doi: 10.2490/prm.20240028 Progress in Rehabilitation Medicine 2024; Vol. 9, 20240028

CASE REPORT

Bilateral Foot Drop Caused by Acute-onset Neuropathy after Diabetic Ketoacidosis: Successful Management and Long-term Follow-up for Employment

Kyohei Shimomura, MD [a] Tomoyo Taketa, MD [b] Yuki Uchiyama, MD, PhD [b] Norihiko Kodama, MD, PhD [b,c] and Kazuhisa Domen, MD, PhD [b]

Background: Peripheral neuropathy is a common complication of diabetes, impacting many patients with type 1 or 2 diabetes. Acute-onset peripheral neuropathy after diabetic ketoacidosis (DKA) is rare yet serious, and reports on long-term functional outcomes and rehabilitation for this condition are limited. We present a case of bilateral foot drop caused by acute-onset peripheral neuropathy following DKA. The case was effectively managed through prompt and continuous intervention. **Case:** A 21-year-old male university student with no notable medical history who was seeking employment presented with impaired consciousness. DKA associated with type 1 diabetes was diagnosed. As blood glucose and acidosis improved, he rapidly regained consciousness. On Day 3 post-onset, bilateral foot drop and lower leg sensory impairment emerged, with nerve conduction studies indicating lower extremity peripheral neuropathy on Day 8. Improvement during hospitalization was modest, so ankle–foot orthoses were prescribed on Day 10. He could walk independently with the orthoses on Day 12 and was discharged home on Day 15. Outpatient follow-up was continued to support the patient's efforts to gain employment. Needle electromyography in the tibialis anterior muscles bilaterally showed denervation at 2 months and polyphasic potentials at 8 months. In the 2 years post-onset, bilateral lower limb muscle strength progressively improved, and the patient successfully secured clerical employment. **Discussion:** Successful rehabilitation for employment was achieved in the rare condition of acute-onset neuropathy after DKA through effective management based on early orthotic prescription, clinical and electrophysiological examinations, and continuous follow-up.

Key Words: neuropathy; orthoses; outcome prediction

INTRODUCTION

Peripheral neuropathy is the most common complication of diabetes, occurring in approximately 45% of patients with type 2 diabetes and 54%–56% of patients with type 1 diabetes.[1)] Diabetic peripheral neuropathy typically develops chronically over the years in patients with longstanding hyperglycemia.[1)]

Acute-onset peripheral neuropathy can also occur in association with newly diagnosed type 1 diabetes, but reports are extremely limited.[2–7)] Among these cases, acute peripheral neuropathy following onset of diabetic ketoacidosis (DKA) in type 1 diabetes has been reported.[3–7)] Although the exact pathogenesis is not yet clear, both metabolic and hemodynamic mechanisms have been suggested.[8,9)] According to previous reports, acute peripheral neuropathy following DKA presents with a range of clinical manifestations, often characterized by bilateral or unilateral distal-dominant motor and sensory impairments.[2–7)] The functional outcomes of these impairments vary, and in some cases, severe residual

Received: May 31, 2024, Accepted: August 27, 2024, Published online: September 11, 2024
[a] Rehabilitation Center, Hyogo Medical University Hospital, Nishinomiya, Japan
[b] Department of Rehabilitation Medicine, School of Medicine, Hyogo Medical University, Nishinomiya, Japan
[c] Department of Physical Therapy, School of Rehabilitation, Hyogo Medical University, Kobe, Japan
Correspondence: Yuki Uchiyama, MD, PhD, 1-1 Mukogawa-cho, Nishinomiya, Hyogo 663-8501, Japan, E-mail: yutti@hyo-med.ac.jp

neurological deficits have been reported.[4,7] However, the literature remains limited on the long-term functional outcomes and rehabilitation management of acute-onset peripheral neuropathy.

This report describes the case of a young man who presented with peripheral neuropathy complicated by bilateral foot drop after the onset of DKA. We initiated gait training with prescribed bilateral ankle–foot orthoses (AFOs) for the bilateral foot drop from the acute phase, and electrophysiological examinations were performed during the subacute period. Based on clinical and electrophysiological outcome predictions during follow-ups, we provided guidance to the patient during employment-seeking activities. As a result of the early and continuous intervention, the patient successfully secured employment within 2 years after onset.

CASE

A 21-year-old man who was fully independent in activities of daily living (ADL) was emergently transferred to our university hospital (Day 1) with the chief complaint of altered consciousness. The patient had been experiencing weight loss for the past few years. He had a body mass index of 17.7 kg/m^2 (weight 60.6 kg, height 185.0 cm). He was a university student actively engaged in employment-seeking activities. He had no significant medical history, and there were no notable findings in the family history. He was a social drinker and a non-smoker. He resided in a two-story detached house with his parents and younger sister. Written informed consent was obtained from the patient for publication of this report.

Upon transfer to our hospital, the patient exhibited impaired consciousness [Glasgow Coma Scale[10] (GCS) E3V4M5] and had tachypnea (respiratory rate 30 breaths/min). Clinical examination revealed severe metabolic acidosis (pH 6.99, HCO_3^- 1.9 mmol/L), fasting blood glucose of 720 mg/dL, hemoglobin A1c of 15.2%, and glutamic acid decarboxylase (GAD) antibody level of 197 U/mL. DKA associated with type 1 diabetes was diagnosed, and the patient was admitted to the intensive care unit (ICU) with the emergency doctor as the attending physician. Interventions including fluid resuscitation, correction of electrolytes, and glycemic control resulted in improved consciousness within 4 h. On Day 2, the patient's blood glucose level was 141 mg/dL, and he was discharged from the ICU to the general ward. A doctor in the Department of Diabetology, Endocrinology, and Metabolism became the attending physician in the general ward.

Figure 1 shows the post-admission clinical course. On Day 3, the patient presented with lower limb weakness, and the attending doctor requested a consultation with our department. During our initial clinical examination on Day 5, the muscle strength and sensation in the upper limbs were normal bilaterally. However, voluntary contraction of the tibialis anterior (TA) muscles and extensor hallucis longus muscles were absent bilaterally. The muscle strength of the gastrocnemius muscles was grade 2 on the Manual Muscle Test[11] (MMT) bilaterally, and tendon reflexes in the lower extremities were absent bilaterally. In addition, moderate superficial sensory disorder and mild deep sensory disorder were observed bilaterally in the lower legs to the soles and tops of the feet. With the aim of discharge to home, physical therapy was started on Day 5. A nerve conduction study (NCS) was performed on Day 8 to investigate the cause of the bilateral foot drop. Compound muscle action potentials (CMAPs) over the extensor digitorum brevis (EDB) muscles could not be evoked from the right peroneal nerve, and decreased motor conduction velocity and amplitude were detected in the left peroneal nerves and in the tibial nerves and sural nerves bilaterally (**Table 1**). These findings suggested peripheral neuropathy in the lower extremities. As physical therapy, we initiated lower limb strength training and gait training with a walker. Throughout the hospitalization, voluntary contractions of TA muscles were not observed bilaterally, and there was poor clearance of the ankle joints during the initial swing phase. While walking, the patient compensated for this poor clearance by hip and knee flexion bilaterally. On Day 10, bilateral rigid plastic AFOs (pAFOs; 3 mm thick) with toe-springs were prescribed, and gait training was recommenced. When walking with the bilateral pAFOs, ankle dorsiflexion during the initial swing phase was improved, and the compensatory bilateral hip and knee flexion was also alleviated. On Day 12, he achieved independent walking and climbing stairs with orthotic support, and we instructed him to wear pAFOs for walking both indoors and outdoors. On Day 15, he was discharged home. At discharge, the gastrocnemius muscles showed improved strength up to grade 3 (MMT) bilaterally, but voluntary contraction of the TA muscles remained absent bilaterally. Although there had been improvement in sensory disorder when compared with admission, mild superficial sensory deficits persisted in the soles and tops of the feet, along with a moderate degree of deep sensory disorder predominantly on the left side. The Functional Independence Measure[12] (FIM) score (an indicator of ADL performance) was 106, with scores of 71 for motor components and 35 for cognitive components.

When the patient indicated his desire decided to recommence his employment-seeking activities, we scheduled

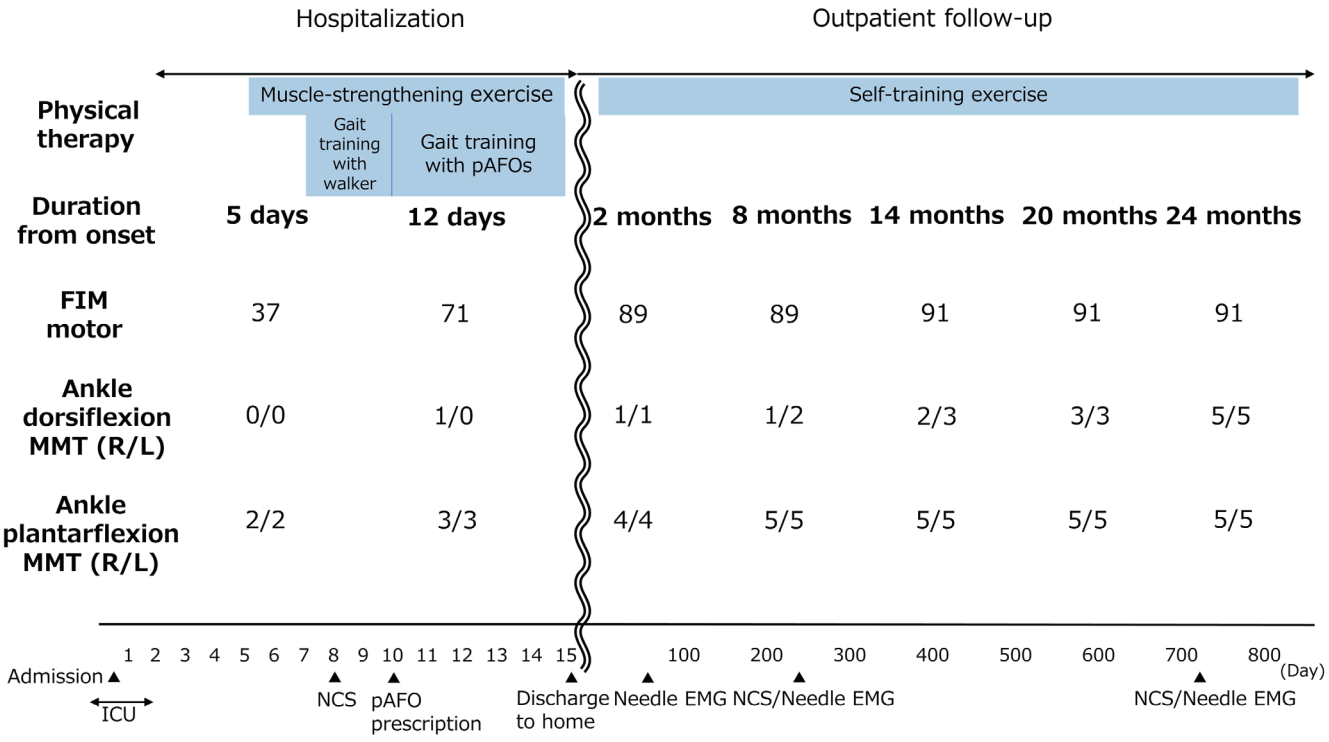

Fig. 1. Clinical course during hospitalization and outpatient follow-up. The patient was admitted to the ICU on Day 1 because of impaired consciousness resulting from diabetic ketoacidosis and was discharged to the general ward on Day 2. Bilateral foot drop was noted on Day 3, and voluntary contraction of the tibialis anterior muscles was not observed bilaterally during hospitalization. NCS was conducted on Day 8. Posterior ankle–foot orthoses were prescribed on Day 10. Following discharge from the hospital on Day 15, follow-up was conducted in the outpatient setting, and gradual improvement was observed clinically over time. The muscle strength of ankle dorsiflexion improved to grade 5 (MMT) bilaterally 2 years after onset.

follow-up appointments at our outpatient clinic. At 2 months from onset, the strength of the TA muscles became grade 1 (MMT) bilaterally and the gastrocnemius muscles improved to grade 4 (MMT) bilaterally. To diagnose the presence of axonal damage, we performed needle electromyography (EMG) 2 months after onset, which revealed denervation potentials as positive sharp waves, fibrillation potentials, and no motor unit potential (MUP) in the TA muscles bilaterally. In the gastrocnemius muscles bilaterally, there were no signs of denervation potentials, but polyphasic potential reduction in interference patterns was observed on needle EMG (**Table 2**). At 8 months of follow-up, the strength of the TA muscles improved to grade 2 (MMT) on the right and grade 1 (MMT) on the left. The strength of the gastrocnemius muscles reached grade 5 (MMT) bilaterally. An NCS still showed that CMAPs over the EDB could not be evoked from the peroneal nerves bilaterally. However, needle EMG showed the emergence of unstable polyphasic MUPs, disappearance of denervation potential, and an increase in interference patterns in the TA muscles bilaterally. In the gastrocnemius muscles, the appearance of polyphasic MUPs and an increase in interference patterns were observed bilaterally (**Table 2**). These findings suggested the possibility of further functional improvement. At 10 months, the patient was permitted to omit use of the pAFOs in daily life while indoors. At 14 months of follow-up, we conducted gait assessment. His walking speed was 1.16 m/s (6-min walk test) with orthoses and 1.17 m/s without orthoses; the 6-min walking distance was 586 m. Use of the pAFOs was discontinued because the patient was able to walk long distances and climb stairs safely without them, and the FIM motor score reached full points (91). At 20 months from onset, the 6-min walking distance was 636 m. At 2 years from onset, needle EMG showed maturity of nerve reinnervation in the TA muscles bilaterally.

Based on clinical and electrophysiological follow-ups, we instructed the patient in self-training exercises, including

Table 1. Results of nerve conduction studies at 8 days, 8 months, and 24 months after onset

Nerve/site	Latency (ms)			Amplitude (mV)			Velocity (m/s)		
	8 days	8 months	24 months	8 days	8 months	24 months	8 days	8 months	24 months
Right tibial									
Ankle	4.9	3.4	3.0	1.3	4.4	5.3	36.7	36.8	40.0
Popliteal fossa	16.2	15.3	14.3	1.1	3.2	4.2			
Left tibial									
Ankle	5.7	3.3	3.2	1.2	1.8	2.2	35.3	33.8	39.5
Popliteal fossa	18.1	16.9	14.3	1.1	1.6	1.8			
Right peroneal									
Ankle	n.e.	n.e.	n.e.	n.e.	n.e.	n.e.	n.e.	n.e.	n.e.
Fibular head	n.e.	n.e.	n.e.	n.e.	n.e.	n.e.			
Left peroneal									
Ankle	6.9	n.e.	4.9	0.105	n.e.	0.194	33.9	n.e.	17.0
Fibular head	18.2	n.e.	25.2	0.084	n.e.	0.068			
Right sural									
Mid calf	3.9	2.9	3.3	0.0055	0.0098	0.0085	36.8	41.1	47.5
Left sural									
Mid calf	2.6	3.4	3.0	0.0078	0.0031	0.0059	40.7	38.5	49.3

n.e., not evoked.

Table 2. Needle electromyography findings

Time after onset	Muscle		Spontaneous		Voluntary contraction			
			Fibrillation	Positive sharp wave	Amplitude (mv)	Duration (ms)	Motor unit potential	Interference pattern
2 months	TA	Right	+	+	−	−	−	−
		Left	+	+	−	−	−	−
	GC	Right	−	−	0.4–1.0	10–13	−	Remarkable decrease
		Left	−	−	0.9–1.1	8–14	−	Pathological interference
8 months	TA	Right	−	−	0.05–0.1	2.5–5	Polyphasic	Pathological interference
		Left	−	−	0.4–1.0	8–15	Polyphasic	Remarkable decrease
	GC	Right	−	−	0.4–1.8	5–12	Polyphasic	Minor decrease
		Left	−	−	0.4–0.9	8–15	Polyphasic	Remarkable decrease
24 months	TA	Right	−	−	0.8–1.4	14–20	Normal	Remarkable decrease
		Left	−	−	1.8–2.0	14–20	Normal	Minor decrease
	GC	Right	−	−	0.4–1.1	7–14	Normal	Remarkable decrease
		Left	−	−	0.8–1.4	5–10	Normal	Remarkable decrease

TA, tibialis anterior muscle; GC, gastrocnemius muscle.

ankle joint range-of-motion exercises when the TA muscle strength was grade 0 to 1 (MMT). We started muscle-strengthening exercises on a horizontal plane at grade 2 (MMT), and we guided him to perform heel walks, calf raises, and TheraBand exercises while holding onto a support when TA muscle strength reached grade 3 to 5 (MMT). Moreover, we provided the patient with guidance regarding employment-seeking activities, commuting methods, and job-related considerations. At 2 months after discharge, he had achieved independence in walking with orthoses, and his diabetes was well controlled. At this point, we agreed with the patient's internist that he could resume seeking employment. In considering the risks of falls, we instructed the patient to avoid long-distance walking on uneven or sloped terrain where the footing might be poor while commuting or working. He successfully secured a clerical position 20 months after discharge.

DISCUSSION

This report describes a rare case of bilateral foot drop caused by peripheral neuropathy associated with DKA. In this case, the patient's wish for early resumption of employment-seeking activities and success in securing employment necessitated early implementation of functional improvements and long-term follow-up. Based on the clinical course and results of electrophysiological examinations, we predicted limited potential for short-term functional improvement. Consequently, we prescribed AFOs for bilateral foot drop early in the clinical course and provided support for employment through repeated clinical and electrophysiological follow-ups. The patient was subsequently successful in securing employment.

There are several reports of acute onset of foot drop after diagnosis of type 1 diabetes complicated with DKA in children and young adults.[2–8] However, the pathogenesis of acute peripheral neuropathy involving the peripheral nerves of the lower limb following DKA is unclear. Moreover, there are few reports on functional outcomes in these cases. Nonetheless, for this patient, we recognized the need for ADL improvement and support toward achieving social goals. Therefore, in this case, it was necessary to predict functional outcomes and conduct follow-up through both clinical and electrophysiological approaches.

The functional outcomes of acute-onset foot drop following the diagnosis of type 1 diabetes with DKA vary in previous reports. In some cases, full recovery was achieved within a few months after onset through the correction of hyperglycemia.[3–6] However, cases accompanied by altered consciousness or severe acidosis tended to have a poor functional prognosis.[4,7] This was attributed to the multifactorial nature of the pathogenesis where peripheral neuropathy after DKA leads to foot drop. Acute-onset peripheral neuropathy after DKA could be a consequence of peripheral ischemia or hemodynamic and metabolic changes linked to the ketoacidosis.[13] In addition, previous reports have indicated that the peripheral nerves in the lower extremities of diabetic individuals are swollen because of the effects of metabolic dysfunction and ischemia, increasing their susceptibility to entrapment effects.[13] Chrzanowska et al.[4] suggested that in cases of acute-onset peripheral neuropathy following severe DKA, those with impaired consciousness may experience lower limb nerve damage because of poor positioning, leading to entrapment-related lower limb peripheral neuropathy and potentially resulting in poor functional improvement. Considering the above and insights from previous reports, the short-term functional prognosis was expected to be challenging clinically.

Electroneurophysiological examinations serve as indicators for predicting the functional outcome of foot drop associated with peroneal nerve neuropathy.[14] Despite the limited sample size, positive recruitment findings in the TA muscle on needle EMG could potentially be associated with a favorable prognosis.[15] At the initial assessment in our patient, motor unit recruitment was not observed on needle EMG bilaterally, suggesting limited favorable prognostic factors. However, despite the initial assessment results indicating axonal injury-type peripheral nerve disorders, previous reports suggest that there is potential for recovery over a time span of years.[14,16] Therefore, although a favorable prognosis was not anticipated in the initial assessment, we performed repeated electrophysiological examinations. Indeed, at the 8-month follow-up, needle EMG showed an increase in interference pattern, suggesting the likelihood of further improvement in functional prognosis.

Application of an AFO to the foot and lower leg is a common treatment for foot drop. In this case, given the anticipated difficulty of achieving short-term functional improvement of the bilateral foot drop both clinically and electrophysiologically from the acute phase, AFOs were prescribed early in the clinical course. As a result, gait improved, allowing the patient to safely engage in activities after discharge, such as walking long distances and climbing stairs, facilitating an early return to employment-seeking activities.

We conducted NCSs three times for the purpose of understanding the pathophysiology of this case. However, no CMAPs could be evoked from the right peroneal nerve, and we were unable to arrive at an accurate diagnosis for the left peroneal nerve palsy. Generally, decreased CMAPs or nerve inexcitability leads to muscle denervation and is considered a poor prognostic factor.[17] In the present case, despite clinical improvement in muscle strength, these findings persisted in NCS. Reports of similar clinical courses in Guillain-Barré syndrome suggest that decreased excitability caused by distal stimulation of peripheral nerves might be associated with severe demyelination with conduction block of the terminal segments of motor axons, in addition to axonal degeneration.[17,18] Although the pathophysiology of acute-onset neuropathy after DKA is not well understood, demyelination has been reported as an initial pathophysiology of chronic diabetic neuropathy.[19] Therefore, it is possible that a combination of these factors was involved in addition to axonal degeneration in this case. We plan to continue follow-up examinations in the future.

This study has some limitations. First, as a case study, the functional outcome and course of bilateral foot drop following DKA cannot be generalized. Second, the timing of diabetes onset was unclear, and the extent of chronic neuropathy before the onset of DKA was unknown. Third, NCS evaluation of the TA should have been performed to assess foot drop. Fourth, as mentioned above, the detailed pathophysiology of acute-onset neuropathy in this case was unclear. Despite these limitations, there are no previous reports detailing functional improvement over such an extended period as observed in this case.

CONCLUSION

This report describes an example of successful rehabilitative management and long-term follow-up for bilateral foot drop after onset of DKA. Areas of this management approach will be relevant to future clinical practice and research on the pathophysiology in similar cases.

ACKNOWLEDGMENTS

The authors are grateful to the staff of the Department of Rehabilitation Medicine, Hyogo Medical University. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ III, Service FJ: The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. Neurology 1993;43:817–824. https://doi.org/10.1212/WNL.43.4.817, PMID:8469345
2. Hamada Y, Takahashi K, Hokkoku K, Kanbayashi T, Hatanaka Y, Kobayashi S, Sonoo M: Severe sensory-motor axonal neuropathy following diabetic ketoacidosis [in Japanese]. Rinsho Shinkeigaku 2020;60:614–619. https://doi.org/10.5692/clinicalneurol.cn-001433, PMID:32779597
3. Corcillo A, Kleinaki Z, Kapnisi S, Fountoulakis N, Maltese G, Thomas SM, Karalliedde J: Painless foot drop: an unusual acute presentation of new onset type 1 diabetes mellitus. Endocrinol Diabetes Metab Case Rep 2021;2021:21-0012. https://doi.org/10.1530/EDM-21-0012, PMID:33845454
4. Chrzanowska J, Seifert M, Salmonowicz B, Zubkiewicz-Kucharska A: Foot drop in children with newly diagnosed type 1 diabetes: three case reports. Endocrinol Diabetes Metab Case Rep 2023;2023:22-0417. https://doi.org/10.1530/EDM-22-0417, PMID:37650300
5. Baszyńska-Wilk M, Wysocka-Mincewicz M, Świercz A, Świderska J, Marszał M, Szalecki M: Peripheral neuropathy as a complication of diabetic ketoacidosis in a child with newly diagnosed diabetes type 1: a case report. J Clin Res Pediatr Endocrinol 2018;10:289–293. https://doi.org/10.4274/jcrpe.5374, PMID:29217500
6. Sada K, Hidaka S, Takemaru M, Ueno D, Shibata H: A case of polyneuropathy associated with diabetic ketoacidosis in new-onset type 1 diabetes. J Diabetes Investig 2022;13:918–922. https://doi.org/10.1111/jdi.13724, PMID:34845866
7. Giza S, Litou E, Kotanidou EP, Kleisarchaki AN, Koliatos P, Tzirtzipis T, Tsinopoulou VR, Tychalas A, Evangeliou A, Galli-Tsinopoulou A: Permanent damage of the sciatic nerve in an 8-year-old girl with newly diagnosed type 1 diabetes. Paediatr Int Child Health 2020;40:69–71. https://doi.org/10.1080/20469047.2019.1575536, PMID:30739577
8. Jensen VF, Mølck AM, Bøgh IB, Lykkesfeldt J: Effect of insulin-induced hypoglycaemia on the peripheral nervous system: focus on adaptive mechanisms, pathogenesis and histopathological changes. J Neuroendocrinol 2014;26:482–496. https://doi.org/10.1111/jne.12170, PMID:24921897
9. Sinnreich M, Taylor BV, Dyck PJ: Diabetic neuropathies. Classification, clinical features, and pathophysiological basis. Neurologist 2005;11:63–79. https://doi.org/10.1097/01.nrl.0000156314.24508.ed, PMID:15733329
10. Teasdale G, Jennett B: Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;304:81–84. https://doi.org/10.1016/S0140-6736(74)91639-0, PMID:4136544
11. Brown M, Avers D: Daniels and Worthingham's Muscle Testing. Techniques of Manual Examination and Performance Testing. 10th ed. Elsevier, New York, 2018.

12. Tsuji T, Sonoda S, Domen K, Saitoh E, Liu M, Chino N: ADL structure for stroke patients in Japan based on the functional independence measure. Am J Phys Med Rehabil 1995;74:432–438. https://doi.org/10.1097/00002060-199511000-00007, PMID:8534387
13. Rota E, Morelli N: Entrapment neuropathies in diabetes mellitus. World J Diabetes 2016;7:342–353. https://doi.org/10.4239/wjd.v7.i17.342, PMID:27660694
14. Robinson LR: How electrodiagnosis predicts clinical outcome of focal peripheral nerve lesions. Muscle Nerve 2015;52:321–333. https://doi.org/10.1002/mus.24709, PMID:25989907
15. Derr JJ, Micklesen PJ, Robinson LR: Predicting recovery after fibular nerve injury: which electrodiagnostic features are most useful? Am J Phys Med Rehabil 2009;88:547–553. https://doi.org/10.1097/PHM.0b013e3181a9f519, PMID:19542779
16. Masakado Y, Kawakami M, Suzuki K, Abe L, Ota T, Kimura A: Clinical neurophysiology in the diagnosis of peroneal nerve palsy. Keio J Med 2008;57:84–89. https://doi.org/10.2302/kjm.57.84, PMID:18677088
17. Triggs WJ, Cros D, Gominak SC, Zuniga G, Beric A, Shahani BT, Ropper AH, Roongta SM: Motor nerve inexcitability in Guillain-Barré syndrome. The spectrum of distal conduction block and axonal degeneration. Brain 1992;115:1291–1302. https://doi.org/10.1093/brain/115.5.1291, PMID:1422789
18. Sedano MJ, Canga A, Pablos C, Polo JM, Berciano J: Muscle MRI in severe Guillain–Barré syndrome with motor nerve inexcitability. J Neurol 2013;260:1624–1630. https://doi.org/10.1007/s00415-013-6845-y
19. Chang MC, Yang S: Diabetic peripheral neuropathy essentials: a narrative review. Ann Palliat Med 2023;12:390–398. https://doi.org/10.21037/apm-22-693, PMID:36786097