A) [12]. RF muscle strength was measured using a digital tension meter (ZTS-500N; Imada Inc., Tokyo, Japan) (Fig. 1B). The root mean square (RMS) values of the RF muscle were measured using an sEMG device (PSL-EMG-Tr1; PhysioLab Co., Ltd., Busan, Korea) (Fig. 2A), and the electrode attachment site was set by referring to the standard electrode position suggested by Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) (Fig. 2B) [13]. To familiarize the participants with the equipment, submaximal isometric contraction trials, corresponding to approximately 20% of MVIC, were attempted as a warm-up [12]. The subjects then performed two 5-s-long MVIC trials, with at least 5 minutes of rest between trials; the maximum value was then selected. If the RMS values of MVIC differed by more than 5% from each other, a third measurement was taken and the largest of the measurements was selected [12]. The RMS value was taken, divided by the MVIC value, and the %MVIC, which is a value converted into a percentage, was used to analyze the normalized RMS value in the ramp exercise test of the RF muscle. The ramp exercise test consists of a gradual increase in knee extension (60° knee angle) force from baseline to the maximum in 10 seconds to reach 70% of MVIC and maintained for 5 seconds [11,12]. Measurements were performed twice with a sufficient rest period of at least 5 minutes between measurements. After the test, the most linear increase in time and muscle strength was selected by visual inspection and used for the analysis. In both tests, visual biofeedback and verbal encouragement were provided to achieve the highest level of muscle strength.

(2) Physical function assessment

Dyspnea was evaluated using the mMRC scale, which consists of five items that assess the severity of dyspnea from none (grade 0) to almost complete incapacity (grade 4). Additionally, baseline pulmonary function, respiratory muscle strength, grip strength, and cardiopulmonary endurance were obtained. The physical function assessments were conducted by a trained physiotherapist (H.J.S.). Pulmonary function and respiratory muscle

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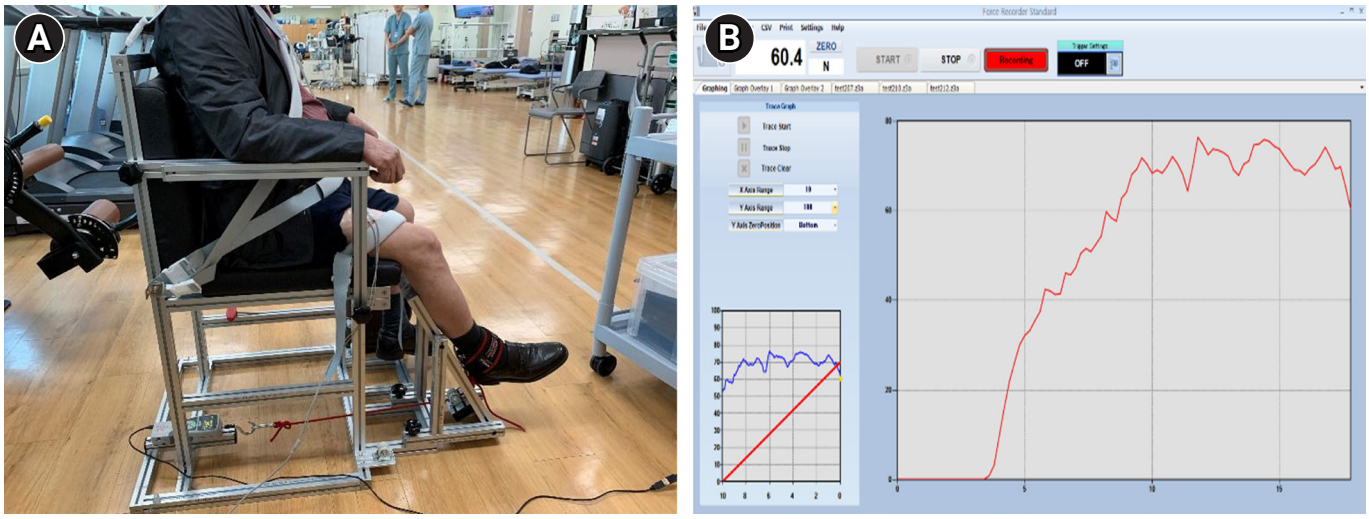

Fig. 1. Chair-type equipment (A) and user interface of digital tension meter software (ZTS-500N; Imada Inc.) (B) for measuring maximum voluntary isometric contraction and ramp contraction of the rectus femoris muscle.

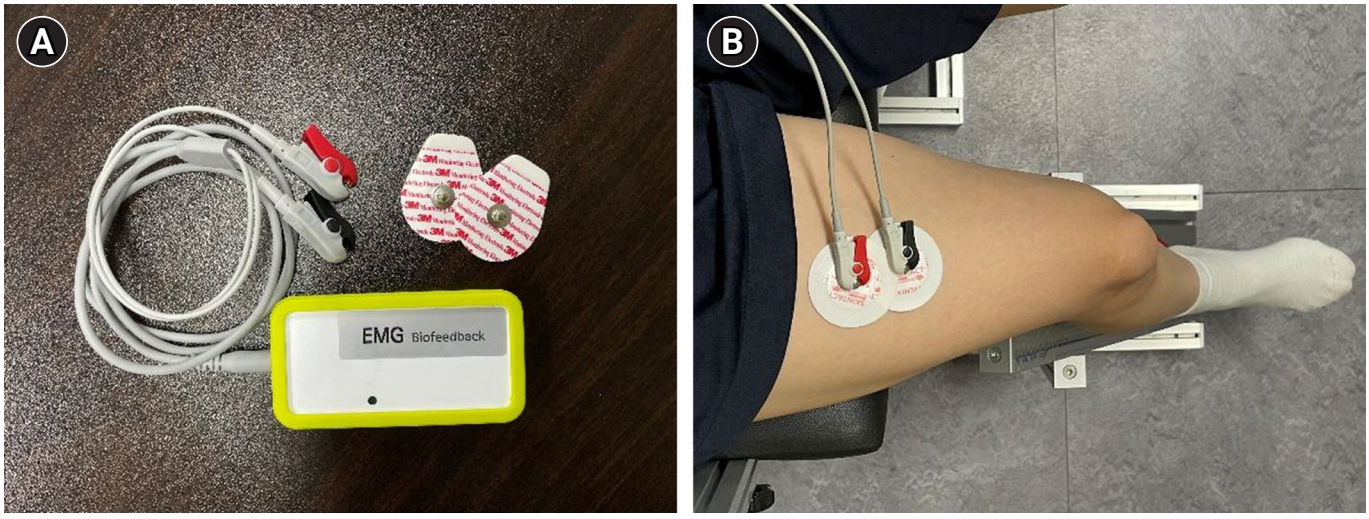

Fig. 2. Surface electromyography (EMG) device (PSL-EMG-TR1; Physiolab Co., Ltd.) (A) and electrode attachment site (B).

strength were measured using a spirometer (Font Fx, Cosmed, Italy) (Fig. 3A), and FVC, FEV_1, FVC/FEV_1, and maximal inspiratory and maximal expiratory pressures were evaluated. Pulmonary function and respiratory muscle strength tests were performed in all subjects during the initial evaluation according to previously described guidelines [14]. Grip strength was measured thrice using a hand dynamometer (SH5001; Saehan Co., Korea), and the maximum value was recorded (Fig. 3B). Cardiopulmonary endurance was measured using the 6-minute walk test (6MWT) according to the American Thoracic Society's Pulmonary Function Standard Committee guideline [15]. The 6MWT was recorded as a value evaluated once using a 30-m-long track with marks every 3 m.

3) Data analysis

The sEMG signal is the electrical activity reflecting the level of muscle contraction, and its parameters can be calculated using frequency analysis. The signal in a ramp exercise can be expressed as a relative value, such as %MVIC [16]. Using the absolute value, such as the RMS of sEMG, may cause signal differences depending on variables that occur when measuring sEMG, such as skin movement and muscle length discrepancies both between and within subjects. Therefore, it is also common to perform comparative analyses using the ratio of the reference

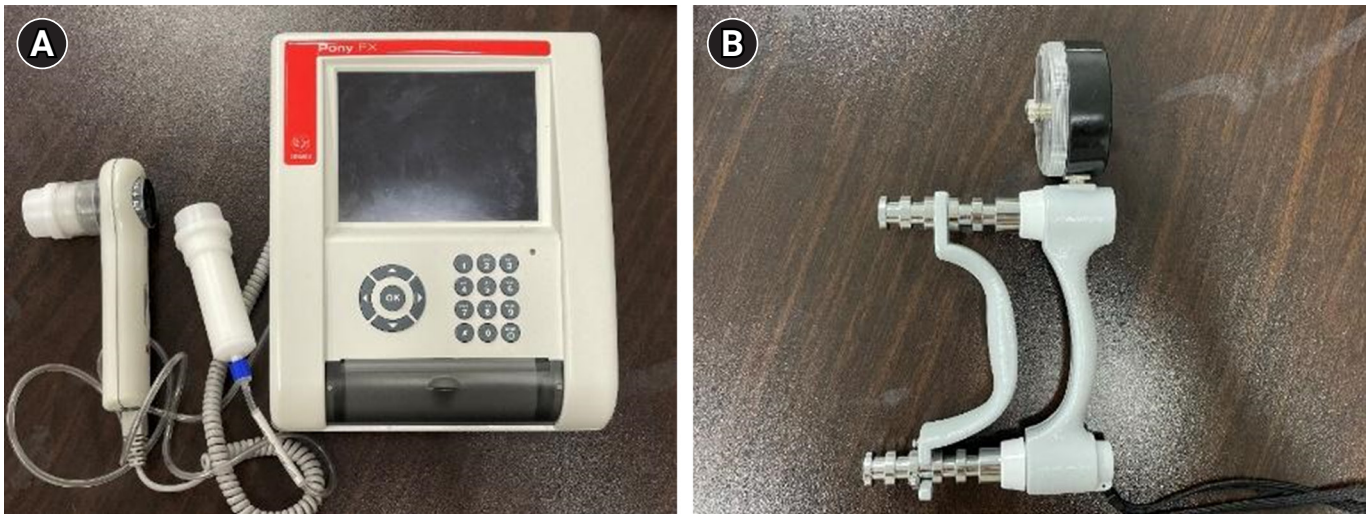

Fig. 3. Spirometer (Font FX) (A) to measure pulmonary function and respiratory muscle strength and hand dynamometer (SH5001) (B) to measure grip strength.

value [17]. In this study, among the RMS values of MVIC, the values for the middle 2 seconds, excluding the first and last seconds, among the collected 5-second signals were analyzed. MVIC was used to normalize %MVIC, and the formula used to determine %MVIC was as follows:

$$\%\,\mathrm{MVIC}\,(\%) = \frac{\mathrm{RMS}_{\mathrm{ramp\ excercise}}}{\mathrm{RMS}_{\mathrm{MVIC}}} \times 100$$

Frequency analysis is the most commonly used method for identifying the characteristics of complicated signals such as those of sEMG [18]. Accordingly, the main frequency band of the sEMG signal and amplitude of each frequency component are known. The methods for calculating the main frequency domain or range are median frequency (MDF) and mean power frequency. In this study, MDF was used. The MDF is the frequency value that divides the power spectrum (P[f]) into two regions with equal amplitudes. Mean values were calculated throughout the frames. The MDF was calculated as follows:

$$\int_0^{\mathrm{MDF}} \mathrm{P}\,(\mathrm{f})\mathrm{df} = \int_{\mathrm{MDF}}^{\infty} \mathrm{P}\,(\mathrm{f})\mathrm{df}$$

The fatigue index is used as a general-purpose indicator for detecting muscle fatigue. When muscle fatigue due to excessive muscle contraction occurs, MDF decreases [19]. The equation for fatigue index is as follows:

$$\mathrm{Fatigue\ \ index}\,(\%) = \frac{\mathrm{MDF}_{\mathrm{max}} - \mathrm{MDF}_{\mathrm{min}}}{\mathrm{MDF}_{\mathrm{max}}} \times 100$$

In the above equation, MDFmax is the maximum value of the MDF immediately before the MDF decreases due to fatigue. MDFmin is the minimum value of the MDF reduced by fatigue.

4) Statistical analysis

One-way analysis of variance (ANOVA) was performed to determine whether there was a significant difference in the values of each parameter between the three groups. We used the Scheffe method and post-analysis one-way ANOVA [20]. The patients were divided into three groups according to the mMRC grade and GOLD stage, and a statistical analysis was performed.

5) Ethical statement

The study protocol was approved by the Pusan National University Hospital Institutional Review Board (IRB number:1904-014-077) on April 29, 2019. This study was conducted in accordance with the Declaration of Helsinki. Written consent was obtained from all participants prior to the study.

Results

Overall, 24 patients were enrolled in the study. Patients were classified into groups according to the mMRC grade and GOLD stage. Patients with mMRC grades 0 and 1 were classified into group A, grade 2 into group B, and grades 3 and 4 into group C. Patients with GOLD stage 1 were classified into group I, stage 2 into group II, and stages 3 and 4 into group III. The mean age of the patients was 69.9 ± 8.7 years, and there were 23 men and 1 woman. Table 1 presents the patients' characteristics. Table 2 shows the mean and standard deviation of physical function as-

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Table 1. Demographic Characteristics of Patients

Characteristic	Value (n = 24)
General characteristic	
Age (y)	69.9 ± 8.7 (46–81)
Sex (male:female)	23:1
Height (cm)	166.5 ± 6.5
Weight (kg)	65.8 ± 10.3
mMRC	
Grade 0	1 (4.2)
Grade 1	4 (16.7)
Grade 2	11 (45.8)
Grade 3	7 (29.2)
Grade 4	1 (4.2)
GOLD	
Stage 1	3 (12.5)
Stage 2	13 (54.2)
Stage 3	6 (25)
Stage 4	2 (8.3)

Values are presented as mean ± standard deviation (range) or number (%).
mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

sessments for each mMRC and GOLD group, while Table 3 shows the mean and standard deviation of sEMG parameters in those groups. As the mMRC grade increased, sEMG parameters tended to decrease, except for %MVIC and the fatigue index. The maximum strength, MDF, and MVIC were inversely proportional to the mMRC grade and directly proportional to the fatigue index. In contrast, the sEMG parameters and GOLD did not show any trend. Table 4 shows whether there were statistically significant differences in the sEMG parameters according to the mMRC and GOLD groups. Among the mMRC groups, there were no significant differences in the mean values for maximal strength, MDF, MVIC, or %MVIC; however, there was a significant difference in the fatigue index. For the fatigue index, a statistically significant difference was found among all groups. The results suggest that the mMRC grade has a higher correlation with muscle quality after contraction than with physical ability and during pre-contraction.

Table 2. Assessment of Physical Function in Each Group of mMRC and GOLD

Variable	mMRC groups			GOLD groups		
	A	B	C	I	II	III
Pulmonary function	5	10	8	2	13	8
FVC (L)	3.6 ± 1.1	2.6 ± 0.7	3.4 ± 0.9	4.7 ± 0.2	3.0 ± 0.8	2.9 ± 0.9
Predicted FVC (%)	88.4 ± 14.3	60.6 ± 12.9	77.0 ± 18.8	97.5 ± 3.5	71.5 ± 17.8	67.5 ± 18.3
FEV_1 (L)	1.8 ± 0.7	1.4 ± 0.6	1.9 ± 0.6	3.0 ± 0.1	1.8 ± 0.4	1.06 ± 0.19
Predicted FEV_1 (%)	62.2 ± 15.8	45.0 ± 16.0	62.1 ± 12.2	84.5 ± 0.7	61.0 ± 7.6	37.0 ± 8.6
FEV_1 /FVC (%)	50.8 ± 16.2	52.1 ± 17.4	57.75 ± 14.66	64.5 ± 0.7	61.8 ± 12.8	38.1 ± 8.5
Respiratory muscle strength	4	11	6	3	11	7
MIP (cmH_2O)	84.5 ± 29.2	76.6 ± 25.2	67.2 ± 24.4	103.0 ± 11.4	71.9 ± 23.9	70.0 ± 25.6
MEP (cmH_2O)	117.0 ± 25.0	98.6 ± 16.1	91.3 ± 36.2	121.3 ± 11.7	94.6 ± 31.2	99.3 ± 12.5
Grip strength	5	11	8	3	13	8
Right (kg)	33.0 ± 5.4	33.4 ± 6.4	33.1 ± 5.3	33.6 ± 3.5	32.9 ± 6.1	33.6 ± 6.0
Left (kg)	31.4 ± 4.0	33.0 ± 7.0	33.0 ± 6.3	29.3 ± 4.6	33.4 ± 7.0	32.8 ± 5.9
6MWT (%)	4	11	7	3	11	8
Walked distance/predicted distance (%)	80.3 ± 12.9	66.9 ± 9.3	64.3 ± 11.3	70.9 ± 12.6	67.6 ± 13.5	69.0 ± 9.8

Values are presented as mean ± standard deviation.
mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; 6MWT, 6-minute walk test.

Table 3. Surface Electromyography Parameters in Each Group of mMRC and GOLD

Variable	Maximum strength (n)	MDF (Hz)	MVIC (μV)	%MVIC (%)	Fatigue index (%)
mMRC groups					
A	73.0 ± 27.8	70.8 ± 6.3	183.0 ± 86.9	35.6 ± 7.5	10.2 ± 5.7
B	59.3 ± 15.0	66.8 ± 8.1	145.7 ± 87.4	33.9 ± 5.9	21.7 ± 7.3
C	53.6 ± 6.9	62.5 ± 5.6	103.3 ± 46.2	40.9 ± 12.7	31.3 ± 8.8
GOLD groups					
I	76.0 ± 30.5	67.7 ± 2.8	176.9 ± 32.0	25.9 ± 5.5	22.3 ± 15.1
II	54.7 ± 9.4	66.4 ± 1.8	138.7 ± 75.9	38.8 ± 10	22.8 ± 10.5
III	63.2 ± 19.7	65.3 ± 3.5	126.2 ± 96.5	37.0 ± 6.2	22.2 ± 10.8

Values are presented as mean ± standard deviation.
mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease; MDF, median frequency; MVIC, maximum voluntary isometric contraction.

Table 4. Parameters with Significant Differences between mMRC and GOLD Groups

sEMG parameter	mMRC group		Average difference	p-value	GOLD group		Average difference	p-value
Maximum strength (n)	A	B	13.7	0.290	I	II	21.3	0.130
	A	C	19.4	0.121	I	III	12.8	0.493
	B	C	5.7	0.741	II	III	8.5	0.493
MDF (Hz)	A	B	3.9	0.589	I	II	1.3	0.960
	A	C	8.3	0.140	I	III	2.5	0.884
	B	C	4.4	0.421	II	III	1.1	0.943
MVIC (μV)	A	B	37.2	0.642	I	II	38.2	0.763
	A	C	79.7	0.182	I	III	50.7	0.655
	B	C	42.5	0.498	II	III	12.5	0.942
%MVIC (%)	A	B	1.7	0.964	I	II	-12.8	0.087
	A	C	-5.3	0.589	I	III	-11.1	0.185
	B	C	-7.0	0.446	II	III	1.8	0.900
Fatigue index (%)	A	B	11.5	0.027*	I	II	-0.5	0.997
	A	C	21.3	0.000*	I	III	0.0	1.000
	B	C	9.6	0.032*	II	III	0.5	0.994

mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease; sEMG, surface electromyography; MDF, median frequency; MVIC, maximum voluntary isometric contraction.
*$p < 0.05$.

Meanwhile, there were no significant differences in any parameters among the GOLD groups.

Discussion

We investigated the relationships between subjective dyspnea, muscle strength, and fatigue using sEMG. No significant difference was found in muscle fatigue according to the GOLD stage, but it was different according to the mMRC grade. Compared to air-flow obstruction, a high score of the mMRC was associated with poor maximum capacity for exercise [21]. Similarly, in our study, when leg fatigue was induced with submaximal contraction, it is thought that the patients' dyspnea symptoms influenced the maximum strength of the lower limb muscle. Furthermore, lower limb muscle fatigue, as determined by the fatigue index, was more strongly correlated with dyspnea than with muscle strength. Using the mMRC questionnaire could be useful in clinical practice because they can predict a patient's exercise capacity and level of physical activity when performing activities of daily living.

The goal of COPD assessment is to evaluate a patient's health status, predict disease exacerbation, and set treatment directions. COPD can be assessed based on the severity of airflow limitation and symptoms [22]. Methods of stratifying the severity of dyspnea in COPD, such as the mMRC scale, and health status questionnaires, such as the COPD assessment test, were used to assess symptoms. The mMRC scale is a simple assessment tool that predicts the mortality risk of patients with COPD. In COPD, the mMRC grade and cardiopulmonary exercise test (CPET) are closely related and predictive of exercise tolerance; patients with higher dyspnea scores on the mMRC scale complained of more severe dyspnea after CPET [21]. Similarly, our study found a close relationship between dyspnea perception and leg fatigue induced by submaximal isometric contraction, which was not related to the severity of airflow obstruction.

The lower limb muscles of patients with COPD are affected by both the quality and quantity of muscles, and leg fatigue is a common cause of exercise intolerance [23]. A decrease in muscle mass and changes in its composition are not only directly caused by muscle weakness, but can also cause a decrease in exercise capacity. Structural abnormalities are present in the quadriceps of patients with advanced COPD due to atrophy, mainly caused by a shift in muscle fibers from type I to type II. Additionally, the number of capillaries per muscle fiber and capillary density are decreased in the limb muscles of patients with COPD [1]. Because of these changes, assessments of limb muscle quality may become more important than those of muscle mass in patients with COPD. It was also reported that quadriceps endurance was lower in COPD patients than in healthy individuals, which is related to muscle oxidative capacity and not muscle mass [21]. Limb muscle fatigue can be explained by blood redistribution during high-intensity exercise and reduced muscle capillarity, which promotes fatigability by causing problems with blood and oxygen delivery [24]. Furthermore, metabolic changes in muscles that increase dependence on glycolytic metabolism are associated with muscle fatigue in patients with COPD [25].

Muscle strength in patients with COPD is generally better preserved in the upper limbs than in the lower limbs. Among the

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lower limb muscles, the quadriceps muscle, which is easily accessible, is mainly evaluated for muscle strength and endurance by volitional and non-volitional assessments [3]. Regardless of the assessment tools, patients with COPD mainly show reduced muscle strength and endurance compared to healthy individuals [26]. Endurance tests in patients with COPD may be discontinued before reaching maximal exercise capacity due to fatigue, dyspnea, and anxiety [27]. The MDF of muscles on sEMG can compensate for the disadvantages of the endurance test and can serve as an indirect marker that can predict contractile fatigue. In our study, we revealed that the lower limb muscle fatigue index can be evaluated using sEMG even in patients with severe COPD for whom exercise stress testing is difficult to perform.

This study had some limitations. First, this study had a small sample size, which can reduce the power of the results, and the findings may be difficult to apply to all patients with COPD. Second, we did not include an age-matched control group. As muscle fatigue is affected not only by the severity of COPD but also by age, the interpretation of the results requires caution. Future studies should overcome these limitations and propose reliable testing methods that can be adapted to patients with COPD as a whole.

Conclusion

The sEMG signal from the lower limb muscle in COPD during fatiguing exercise was correlated with the patient's subjective dyspnea. Furthermore, we confirmed that the muscle fatigue index in patients with severe COPD could be quantified using sEMG. The importance of the mMRC score was confirmed for the rehabilitation of COPD patients, and the potential of sEMG as a complementary measure was demonstrated.

Conflict of Interest

Jun Woo Lee is a technical team leader at a healthcare device manufacturer and had no no involvement in terms of funding of this manuscript.

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The Hmax/Mmax Ratio as a Diagnostic Tool in Assessing Spasticity in a Patient with Hereditary Spastic Paraplegia

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Hereditary spastic paraplegia (HSP) refers to a group of inherited diseases caused by progressive degeneration of the corticospinal tracts. We report a case of an HSP patient with ankle spasticity treated with an intrathecal baclofen (ITB) pump, for whom the Hmax/Mmax ratio was used as a diagnostic tool for spasticity. A man in his early 30s who was born without any complications and developed normally in childhood was diagnosed with HSP when he was 29 years old. Equinus gait pattern and bilateral genu recurvatum improved after manual therapy and botulinum toxin injections in both gastrocnemius muscles; however, after a few months, his gait disturbance became more severe as a natural course of the disease. To treat ankle spasticity and clonus, he was considered a suitable candidate for an ITB therapy. However, as spasticity is a finding that is easy to recognize but difficult to evaluate, we conducted electrophysiological testing, including H-reflex and the ratio of H-reflex amplitude to compound muscle action potential amplitude. The Hmax/Mmax ratio was 75.2% on the right side and 65.2% on the left side before an ITB pump, and 37.6% on the right side and 47.0% on the left side after an ITB pump. This case illustrates the usefulness of testing electrophysiological parameters such as the Hmax/Mmax ratio to measure spasticity objectively in late-onset HSP patients. The Hmax/Mmax ratio is also a good tool for measuring the degree of improvement in spasticity after ITB or additional treatment in these patients.

Keywords: Spastic paraplegia; Hereditary spastic paraplegia; Intrathecal baclofen; H-reflex

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Introduction

Hereditary spastic paraplegia (HSP) refers to a clinically and genetically heterogeneous group of inherited neurodegenerative and neurodevelopmental disorders caused by progressive degeneration of the corticospinal tracts [1]. Clinically, these conditions manifest as lower limb spasticity, weakness, hyperreflexia, and other corticospinal signs. The genetic basis of HSPs includes mutations inherited through autosomal dominant, autosomal recessive, and X-linked patterns. Its classification is based on the sequential numbering of chromosomal loci or specific genes, as they were identified, using a spastic paraplegia gene (SPG) designation [2]. Currently, more than 70 SPG genes have been described, and yet, since many conditions mimic HSP, accurate diagnosis can be challenging [1].

HSP patients show slow and progressive gait disturbances, as well as spasticity from infancy to adulthood. Currently, there is no specific disease modification therapy for HSP. Symptomatic

treatment includes physiotherapy, anti-spasticity drugs (baclofen, tizanidine and diazepam), and botulinum toxin. An orthosis is important for preventing complications, which can include multiple contractions, pain, and fractures, as well as for improving the patient's quality of life [3,4].

Here, we report a case of an HSP patient with ankle spasticity who was assessed with the Hmax/Mmax ratio and treated with an intrathecal baclofen (ITB) pump. The patient complained of severe ankle spasticity and gait disturbance. Initially, the spasticity of both ankles scored grade 1+ on the modified Ashworth scale (MAS). Despite undergoing rehabilitation therapy and receiving injections, the patient's ankle clonus and spasticity worsened. We decided on an ITB pump after assessing the patient's spasticity using the Hmax/Mmax ratio. We aim to illustrate the difficulties in the decision of ITB insertion in this HSP patient with spasticity, and to emphasize the importance of using the Hmax/Mmax ratio in making this decision.

Case Report

A male patient in his early 30s, who was born without complications and developed normally during childhood, began to experience ankle spasticity and gait disturbance at the age of 26. These conditions progressively worsened. Despite his conscious efforts to walk normally, he gradually began to trip and drag both feet as if they were not under his control. His walking pattern exhibited pes equinus, genu valgus, and a waddling gait. He was admitted to the neurology department of our hospital, where genetic studies revealed a pathogenic mutation in *SPAST* gene (MIM 604277), specifically an exon 9-16 duplication. At the age of 29, he was diagnosed with HSP. Brain magnetic resonance imaging demonstrated no definite abnormality.

The patient exhibited grade 3 muscle weakness in both ankle dorsiflexion and plantar flexion, as classified by the Medical Research Council. He was able to walk independently, and his functional independence measure was 123. He scored 53 on the Berg balance test. Both knee and ankle jerks were hypertonic, and ankle clonus was sustained. In terms of spasticity, both ankles' plantar flexors had MAS scores of 1+. A sensory examination showed hypesthesia on both ankles. Due to ankle spasticity and clonus, he presented to our rehabilitation center and started pool therapy, and circuit training (chest press, rowing, back machine, leg extension, and leg curl) for 2 months. Due to HSP, the patient presented with core muscle weakness, lower limb muscle weakness, and spasticity. We performed manual therapy to relieve his symptoms. Although this treatment helped with his muscle strength and gait disorders, joint contracture, and spasticity, thereby improving the patient's daily life functions and relieving pain, the discomfort persisted. However, as his spasticity worsened, we administered an initial injection of 300 units of Dysport (Ipsen, Boulogne-Billancourt, France) was injected first into both gastrocnemius muscles. Six months later, due to continued spasticity, we administered 200 units of Botox (Allergan, Dublin, Ireland) into both gastrocnemius muscles. Following these injections, both the equinus gait pattern and genu recurvatum showed improvement. However, a few months later, the patient's gait disturbance worsened, reflecting the natural progression of the disease.

This patient was deemed an appropriate candidate for an ITB therapy, aimed at managing severe ankle spasticity and clonus. However, given that spasticity is a symptom that is easy to identify but challenging to evaluate, we carried out electrophysiological tests, including the H-reflex and the ratio of the H-reflex to that of compound muscle action potential amplitude (Fig. 1). The H-reflex and M-response of the bilateral gastrocnemius-soleus (triceps surae) muscles and the F-wave of the tibial nerve recorded from each abductor hallucis longus muscle were assessed. The patient was positioned supine with a slight knee flex (approximately 30°). The ankle joint was secured in a mild plantar flexion position (around 20°), as the H-wave of the soleus muscle is inhibited by ankle dorsiflexion. The Hmax/Mmax ratio was 75.2% on the right side and 65.2% on the left side, leading us to decide on the use of an ITB pump (Tables 1, 2).

No significant side effects were observed following the ITB bolus injection, which led us to proceed with the ITB pump insertion. The infusion dose was initiated at 25 μg/day and was incrementally increased to 60 μg/day. Following the continuous ITB infusion, there was a reduction in ankle spasticity and clonus. The MAS score for both ankles improved with plantar flexor scores from 1+ to 1. Improvements were also noted in both the equinus gait pattern and genu recurvatum. A subsequent study of the Hmax/Mmax ratio showed values of 37.6% on the right side and 47% on the left side (Table 1).

Discussion

One of the primary objectives of rehabilitation is to recover from gait disorders, which significantly hinder functional independence in HSP patients. In our patient, spasticity was particularly evident in both ankles, specifically in the ankle plantar flexors. This patient experienced gait disturbance, and it is important to note that spasticity is one of the most common causes of gait disorders.

The MAS is commonly used to measure spasticity, but it is not sensitive enough to determine small changes in spasticity, and its

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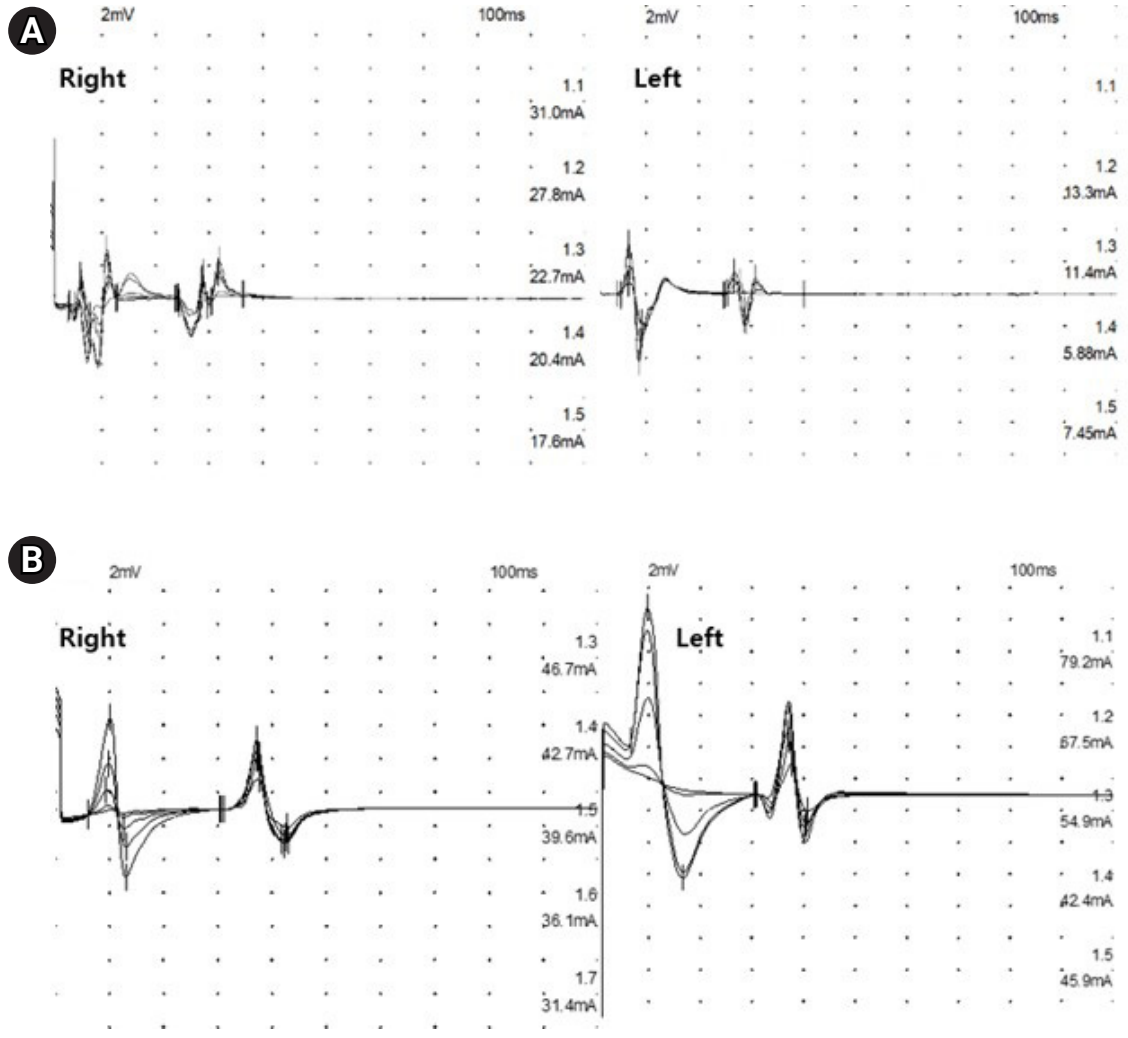

Fig. 1. Electrophysiological evaluation of lower motor neuron excitability, H-reflex and M-wave in a patient with hereditary spastic paraplegia. (A) The H-reflex and M-wave forms before intrathecal baclofen pump treatment. (B) The H-reflex and M-wave forms after intrathecal baclofen pump treatment.

Table 1. Results of the Nerve Conduction Studies

Parameter	Before ITB insertion		After ITB insertion	
	Right	Left	Right	Left
H-reflex latency (ms)	29.8	29.6	30.4	30.6
Hmax/Mmax ratio (%)	75.2	65.2	37.6	47.0
H-reflex amplitude (mV)	5.9	5.6	4.2	3.9

ITB, intrathecal baclofen.

reliability has been reported to be variable depending on the muscle and joint in question [5]. The MAS is thought to be more reliable among those assessing upper extremity spasticity, but it is not reliable for spasticity in the lower extremities [6,7]. In plantar flexion spasticity, the short-lever arm of the ankle makes it difficult to determine resistance to movement [6,7].

Currently, no treatment regimens for HSP are available. As the disease typically progresses, effective symptomatic treatment can significantly reduce the patient's disease burden. HSP is characterized by the degeneration of the corticospinal tract and dorsal column in a length-dependent manner. This degeneration manifests as key clinical features such as bilateral lower limb spasticity, a positive Babinski sign, and hyperreflexia [8]. ITB can improve spasticity and gait ability in patients with HSP [9]. However, in some cases, like our patient, it may be difficult to assess spasticity precisely with a physical examination. In such cases, electrophysiological parameters (H-reflex, Hmax/Mmax ratio, and F-wave response) can measure spasticity more objectively and can be used as a part of the clinical evaluation [10]. The Hmax/Mmax ratio is a comparison of the total and maximum counts of motor

Table 2. Results of the Motor Nerve Conduction Studies

Nerve	Stimulation site	Recording site	Before ITB trial F-wave (ms)	After ITB trial F-wave (ms)
Median	Rt. wrist	APB	24.7	24.8
	Lt. wrist	APB	23.8	23.7
Ulnar	Rt. wrist	ADM	24.3	25.2
	Lt. wrist	ADM	25.6	25.5
Peroneal	Rt. ankle	EDB	48.3	49.3
	Lt. ankle	EDB	47.6	47.0
Tibial	Rt. ankle	AH	46.7	46.5
	Lt. ankle	AH	46.4	46.8

ITB, intrathecal baclofen; Rt., right; APB, abductor pollicis brevis; Lt., left; ADM, abductor digiti minimi; EDB, extensor digitorum brevis; AH, abductor hallucis.

neurons that are reflexively activated by excitatory and inhibitory stimuli. This ratio decreases in the presence of presynaptic inhibition and reduced motor neuron excitability [11]. Previous studies have found that, compared to healthy individuals, the H-reflex amplitude is significantly higher on the spastic side in patients with spasticity [12,13]. Another study demonstrated that the Hmax/Mmax ratio is a feasible and objective method for quantifying the decrease in motor neuron excitability in patients with cerebral palsy [14]. However, there are notable variations in the Hmax/Mmax ratio among individuals with the same degree of hypertonia, which accounts for the poor correlation [15].

Only one report has utilized the Hmax/Mmax ratio to evaluate spasticity in a patient with HSP [16]. Unlike the other study, our case emphasizes the usefulness of the Hmax/Mmax ratio in a patient with HSP who complained of spasticity and had a MAS score that did not align with that complaint. In our patient, the MAS scores were 1+ in both ankles, and the degree of discomfort expressed by the patient did not match those findings. Thus, it was difficult to decide whether to proceed with ITB insertion. An electrophysiological test was conducted to assess the degree of spasticity via the Hmax/Mmax ratio, which was 75.2% and 65.2% on right and left side, respectively. We decided to insert the ITB pump. After the ITB pump therapy, we assessed the Hmax/Mmax ratio again, and it showed improvement. The Hmax/Mmax ratio accurately measured the patient's spasticity, enabling rapid ITB pump insertion, which improved the patient's quality of life.

In conclusion, our HSP patient had spasticity and mild motor weakness. The symptoms began in adulthood and progressed slowly and steadily; therefore, it was not easy to assess spasticity in a precise manner. The MAS score and degree of spasticity experienced by the patient did not match. In such a case, it may be useful to test electrophysiological parameters, such as the Hmax/Mmax ratio, to measure spasticity objectively. Furthermore, the Hmax/Mmax ratio is a good measure to estimate the degree of improvement in spasticity after ITB insertion or other treatments in HSP patients.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Bilateral Ischemic Lumbosacral Plexopathy after Proximal Aortic Surgery

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In paraplegia after proximal aortic surgery, in addition to spinal cord ischemia, injuries to the plexuses and other peripheral nerves should be considered. Spinal cord ischemia—the most common etiology of paraplegia—can be caused by the occlusion of several radicular arteries resulting from aortic clamping. We report a case of bilateral ischemic lumbosacral plexopathy with a spared spinal cord occurring after proximal aortic surgery. A 76-year-old woman underwent aortic valve replacement with ascending aorta and total arch replacement, along with multiple hematoma evacuations. Postoperatively, she developed paraplegia with sensory deficits in the bilateral lower limbs. Spinal magnetic resonance imaging revealed no remarkable findings at any level of the spinal cord. In electrophysiological studies, the compound motor action potential and sensory nerve action potential of the bilateral lower extremities did not respond to stimuli; all examined muscles displayed abnormal spontaneous activities without motor unit action potentials. Based on these findings, a diagnosis of bilateral lumbosacral plexopathy was ultimately made.

Keywords: Lumbosacral plexopathy; Aortic surgery; Paraplegia

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Introduction

The aorta is directly connected to the heart. Diseases of the aorta include aortic dilatation, aortic aneurysm, and aortic dissection, and several complications may arise after corrective surgery to treat these conditions [1,2]. Paraplegia is a notable complication of aortic surgery that warrants careful evaluation due to its potential to diminish a patient's quality of life and independence in daily activities. The reported prevalence of this complication varies in the literature, with rates ranging from 0.3% to 38% [1,3]. Spinal cord ischemia has been suggested as the most common cause of lower-limb weakness after aortic surgery. During aortic surgery, the proximal descending aorta is clamped to correct pathologies in the thoracic aorta, disrupting blood flow to the distal part of the aorta. If the clamping time is prolonged, ischemia or infarction of the distal portion may occur. This area includes several radicular arteries, most notably the artery of Adamkiewicz, that supply oxygen to the thoracic spinal cord. Consequently, prolonged clamping can result in paraplegia due to ischemic injury of the thoracic spinal cord [3,4].

However, paraplegia following aortic surgery may not always be attributable to ischemic spinal cord injury [4,5]. In the present case, features of peripheral nerve injury were observed, including lumbosacral plexopathy and femoral neuropathy. Ischemic lumbosacral plexopathy with paraplegia can occur after surgery of the distal abdominal aorta or iliac artery [4,6].

However, no case reports have been published on lumbosacral plexopathy following proximal aortic surgery. Therefore, this case report is intended to discuss the occurrence of bilateral ischemic lumbosacral plexopathy after ascending aorta and total arch replacement, which is classified as proximal aortic surgery.

Case Report

A 76-year-old woman presented with dyspnea on exertion that had begun 2 years prior. Echocardiography performed in February 2019 revealed severe aortic regurgitation and ascending aortic dilatation. On February 14, 2020, due to progressive symptoms and aggravated aortic regurgitation, the patient underwent aortic valve replacement with ascending aorta and total arch replacement. The following day, venoarterial extracorporeal membrane oxygenation (VA-ECMO) was administered to the right thigh due to cardiac tamponade. The patient subsequently underwent two hematoma removal procedures to address bleeding at the cardiac surgery site, after which she was admitted to the intensive care unit. On February 22, which was postoperative day (POD) 8, the patient regained consciousness after sedatives were tapered. However, she was unable to move her bilateral lower extremities. On the same day, ischemic colitis was confirmed via sigmoidoscopy. A physical examination revealed that the patient's consciousness and orientation were intact; however, the muscle strength of her bilateral lower extremities was assessed as grade 0, and sensation was impaired below both thighs. The patient's deep tendon reflexes were reduced, but no abnormalities were observed in the upper extremities, and no pathological reflexes were induced.

VA-ECMO was removed on POD 17. Subsequent electroencephalography (EEG) and brain computed tomography (CT) scans performed on POD 19 revealed no abnormalities. Once the patient's condition stabilized, she was transferred from the intensive care unit to the general ward on POD 51. Two days later, on POD 53, thoracic diffusion-weighted magnetic resonance imaging (MRI) indicated no signal changes suggestive of ischemic damage to the spinal cord. In a nerve conduction study (NCS) performed on POD 54, no response was observed in either the motor (femoral, peroneal, and tibial) or the sensory (lateral femoral cutaneous, sural, saphenous, and superficial peroneal) nerves in the bilateral lower limbs (Table 1).

Therefore, due to the potential for bilateral lumbosacral plexopathy, conservative treatment, and rehabilitation were initiated. This included passive range-of-motion exercises, standing training via a tilting table, ergometer use, and gait training with a lifting device. To investigate the persistent paraplegia, electromyography (EMG) was performed on POD 73. However, this evalua-

Table 1. Nerve Conduction Study on Postoperative Day 51 Suggesting Bilateral Lumbosacral Plexopathy

Variable	Stimulation site	Recording site	Latency (m/sec)	Amplitude (μV)	Velocity (m/sec)
Sensory					
Lt. median	Wrist	Third finger	3.70	21.0	
Lt. ulnar	Wrist	Fifth finger	2.70	17.5	
Rt. superficial peroneal	Lateral leg	Ankle	NR	NR	
Lt. superficial peroneal	Lateral leg	Ankle	NR	NR	
Rt. sural	Calf	LM	NR	NR	
Lt. sural	Calf	LM	NR	NR	
Rt. saphenous	Calf	MM	NR	NR	
Lt. saphenous	Calf	MM	NR	NR	
Rt. LFCN	Inguinal ligament	Lateral thigh	NR	NR	
Lt. LFCN	Inguinal ligament	Lateral thigh	NR	NR	
Motor					
Lt. median	Wrist	APB	4.60*	9.6	
	Elbow	APB	8.10	8.9	54.2
Lt. ulnar	Wrist	ADM	2.20	9.4	
	Elbow	ADM	5.30	8.3	59.6
Rt. deep peroneal	Ankle	EDB	NR	NR	
	Fibular head	EDB	NR	NR	
Lt. deep peroneal	Ankle	EDB	NR	NR	
	Fibular head	EDB	NR	NR	
Rt. femoral	Inguinal ligament	VM	NR	NR	
Lt. femoral	Inguinal ligament	VM	NR	NR	
Rt. tibial	Ankle	AH	NR	NR	
	Knee	AH	NR	NR	
Lt. tibial	Ankle	AH	NR	NR	
	Knee	AH	NR	NR	

Lt., left; Rt., right; NR, no response; LM, lateral malleolus; MM, medial malleolus; LFCN, lateral femoral cutaneous nerve; APB, abductor pollicis brevis; ADM, abductor digiti minimi; EDB, extensor digitorum brevis; VM, vastus medialis; AH, abductor hallucis.
*The terminal latency of the left median compound muscle action potential was delayed; otherwise, results for the upper extremities fell within normal range. We considered this a non-significant finding.

tion was limited by poor patient cooperation. Based on the study, all muscles examined (including the vastus medialis, iliopsoas, and right tibialis anterior muscles) displayed diffuse abnormal spontaneous activities (specifically, positive sharp waves and fibrillation potentials), and no motor unit action potentials were observed (Tables 2, 3). On POD 197, T2-weighted lumbosacral plexus MRI revealed diffuse increased signal intensity in the right lumbar third, fourth, and fifth nerve roots, as well as both lumbosacral plexuses. This suggested diffuse swelling of the nerve. No abnormal findings were observed in the spinal cord at the lumbosacral level (Fig. 1). At discharge, no improvement in muscle strength was noted for any muscle group. The patient continued her treatment at a hospital in her hometown.

Table 2. Nerve Conduction Study* on Postoperative Day 73 Corresponding to Bilateral Lumbosacral Plexopathy

Variable	Stimulation site	Recording site	Latency (m/sec)	Amplitude (μV)	Velocity (m/sec)
Sensory					
Rt. superficial peroneal	Lateral leg	Ankle	NR	NR	NR
Motor					
Rt. deep peroneal	Ankle	EDB	NR	NR	NR
	Fibular head	EDB	NR	NR	NR
Lt. deep peroneal	Ankle	EDB	NR	NR	NR
	Fibular head	EDB	NR	NR	NR
Rt. femoral	Inguinal ligament	VM	NR	NR	NR
Lt. femoral	Inguinal ligament	VM	NR	NR	NR

Rt., right; NR, no response; EDB, extensor digitorum brevis; Lt., left; VM, vastus medialis.
*Due to the existence of the previous study and the patient's poor cooperation, this study was performed in a limited fashion.

Table 3. Electromyography Study on Postoperative Day 73 Corresponding to Bilateral Lumbosacral Plexopathy

Muscle	Spontaneous		MUAP			Recruitment pattern	Interference pattern
	Fib	PSW	Amplitude	Duration	Phase		
Rt. tibialis anterior	3+	3+		No MUAP			
Rt. vastus medialis	2+	2+		No MUAP			
Rt. iliopsoas	2+	2+		No MUAP			
Lt. vastus medialis	1+	1+		No MUAP			
Lt. iliopsoas	1+	1+		No MUAP			
Rt. first dorsal interossei	None	None	NL	NL	NL	NL	NL
Rt. deltoid	None	None	NL	NL	NL	NL	NL

Fib, fibrillation; PSW, positive shock wave; MUAP, motor unit action potential; Rt., right; Lt., left; NL, normal.

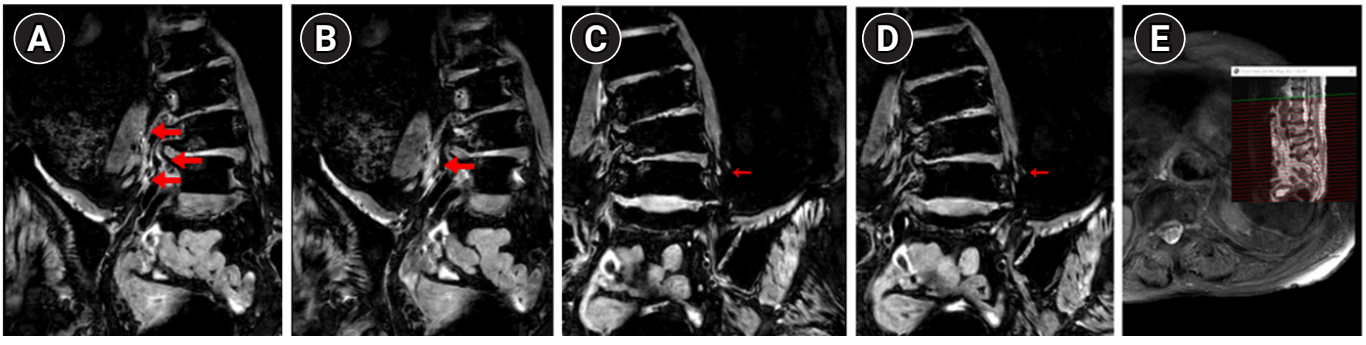

Fig. 1. Magnetic resonance images of the lumbosacral plexus, obtained on postoperative day 197, from a patient who developed paraplegia after proximal aortic surgery. T2-weighted images reveal (A, B) diffuse swelling of the right L3, L4, and L5 nerve roots and lumbar plexus (thick arrows), as well as (C, D) suspicious increased T2 signal intensity of the left lumbar plexus, indicating bilateral lumbar plexopathy (arrows). (E) No signal changes were observed that would indicate a spinal cord lesion.

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Discussion

The lumbosacral plexus is composed of the lumbar plexus, which includes the ventral branches of the L1-L4 nerve roots, and the sacral plexus, which includes the ventral branches of the L4 and L5 and the S1-S3 nerve roots [7]. The lumbar plexus gives rise to nerves such as the femoral, obturator, and lateral femoral cutaneous nerves, which are responsible for movement and sensation in the upper parts of the lower limbs. The sacral plexus primarily consists of the sciatic nerve, which branches into the peroneal and tibial nerves, responsible for movement and sensation in the distal lower limbs. Lumbosacral plexopathy can result from both structural and non-structural lesions in this area. Structural issues include hematoma, aneurysm, and trauma, while non-structural issues encompass ischemic injury, surgery-related stretch injury, inflammation, and radiation injury [7]. In most cases, plexopathy presents unilaterally, with bilateral involvement primarily reported following radiation therapy [8]. Ischemic lumbosacral plexopathy is not widely recognized due to its low incidence rate, but bilateral symptoms have been reported in some postoperative cases, including bilateral aortic iliac artery occlusion and descending aortic dissection [3,9,10].

Aortic surgery causes substantial hemodynamic fluctuations and can impact the human body in numerous ways. A previous study suggested that the risk of postoperative complications increases when the aortic cross-clamping (ACC) time exceeds 150 minutes [11]. Therefore, when evaluating paraplegia after surgery, it is crucial to conduct a thorough evaluation of the corticospinal tract structures originating from the primary motor cortex [9]. The cerebral cortex, spinal cord, lumbosacral nerve root, lumbosacral plexus, and other peripheral nerves should also be evaluated [10]. While no systematic reviews are available on complications after aortic surgery, several studies have reported incidence rates including stroke in 1.2% to 17% of patients, spinal cord injuries in 0.25% to 11.1% of cases, lumbosacral plexopathy in 0% to 0.3% of cases, and peripheral nerve injuries in 3.4% of cases [2,4-6,12-14]. As demonstrated in the present case, brain CT and EEG can be utilized to detect cerebral abnormalities, and MRI scans of multiple sites can be performed to confirm ischemic spinal cord injuries commonly seen in aortic surgery. Additionally, NCS and EMG can be used to assess the condition from the nerve root to the peripheral nerve, helping to identify the location of the lesion.

In this case, abnormal findings were observed on the sensory NCS of both lower limbs. This suggests a potential lesion in the lumbosacral plexus or peripheral nerve, distal to the dorsal root ganglion [7]. Subsequent EMG revealed abnormalities in all nerves, suggesting lumbosacral plexopathy rather than diffuse mononeuropathies [7]. Clinically, paraplegia results from extensive ischemic injury that occurs distal to the site of proximal aortic surgery. In the present case, the total ACC time during the operation with cardiopulmonary bypass was 266 minutes. Severe hypotension ensued postoperatively due to cardiac tamponade; this necessitated two additional hematoma removal procedures, and accompanying ischemic colitis was confirmed. MRI revealed a diffuse edematous lesion on the bilateral lumbosacral plexus, which may have been caused by ischemic neuropathy.

This report presents a case of bilateral lumbosacral plexopathy with an intact spinal cord following proximal aortic surgery, which had not been previously documented. This case underscores the need to consider the possibility of lumbosacral plexopathy and ischemic spinal cord injury in patients who experience paraplegia after proximal aortic surgery. Furthermore, given the risk of these complications, it is advisable to employ more active intraoperative neurophysiological monitoring during aortic surgery.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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CASE REPORT

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Granular Cell Tumor: An Unusual Cause of Common Peroneal Neuropathy

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Granular cell tumors, also known as Abrikossoff's tumors, are rare soft-tissue tumors, and their occurrence in the peripheral nerves has been very rarely reported. We present the case of a 35-year-old woman with common peroneal neuropathy due to a granular cell tumor, who complained of foot dragging. Common peroneal neuropathy was confirmed by electrophysiology. The tumor mass was observed using ultrasonography and magnetic resonance imaging. The tumor was surgically excised, the tumor cells stained positive for S-100, and eosinophilic granular cytoplasm was observed using microscopy. To the best of our knowledge, this is the first report of a granular cell tumor involving the common peroneal nerve.

Keywords: Granular cell tumor; Common peroneal neuropathies; Peripheral nervous system neoplasms

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Introduction

Granular cell tumors (GCTs) were first described by Abrikossoff in 1926, as "myoblastomas" [1,2], and recent studies have indicated they are derived from Schwann cells [1]. GCTs typically contain large, monotonous polygonal cells with abundant eosinophilic granular cytoplasm on microscopy and are mostly benign; however, a few are malignant [2]. GCTs are rare soft-tissue tumors that typically involve the skin and soft tissues of the head, neck, and trunk [3]. GCTs involving the peripheral nerves are rare [3,4] and, to our knowledge, GCTs arising from the common peroneal nerve have not been reported. Herein, we present the first reported case of a GCT of the common peroneal nerve.

Case Report

1) Patient history and physical examination

A 35-year-old woman presented to our hospital with a 2-year history of progressively worsening right foot dragging. The motor power of the right ankle dorsiflexor and long toe extensor was measured as grades 1 and 2, respectively, on the Medical Research Council scale [5]. The motor power of the right ankle plantar flexion was graded as 5. There was no sensory loss in either lower extremity. On palpation of the right popliteal area, a tingling sensation was provoked in the anterior calf; however, there was no palpable mass.

This study was approved by the Institutional Review Board of Kangwon National University Hospital (2022-06-001) and requirement for informed consent was waived.

2) Electrodiagnostic study

The common peroneal compound motor action potential (CMAP) was not obtainable in the right extensor digitorum brevis (EDB) and showed low amplitude in the right tibialis anterior (TA), with normal latency and conduction velocity (Table 1). In the sensory nerve conduction study, the nerve conduction velocity (NCV) of the right superficial peroneal nerve was slower than normal limit (39.8 m/sec) (Table 1). Skin temperature was measured at > 31°C during the study period.

Needle electromyography of the right lower extremity revealed abnormal spontaneous activities of the EDB and TA muscles at rest (Table 2). In the EDB, the motor units were not recruited with volition. In the TA, the motor unit action potentials were noted to be polyphasic and long-duration, and motor unit recruitment was reduced. No abnormalities were observed in the vastus medialis, gastrocnemius, abductor hallucis, short head of the biceps femoris, or peroneal longus.

Based on these findings, the possibility of deep peroneal neuropathy was initially considered. However, given the observed slowing of the NCV in the superficial peroneal nerve, the diagnosis was more closely suggestive of common peroneal neuropathy. Consequently, we concluded that the electrophysiological diagnosis for the patient was common peroneal neuropathy.

3) Ultrasonography and magnetic resonance imaging

Ultrasonography (US) was performed using a GE LOGIQ P6 Pro (General Electric, Milwaukee, WI, USA) with a 3.42 to 10.85 MHz linear probe. The imaging revealed a hypoechoic oval mass with clear margins, measuring 4.0 × 1.0 cm^2, on the lateral posterior region of the right knee (Fig. 1A, B). No vascu-

Table 1. Nerve Conduction Study Findings

Nerve	Stimulating site	Recording site	Latency (ms)	Amplitude (mV)	Velocity (m/sec)
Motor nerve conduction studies					
Rt. peroneal (EDB)	Ankle	EDB	No response		
	Fibular head	EDB	No response		
Lt. peroneal (EDB)	Ankle	EDB	4.58	6.5	-
	Fibular head	EDB	11.04	5.9	46.5
Rt. peroneal (TA)	Fibular head	TA	1.93	3.5	-
	Knee	TA	3.80	3.3	58.7
Lt. peroneal (TA)	Fibular head	TA	2.14	16.8	-
	Knee	TA	4.38	15.1	49.1
Rt. tibial	Ankle	AH	3.85	14.9	-
	Knee	AH	11.77	14.2	41.7
Lt. tibial	Ankle	AH	3.91	11.7	-
	Knee	AH	11.15	11.6	44.2
Sensory nerve conduction studies					
Rt. superficial peroneal	Lateral leg	Foot	4.01	16.2	34.9
Lt. superficial peroneal	Lateral leg	Foot	3.44	9.5	40.7
Rt. sural	Calf	Lateral malleolus	4.11	15.3	34.0
Lt. sural	Calf	Lateral malleolus	3.65	14.0	35.7

Rt., right; EDB, extensor digitorum brevis; Lt., left; TA, tibialis anterior; AH, abductor hallucis.

Table 2. Needle Electromyography of the Right Lower Extremity

Muscle	Insertional activity	Spontaneous activity			MUAP			Recruitment
		Fibrillation	Positive sharp wave	Fasciculation	Amplitude	Duration	Polyphasia	Pattern
Vastus medialis	N	None	None	None	N	N	N	N
Tibialis anterior	N	3+	3+	None	N	Long	Many	Reduced
Peroneal longus	N	None	None	None	N	N	N	N
Gastrocnemius medial head	N	None	None	None	N	N	N	N
Extensor digitorum brevis	N	3+	3+	None	No MUAP recruited			
Abductor hallucis	N	None	None	None	N	N	N	N
Biceps femoris short head	N	None	None	None	N	N	N	N

MUAP, motor unit action potential; N, normal.

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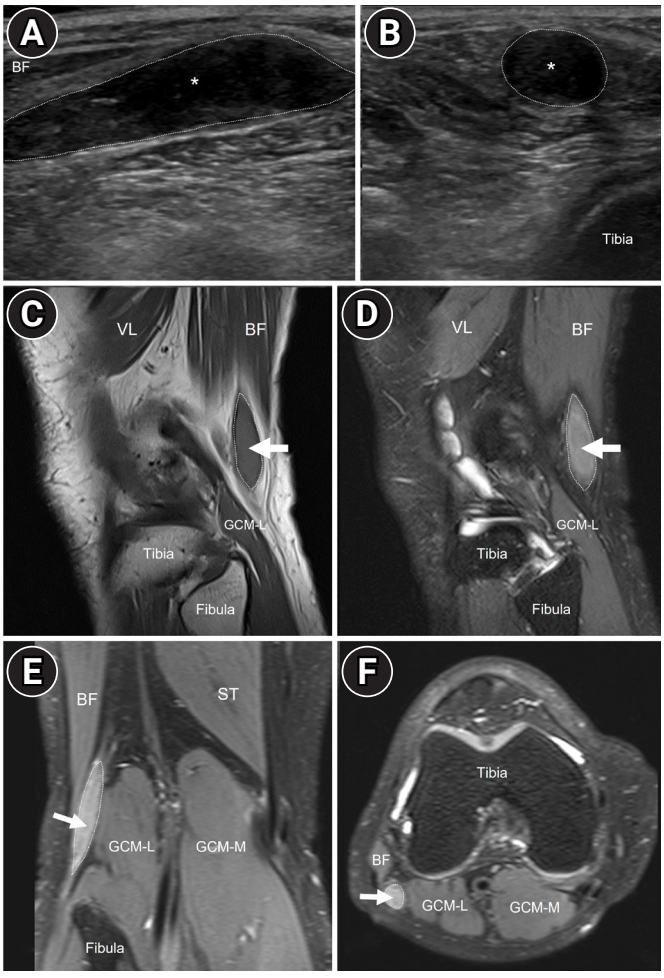

Fig. 1. Ultrasonography (A, B) and magnetic resonance imaging (C-F) of the right knee. In the longitudinal view (A) and transverse view (B), a hypoechoic oval mass (*) was observed. A sagittal T1-weighted image (C), and sagittal (D), coronal (E), and axial T2-weighted (F) images demonstrated a well-circumscribed fusiform mass (white arrows) in the posterior side of the biceps femoris tendon. VL, vastus lateralis; BF, biceps femoris; GCM-L, lateral head of the gastrocnemius; ST, semitendinosus; GCM-M, medial head of the gastrocnemius.

larity of the mass was detected on Doppler US. Magnetic resonance imaging (MRI) revealed a well-circumscribed fusiform mass measuring 4.1 × 0.9 × 0.9 cm^3. The mass exhibited similar signal intensity to the muscles on T1-weighted imaging (Fig. 1C) and showed high signal intensity on fat-suppressed T2-weighted imaging (Fig. 1D-F).

Both the US and MRI examinations indicated that the mass was located on the posterior side of the distal biceps femoris tendon and adjacent to the common peroneal nerve. These findings supported the electrophysiological diagnosis, which had suggested common peroneal neuropathy.

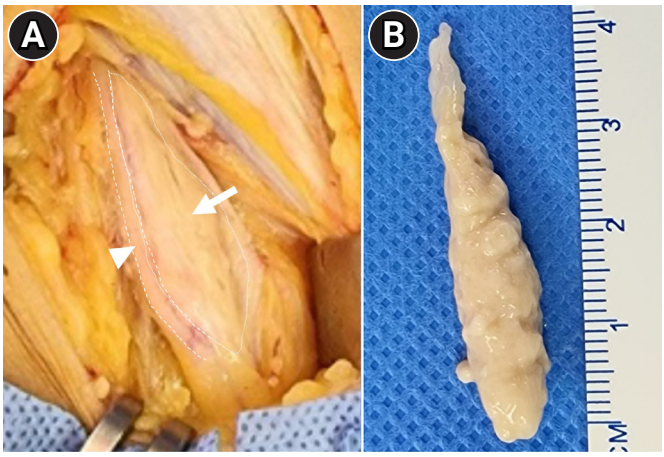

Fig. 2. Intraoperative photograph. The image shows a yellowish, non-hard, fusiform mass (white arrow) adjacent to the common peroneal nerve (white arrowhead) (A), and the mass was totally dissected from the nerve (B).

4) Surgery

In a posterior right knee approach, a longitudinal skin incision was made on posterolateral aspect under spinal anesthesia. A yellowish fusiform mass encircling the common peroneal nerve below the biceps femoris muscle was noted (Fig. 2A). Although the mass could not be easily dissected from the common peroneal nerve, complete removal was achieved without nerve injury. The excised mass measured approximately 4 × 1 × 1 cm^3 (Fig. 2B).

5) Immunohistochemistry

Histopathology revealed polygonal cells with abundant eosinophilic granular cytoplasm and hyperchromatic nuclei, with no evidence of mitosis or necrosis on hematoxylin and eosin staining (Fig. 3A, B). The tumor cells stained positive for S-100 and CD68 proteins (Fig. 3C, D).

6) Follow-ups

Ten months after surgery, a follow-up electrodiagnostic study showed a slight improvement in the peroneal CMAP amplitude (4.5 mV) compared to the initial examination (3.5 mV) recorded in the right TA; however, overall, there was no significant improvement in the strength of the right ankle.

Discussion

GCTs rarely arise in the peripheral nerves and even more rarely in the lower extremities and, to our knowledge, no cases involving the common peroneal nerve have been reported [6]. The gradual onset of symptoms is often associated with a pro-

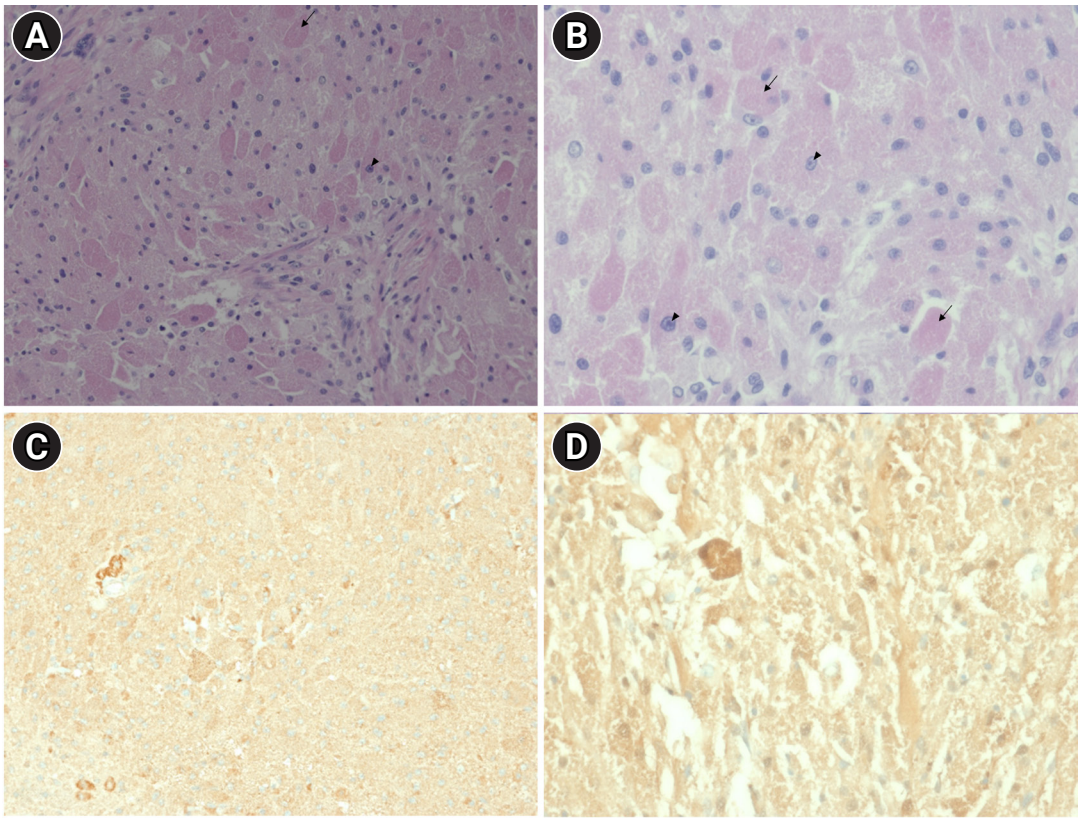

Fig. 3. Histopathological and immunohistochemical examination of the excised tumor. Polygonal cells (black arrows) with a light pink granular eosinophilic cytoplasm and hyperchromatic nuclei (black arrowheads) on hematoxylin and eosin staining (A: × 200; B: × 400 magnification). Immunohistochemical analyses indicate that the tumor cells were strongly positive for CD68 protein (C: × 100 magnification) and S-100 protein (D: × 400 magnification).

gressively growing mass around the common peroneal nerve [7]. An electrophysiological study can diagnose common peroneal neuropathy, but the underlying cause of neuropathy may be attributed to a mass (intraneural ganglion cyst) or tumors (schwannoma or neurofibroma) [7], and some may be malignant [2].

In certain cases, mass lesions in the deep popliteal region are not palpable [8]. However, in our case, although the mass was not palpable, palpating the popliteal fossa induced tingling sensations in the anterior calf. The positive Tinel sign supported the possibility of a lesion involving the common peroneal nerve of the popliteal area. Testing for the Tinel sign is a crucial physical examination technique when a mononeuropathy is suspected. A further imaging evaluation is necessary to differentiate the various potential causes of the lesion [8].

MRI of GCTs reveals quite different patterns between the soft tissue and peripheral nerves. GCTs occurring in the breast show unclear or irregular boundaries with the surrounding soft tissue [9], but GCTs occurring in the peripheral nerves appear as well-circumscribed masses with low or intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images, which is similar to our case [3,4,6].

US is a highly useful imaging modality for peripheral nerves because it is accessible at the bedside and can be used in conjunction with electromyography. No generally shared features of peripheral nerve GCTs have been described in previous reports. In the breast, a common site of GCT occurrence, the tumor presents as an irregular shape with hypoechoic or heteroechoic masses and ill-defined margins on US [9]. Intramuscular GCT was observed as an oval-shaped mass with inhomogeneous echogenicity and internal vascular signals on US [1]. The US features of GCTs in peripheral nerves have rarely been described. Qiyong et al. [3] described a GCT in the facial nerve; the tumor was irregular in shape, with hypoechogenicity, unclear borders, and blood flow signals. In our case, the tumor was oval and appeared as a hypoechoic mass with clear margins on US, which was compatible with the MRI features of a well-circumscribed fusiform mass.

Histological and immunohistochemical analyses are useful di-

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agnostic tools for GCTs [4], which have distinct features such as polygonal cells with an intensely eosinophilic granular cytoplasm on microscopy [1,2,9]. Immunohistochemistry typically reveals positive staining for S-100 protein, nestin, inhibin, CD68, CD63, and neuron-specific enolase [1,2], suggesting that GCTs are derived from Schwann cells.

Most GCTs are benign, as in our case, but approximately 0.5% to 2.0% are malignant [2]. Benign GCTs have a good prognosis after surgical excision; however, malignant GCTs have a poor prognosis, with a mortality rate of 40% [2]. Malignant GCTs are characterized by large cells (> 5 cm), rapid growth, high recurrence, metastasis [2], and histologically increased cellularity with marked pleomorphism and increased mitotic activity [2,6]. Therefore, the possibility of malignancy should be considered.

In a few reports, there was symptom improvement after 9 to 14 months since surgical resection of a GCT in the peripheral nerve [3,4,10]. In our case, the ankle dorsiflexion power did not show an obvious change in 10 months after complete excision of the GCT without nerve injury, even though there was an increase in the peroneal CMAP amplitude in the motor nerve conduction study. The recurrence rate of GCT could be 2% to 8% in cases with clear resection margins, and up to 50% in cases where margins are unclear [4]. Long-term follow-up would be necessary to confirm the absence of recurrence and observe symptom improvement.

We present a patient who complained of progressive right foot dragging. Common peroneal neuropathy associated with an unpalpable mass lesion was assessed using electrophysiology, US, and MRI. The diagnosis of GCT was confirmed histologically after surgical excision. To the best of our knowledge, this is the first report of a GCT involving the common peroneal nerve. We believe that this case report will be helpful in the diagnosis of GCT of the common peroneal nerve.

Conflict of Interest

Sora Baek is an editorial board member of the journal, but he was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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CASE REPORT

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Paraneoplastic Neurologic Syndrome in Small Cell Lung Carcinoma

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A 54-year-old male smoker, previously in good health, was admitted to the hospital due to a tingling sensation in his upper and lower extremities. He reported difficulty walking due to a loss of balance and numbness, leading to an initial diagnosis of chronic inflammatory demyelinating polyneuropathy. Brain and spine magnetic resonance imaging, along with needle electromyography, yielded inconclusive findings. However, a nerve conduction study indicated a length-dependent pattern of sensory-dominant polyneuropathy. A cerebrospinal fluid study did not reveal any specific findings in terms of cell numbers, proteins, or immune tests. Following hospitalization, the patient reported progressive dizziness upon standing, leading to a preliminary diagnosis of orthostatic hypotension. However, a positive anti-Hu autoantibody test, along with chest computed tomography and positron emission tomography scans, revealed a mass in the left interlobar lymph node, suggestive of lung cancer. An endoscopic biopsy confirmed the presence of small cell lung cancer (SCLC). The patient underwent chemo-radiation treatment for the SCLC and immunoglobulin therapy for sensory ganglionopathy. As a result, a definitive diagnosis of paraneoplastic neurologic syndrome was made. Although such cases are rare, our observations suggest that symptoms of dysautonomia and sensory ganglionopathy may be associated with the production of anti-Hu antibodies.

Keywords: Small cell lung carcinoma; Paraneoplastic syndromes; Sensory ganglionopathy; Hypotension, orthostatic

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Introduction

Cancer can cause various types of lesions in both the central and peripheral nerves. These lesions may present as direct cancer invasion, immune response suppression, neuropathy, or paraneoplastic syndrome related to cancer treatment, which occurs in less than 1% of cancer patients [1]. We successfully diagnosed a male patient with small cell lung cancer (SCLC) who presented with neuropathic symptoms such as paresthesia, ataxia, and dizziness [2]. This patient was diagnosed with SCLC and paraneoplastic syndrome, specifically sensory ganglionopathy and orthostatic hypotension (OH), associated with anti-Hu antibody syndrome. This syndrome is occasionally found in patients with SCLC.

We encountered an unusual case of paraneoplastic syndrome, characterized by sensory symptoms and accompanied by dysautonomia [3,4].

Case Report

A 54-year-old man with no notable medical history was admitted to Department of Neurology, Inha University Hospital on June 15, 2021, due to a tingling sensation in his upper and lower extremities. He reported that he had been experiencing difficulty walking due to an imbalance and numbness that began a month beforehand. Furthermore, he confirmed that he had not experi-

enced any infection-related events, such as diarrhea or fever, in the past 3 months.

The initial neurologic examination revealed normal motor power and function, cranial nerve function, and mental status. Deep tendon reflexes, including those in the knees, ankles, biceps, and triceps, were also normal. However, the patient exhibited a diminished sense of position and vibration in the limbs. Furthermore, there was a progressive decrease in sensation to pinprick and light touch moving towards the distal parts of the limbs. No pathological reflex was detected, but the Romberg test yielded a positive result. The patient's history included working as a crane operator and heavy drinking (1–2 bottles of soju/day, 3–4 times a week, for over 10 years until a decade ago). He also had a 25-year history of smoking about a pack a day.

During hospitalization, the patient consistently reported experiencing dizziness upon standing. Consequently, we conducted a tilt test to aid in the differential diagnosis of OH. The diagnosis of OH was confirmed based on his blood pressure readings, which were 129/91 mm Hg when lying down and 102/76 mm Hg when standing, accompanied by persistent dizziness. Despite implementing a treatment regimen that included compression stockings, increased salt intake, oral hydration, and an alpha-1 agonist, there was no improvement in the patient's OH symptoms. In fact, his blood pressure further declined to 80/40 mm Hg upon standing.

In his initial admission evaluation, the patient reported experiencing dizziness and a struggle to maintain balance while standing. This resulted in a score of 24 on the Berg Balance Scale, due to his inability to complete the standing balance assessment item. This suggested a potential balance impairment or an underlying neurological condition, prompting further evaluation and management.

The differential diagnosis considered cervical myelopathy, polyneuropathy, and Guillain-Barré syndrome (GBS); to distinguish between these possibilities, magnetic resonance imaging (MRI) studies for the brain and spine were performed. Brain MRI did not reveal any specific findings; however, contrast-enhanced spine MRI showed possible inflammatory lesions (Fig. 1).

An initial nerve conduction study (NCS) revealed dominant sensory neuropathies in the upper and lower extremities (Tables 1-4), but no motor unit changes were observed on needle electromyography (Table 5). A cerebrospinal fluid (CSF) analysis revealed an albuminocytologic dissociation, characterized by an elevated protein level in the CSF without a corresponding increase in white blood cells. This phenomenon is frequently observed in certain neurological conditions, including GBS, chronic inflammatory demyelinating polyneuropathy, and some types of neuropathy. It generally indicates a chronic or subacute neuropathy rather than an acute inflammatory process. The CSF test revealed a white blood cell count of 3/mm^3 (normal range, 0 to 8)

Table 1. Motor Nerve Conduction Study Results

Variable	Latency (ms)	Amplitude (mV)	Conduction velocity (m/sec)
Left median: APB			
Wrist	3.1	10.7	
Elbow	7.3	10.1	50.0
Left ulnar: ADM			
Wrist	2.3	11.8	
Elbow	6.8	10.7	48.8
Left peroneal: EDB			
Ankle	4.7	4.2	
Popliteal fossa	11.9	3.7	36.8
Left tibial: AH			
Ankle	3.5	12.0	
Popliteal fossa	11.8	11.6	42.1

APB, abductor pollicis brevis; ADM, abductor digiti minimi; EDB, extensor digitorum brevis; AH, abductor hallucis.

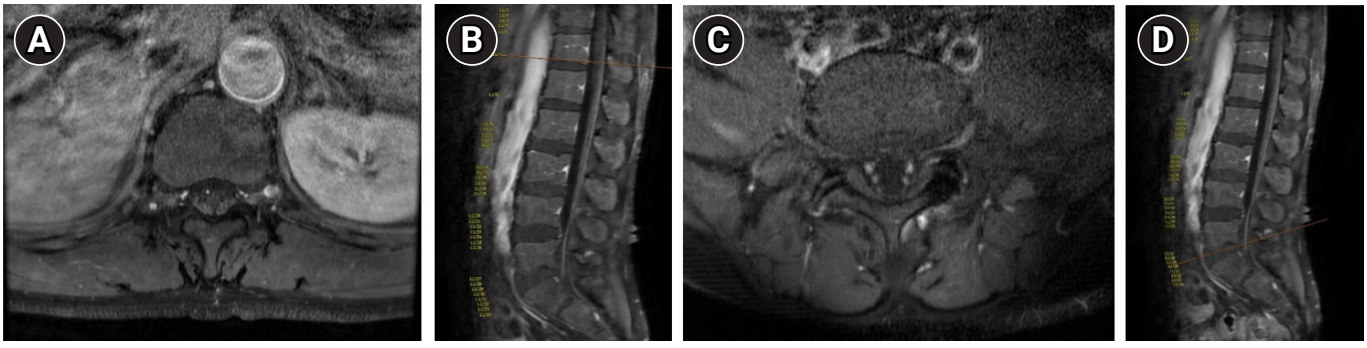

Fig. 1. Contrast-enhanced spine magnetic resonance imaging (MRI), showing thickening and prominent enhancement of the anterior/posterior nerve roots from the filum terminale. (A) An axial image at the level marked by the orange line in (B). (C) An axial image at the level marked by the orange line in (D). (B, D) Sagittal images of contrast-enhanced spine MRI.

Table 2. Sensory Nerve Conduction Study Results

Variable	Peak latency (ms)	Amplitude (μV)	Conduction velocity (m/sec)
Left median: Wrist-elbow	4.4	5.8	43.1
Left ulnar: Wrist-elbow	4.6	10.5	43.4
Left sural: Lower leg	No response	No response	No response
Right sural: Lower leg	No response	No response	No response
Left superficial peroneal: Lower leg	No response	No response	No response
Right superficial peroneal: Lower leg	No response	No response	No response

Table 3. F-Wave Study Results

Nerve	M-Latency (ms)	F-Latency (ms)
Left median	10.0	28.7
Left ulnar	9.7	29.0
Left tibial	11.8	49.4
Right tibial	11.9	51.6
Left peroneal	11.9	55.9
Right peroneal	11.4	53.0

Table 4. H-Wave Study Results

Nerve	Latency (ms)	Amplitude (max) (mV)
Right tibial		
M-wave	5.0	10.0
H-wave	34.3	2.0
Left tibial		
M-wave	4.3	10.0
H-wave	36.0	0.5

Table 5. Needle Electromyographic Findings of the Right Upper Extremity and Right Lower Extremity in This Case

Muscle	Spontaneous					MUAP			Recruitment
	IA	Fib	PSW	Fasc	CRD	Amp	Dur	Poly	Pattern
Right biceps brachii	None	None	None	None	None	N	N	N	Full
Right first dorsal interosseous	None	None	None	None	None	N	N	N	Full
Right vastus lateralis	None	None	None	None	None	N	N	N	Full
Right tibialis anterior	None	None	None	None	None	N	N	N	Full
Right peroneus longus	None	None	None	None	None	N	N	N	Full
Right gastrocnemius (medial head)	None	None	None	None	None	N	N	N	Full
Right C5,8 paraspinal muscles	None	None	None	None	None				
Right L3,4,5 paraspinal muscles	None	None	None	None	None				
Right S1 paraspinal muscles	None	None	None	None	None				

MUAP, motor unit action potential; IA, insertional activity; Fibs, fibrillation potential; PSW, positive sharp wave; Fasc, fasciculation; CRD, complex repetitive discharge; Amp, amplitude; Dur, duration; Poly, polyphasic MUAP; N, normal.

and a protein level of 233.8 mg/dL (normal range, 12 to 60).

Based on the results of the examinations and NCS, the patient was initially treated for GBS with intravenous immunoglobulin (IVIG) and steroids during his first hospitalization in the neurology department. Subsequently, he was transferred to the rehabilitation department. An evaluation of autonomic nerve function was conducted for dizziness both before and after the treatment. The results indicated abnormal sympathetic skin responses, with no response in either the upper or lower extremities. Additionally, a heart rate response to deep breathing test suggested autonomic dysfunction related to vagal parasympathetic control.

A follow-up NCS was conducted 6 months after the initial NCS to evaluate any changes or improvements after the initial examination (Tables 6-9). The motor nerve test results showed a decrease in both latency and amplitude, indicating a deteriorating condition. The sensory nerve test revealed a more significant

Table 6. Follow-up Motor Nerve Conduction Study Results 6 Months after the Initial Nerve Conduction Study

Variable	Latency (ms)	Amplitude (mV)	Conduction velocity (m/sec)
Left median: APB			
Wrist	3.3	9.8	
Elbow	7.6	9.2	46.8
Left ulnar: ADM			
Wrist	2.6	10.1	
Elbow	6.8	9.3	45.6
Left peroneal: EDB			
Ankle	4.8	2.6	
Popliteal fossa	13.1	2.6	40.8
Left tibial: AH			
Ankle	3.7	9.7	
Popliteal fossa	12.1	7.3	41.1

APB, abductor pollicis brevis; ADM, abductor digiti minimi; EDB, extensor digitorum brevis; AH, abductor hallucis.

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Table 7. Follow-up Sensory Nerve Conduction Study Results 6 Months after the Initial Nerve Conduction Study

Variable	Peak latency (ms)	Amplitude (μV)	Conduction velocity (m/sec)
Left median: Wrist-elbow	No response	No response	No response
Left ulnar: Wrist-elbow	No response	No response	No response
Left sural: Lower leg	No response	No response	No response
Right sural: Lower leg	No response	No response	No response
Left superficial peroneal: Lower leg	No response	No response	No response
Right superficial peroneal: Lower leg	No response	No response	No response

Table 8. Follow-up F-Wave Study Results 6 Months after the Initial F-Wave Study

Nerve	M-Latency (ms)	F-Latency (ms)
Left median	10.5	29.6
Left ulnar	9.7	28.5
Left tibial	11.7	50.7
Right tibial	11.5	51.3
Left peroneal	13.3	58.6
Right peroneal	11.4	53.0

Table 9. Follow-up H-Wave Study Results 6 Months after the Initial H-Wave Study

Nerve	Latency (ms)	Amplitude (max) (mV)
Right tibial		
M-wave	5.6	10.2
H-wave	40.6	1.7
Left tibial		
M-wave	4.6	10.1
H-wave	38.6	0.7

decline, with no response detected in any of the nerves tested.

To investigate the possibility of paraneoplastic syndrome due to a lengthy history of smoking, we examined neuronal autoantibodies. The test results did not reveal any autoantibodies, including Ri, Yo, amphiphysin, CV2/collapsing response mediator protein 5 (CRMP-5), paraneoplastic antigen Ma 2 (PNMA2), recoverin, sex-determining region Y protein-related high mobility group box 1(SOX1), and titin. However, we did identify the presence of the anti-Hu antibody. As a result, we performed a chest computed tomography (CT) and positron emission tomography (PET) scan to assess the possible presence of lung cancer associated with paraneoplastic neurologic syndrome. Chest CT revealed a mass in the left interlobar lymph node, which was further highlighted in the PET study (Fig. 2). A transbronchial needle aspiration biopsy of the mass confirmed the diagnosis of SCLC (stage T4N1M0).

Based on these findings, concurrent chemo-radiation therapy was initiated for small cell carcinoma. This involved chemotherapy (etoposide/cisplatin), radiation therapy (left upper lobe, 6,000 cGy/30 sessions), and prophylactic cranial irradiation of the whole brain (2,500 cGy/10 sessions). However, despite the chemo-radiation therapy for SCLC and immunoglobulin therapy for sensory and autonomic neuropathy, there was no improvement in numbness, gait disturbance, dizziness, or syncope.

We arrived at a definitive diagnosis of paraneoplastic neurologic syndrome. Here we report a rare case in which dysautonomia (OH) manifested with sensory neuronopathy caused by anti-Hu antibody production by SCLC.

Discussion

Gait disturbance has various causes. Most commonly, it is caused by pathologies in areas of the central nervous system that control motor function, such as stroke, Parkinson's disease, and myelopathy. Other potential causes include peripheral neuromuscular disorders like spinal stenosis, radiculopathy, entrapment neuropathies, myopathies, or foot drop resulting from peroneal nerve damage. Most peripheral nerve injuries are localized lesions that result in simple sensory changes or focal motor weakness. However, in this case, neurophysiologic studies revealed sensory-dominant, length-dependent polyneuropathy, which usually results from a metabolic or toxic cause of neuropathy, such as alcoholic, diabetic, or chemotherapy-induced neuropathy, although rarely, sensory axonal-type sensory neuropathy occurs in GBS and sensory neuronopathy is observed in paraneoplastic syndrome. Additionally, this polyneuropathy was accompanied by OH, which progressively led to autonomic dysfunction.

In the differential diagnosis of axonal-type sensory neuropathy of this patient, sensory ganglionopathy and sensory neuropathy were considered. While both conditions impact the sensory nerves, they are distinct in that each affects a specific location associated with different underlying diseases.

Sensory ganglionopathies specifically target the dorsal root ganglia or trigeminal ganglion sensory neurons. This results in a

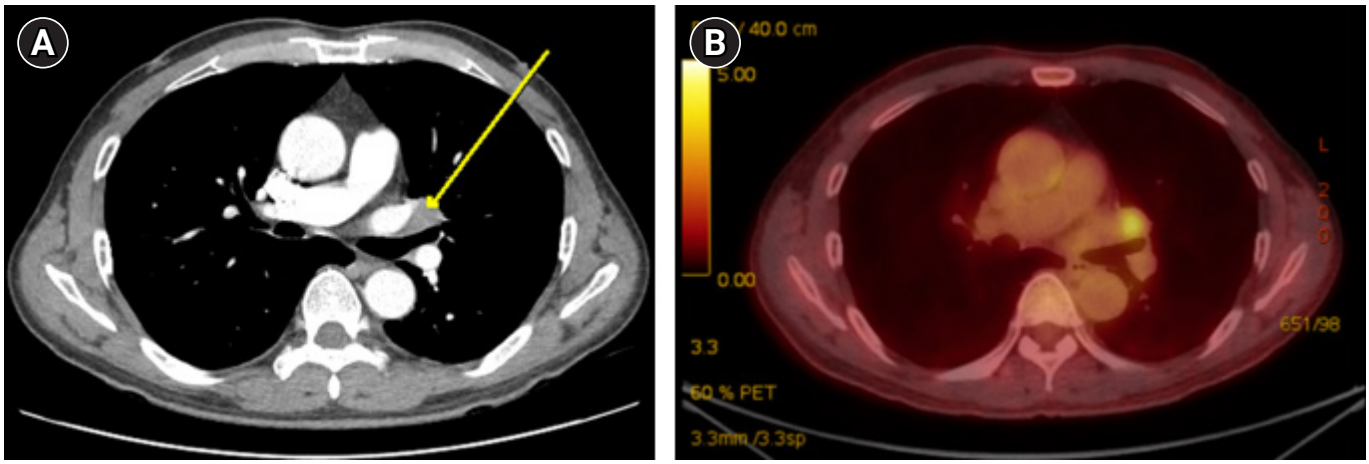

Fig. 2. (A) Computed tomography and (B) positron emission tomography images showing an enlarged left interlobar lymph node (arrow).

loss of balance (gait ataxia), generalized areflexia, and asymmetric sensory symptoms. When caused by cancer, as in the case of our patient, sensory ganglionopathy tends to progress more rapidly than typical sensory neuropathy. In contrast, sensory neuropathy is characterized by damage to the peripheral nerves responsible for transmitting sensory information to the brain and spinal cord. This can lead to a range of symptoms, including numbness, tingling, and pain. Diagnostic tests for sensory neuropathy may include NCS, skin biopsies, and blood tests to check for underlying conditions such as diabetes, toxic or autoimmune disorders [5]. While the clinical symptoms of these two diseases can appear similar, their underlying pathophysiology is distinct. Sensory ganglionopathy is primarily associated with autoimmune conditions like Sjögren's syndrome and cancer. Sensory neuropathy, on the other hand, can be caused by factors such as metabolic-toxic issues, compressive conditions, or ischemic lesions. As a result, the age, medical history, and other clinical characteristics of patients may also differ. In this specific case, the patient's medical history revealed slight changes in sensation, primarily in light touch and pinprick tests. These changes were thought to be due to skin damage on the legs or hands, in addition to the patient's subjective experience. The neurological examination showed a length-dependent sensory loss. Importantly, the patient exhibited new symptoms, which seemed to be a mix of tingling with pain in one area and balance and gait disturbances in another. These symptoms prevented the patient from continuing their work, suggesting the presence of two concurrent lesions.

The patient reported chronic tingling and pain in both hands and feet for several years. The loss of sensation seems to follow a symmetrical and length-dependent pattern in touch and vibration. During the initial presentation, a physical examination and NCS were conducted. The patient's history of alcohol consumption and the observed symptoms suggested a progressive form of alcohol-induced sensory neuropathy, which is characterized by a chronic progressive pattern.

However, the patient sought medical attention due to a gait disturbance, which was caused by rapidly deteriorating balance abnormalities over a 1-month period. Additionally, the patient experienced an increase in numbness in the upper extremities, particularly in the proximal region, which was more severe than previously reported. Initially, these symptoms were present in the left upper and right lower extremities. However, upon evaluation approximately 2 weeks later, numbness was also observed in the right upper and left lower extremities. These findings suggested an acute progressive pattern of sensory ganglionopathy.

The exacerbation of OH was likely also affected by sensory ganglionopathy. Moreover, a subsequent NCS carried out 6 months after the initial consultation showed an overall delay in latency and a reduction in amplitude in motor nerves. No response was detected in the left median nerve and left ulnar nerve, both of which had previously demonstrated responses in the sensory NCS. These alterations suggest a deterioration in the patient's condition. The swift decline noted in the NCS results over a few months further implies the influence of ganglionopathy.

It is important to note that our patient differed from those in the study of Lauria [6], as they did not present with areflexia. However, similarities were noted in the presence of ataxia, glove and stocking sensory changes, and autonomic impairment. Consequently, these factors posed challenges in the initial diagnosis of paraneoplastic syndrome. The pattern of elevated thresholds observed in quantitative sensory testing, as demonstrated in the

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study by Lauria [6], is likely mirrored in the sympathetic skin response of our patient.

Autoimmune autonomic ganglionopathy (AAG) is a rare autoimmune disorder that affects the autonomic ganglia, resulting in autonomic dysfunction. In AAG, autoantibodies specifically target the ganglionic acetylcholine receptors responsible for nerve impulse transmission. This leads to impaired autonomic function, which can manifest as symptoms such as OH, anhidrosis, gastrointestinal dysmotility, and urinary retention.

Diagnosing AAG can be challenging, since its symptoms often mimic those of other conditions. Nevertheless, the identification of autoantibodies against ganglionic acetylcholine receptors is a critical step in confirming an AAG diagnosis. The standard treatment for AAG usually includes immunomodulatory therapies such as steroids, plasma exchange, or IVIG.

Laboratory tests, including ganglionic acetylcholine receptor antibody (gAChR Ab) testing or alpha-3 ganglionic acetylcholine receptor antibody (α3gAChR Ab) testing, can help confirm the diagnosis of AAG and distinguish it from other types of autonomic neuropathy. Unfortunately, these specific tests were not conducted in this case, which is a limitation of the present case report.

We ruled out various potential causes of the subacute sensory neuronopathy, such as vitamin deficiency, toxic and metabolic disorders, chronic inflammatory demyelinating polyneuropathy, Sjögren's syndrome, infections like human immunodeficiency virus (HIV) and leprosy, and anti-myelin associated glycoprotein associated peripheral neuropathy. After excluding these possibilities, we considered the possibility of an unknown sensory neuropathy. Other tests related to rheumatism or vascular inflammation did not provide significant findings, except for the presence of anti-Hu antibodies. To further investigate, we conducted chest CT and PET scans since sensory neuropathies are commonly associated with lung cancer in patients with a long history of smoking [7].

During the patient's hospitalization, his peripheral neuropathy and OH gradually worsened. We conducted a search for similar cases using "anti-Hu syndrome" as a keyword, but only a few cases or clearly related pathological findings were found. OH is rarely found as a comorbidity associated with subacute sensory neuronopathy, and to date, only two cases of OH with albuminocytologic dissociation have been reported in patients with paraneoplastic syndrome [8].

Cancer can cause lesions in both central and peripheral nerves via direct invasion, immune responses, neuropathy, or paraneoplastic syndrome associated with cancer treatment. Paraneoplastic syndrome is observed in roughly 1% of cancer patients, and neuropathy resulting from this syndrome is diagnosed according to the criteria set forth by the PNS-Euro network consortium in 2004 and 2021 [9,10].

Paraneoplastic syndrome can involve the nervous system and can be categorized into various types depending on the areas affected. These categories include central nervous system neuropathies (such as encephalomyelitis, limbic encephalitis, subacute cerebellar degeneration, opsoclonus-myoclonus, stiff person syndrome, and motor neuron disease), peripheral nervous system syndromes (including subacute sensory neuronopathy, acute sensory motor neuropathy like GBS or brachial neuritis, paraprotein-associated neuropathy, autonomic neuropathy, and vasculitis neuropathy), and neuromuscular junction pathologies (such as myasthenic syndrome, acquired neuromyotonia, dermatomyositis, and acute necrotizing myopathy).

In this case, the presence of anti-Hu antibodies confirmed the diagnosis of SCLC through a PET study and biopsy. With the positive anti-Hu antibody and the confirmed diagnosis of SCLC, a definitive diagnosis of paraneoplastic neurologic syndrome was made according to the recognized criteria for this condition [9,10].

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Instructions for Authors

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Journal of Electrodiagnosis and Neuromuscular Diseases (*J Electrodiagn Neuromuscul Dis*, JEND), an official journal of the Korean Association of EMG Electrodiagnostic Medicine, is published Three times a year. It regards all aspects of EMG, electrodiagnostic medicine, and neuromuscular diseases, including clinical practice, experimental and applied research, and education, and its formal abbreviated journal name is J Electrodiagn Neuromuscul Dis.

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Editorial Board will make the final decision on approval for the publication of submitted manuscripts and the publication order of accepted manuscripts. Editorial Board reviews ethics, rationality, originality, and scientific significance in accepting submitted manuscripts, and can request any further corrections, revisions, and deletions of the article if necessary.

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Authors should be limited to members of Korean Association of EMG Electrodiagnostic Medicine, associate members of Korean Association of EMG Electrodiagnostic Medicine or those who are associated with clinical practice, experimental and applied research, and education in the field of EMG, electrodiagnostic medicine, and neuromuscular diseases.

Authorship is credited to those who have direct involvement in the study and have made significant contributions to (a) conceptualization and design of the research, or acquisition, analysis, and interpretation of the data, (b) drafting of the manuscript or critical revision, and (c) approval of the submitted and final versions of the manuscript. The primary investigator is designated the first author of the study unless contested by the other authors. The corresponding author is directly responsible for communication and revision of the submitted manuscript.

In the case that more than one author contributed equally as the first author or the corresponding author, the acceptance of co-first or co-corresponding author should be determined through discussion of the Editorial Board. Everyone who is listed as coauthors should have made a substantial, direct, intellectual contribution to the work.

In the case of a change of authorship, a written explanation must be submitted. Change in either the first author or the corresponding author requires approval by the Editorial Board, and any changes of other authors require approval by the Editor-in-Chief.

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Manuscripts include Original Articles, Case Reports, Brief communications, and Reviews, commissioned by the Editorial Committee on EMG, electrodiagnostic medicine, and neuromuscular diseases.

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Submitted manuscripts will be reviewed by three peer reviewers selected from the Board's database of expert reviewers. Following review, the Editorial Board will decide whether the manuscript will be 1) accepted for publication 2) publication with minor revision, or accepted for publication following revision, 3) subject to major revision, or 4) denied publication.

For manuscripts which are either accepted for publication following revision or subject to major revision, the corresponding author must reply to reviewers' comments point by point and revise the manuscript with changes in red color and explain in detail what changes were made in the manuscript in "summary of revision" as soon as possible.

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The reviewer and Editorial Board can request correcting English of the manuscript to a considerable level, and the author should accept it.

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When a manuscript is not resubmitted within two months of notification, it will be considered that the authors have withdrawn the manuscript from submission.

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There are no charges for reviewing, publication and printing, but illustrations that require extraordinary printing processes will be charged to the authors. The corresponding author is also charged a fee for the plate, English proof leading, offprints, and specialty printing.

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2-1. Forms of the manuscript

Use Microsoft Office Word (versions after 2003) and ensure correct spelling and grammar. Set up the MS Word document for 1-inch margins on a letter or A4-sized paper. The manuscript must be written in 12-point font, and the sentences must be double-spaced including tables and figure legends. The length of the manuscript should not exceed 20 pages in original articles, 7 pages in the case report, and 30 pages in review article except for the tables and figures.

2-2. Use of language and unit

Draw up a manuscript in proper and clear English as per the orthography. When there is no appropriate translation of foreign medical terms, proper nouns, drug names, units, etc., use their originals in the manuscript. If foreign-language words are needed, capital and small letters should be clarified: in principle, proper nouns, place names, and names of persons should be written with a capital letter as the first letter and then small letters for the rest. If an original term has its translation whose meaning is unclear, place the original in a small parenthesis after its translation when it appears for the first time and then uses its translation alone.

Numbers should be written in Arabic numerals, and measurements should be reported using the metric system, and hematologic and biochemical markers should be reported in the International System (SI) of Units. (http://physics.nist.gov/cuu/Units/index.html)

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The use of abbreviations should be minimized and restricted to those that are generally recognized. When using an abbreviated word, it should be spelled out in full on the first usage in the manuscript, followed by the abbreviation in parentheses.

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The manuscript for original articles should be organized in the following order: 1) title page as a separate file, 2) Title of the manuscript 3) abstract and keywords, 4) introduction, 5) materials (or subjects) and methods, 6) results, 7) discussion, 8) conflict of interest, 9) acknowledgements (if necessary), 10) references, 11) figure legends 12) tables as separate files, and 13) figures as separate files.

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Authors: Book title. edition. place: publisher; year, the first and last page number.

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Authors: title of the chapter. In: editor. The book title. edition. place: publisher; year, the first and last page number.

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4) Online resource

National Library of Medicine: Fact sheet: AIDS information resources [Internet]. Bethesda: National Library of Medicine; 2003 [cited 2007 Mar 26]. Available from: http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html.

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