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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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Ultrasound-Guided Subcutaneous Injection with 5% Dextrose for Postherpetic Neuralgia: A Case Series

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Increasingly many studies have documented the clinical benefits of perineural injection therapy using 5% dextrose in water for various peripheral entrapment neuropathies. Postherpetic neuralgia is a condition involving chronic neuropathic pain caused by varicella-zoster virus, which may persist for an extended period despite continued treatment. This case series discusses three patients with postherpetic neuralgia who received ultrasound-guided subcutaneous injections with 5% dextrose, resulting in remarkable pain improvement.

Keywords: Glucose; Neuralgia, postherpetic; Injections, subcutaneous

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Introduction

Postherpetic neuralgia (PHN) is a type of neuropathic pain caused by the varicella-zoster virus, which can persist long after the characteristic rash has healed. Patients with PHN often report experiencing burning, sharp, or throbbing pain, as well as altered sensations in the area of the affected dermatome. The diagnosis of PHN is made by taking a patient's history, which includes the quality of the pain and any episodes of acute herpetic zoster, and through a physical examination that assesses allodynia, hyper- or hyposensitivity to pain, and the presence of cutaneous scarring in the affected area. Pharmacological interventions, such as topical agents, oral analgesics, tricyclic antidepressants, and anticonvulsants, are the primary methods used to manage pain [1].

Perineural injection therapy (PIT) with 5% dextrose in water (5DW) is thought to inactivate transient receptor potential vanilloid receptor-1 (TRPV-1), an important integrator of responses to inflammatory mediators that is found on peripheral nerves [2-4]. This therapy has been used clinically to treat several common entrapment neuropathies, such as carpal tunnel syndrome, radial nerve palsy, and ulnar neuropathy at the elbow [5]. However, to date, there are no case reports on the use of subcutaneous 5DW injections for the treatment of Here, we present three cases of PHN where patients experienced significant improvement following ultrasound-guided subcutaneous injections with 5DW.

Case Reports

Ultrasound-guided subcutaneous injections with 5DW were administered to patients with PHN. These patients received the injections directly into the affected areas. We retrospectively analyzed the outcomes for these individuals. A summary of all three cases is presented in Table 1.

1) Case 1

A 57-year-old man, previously diagnosed and treated for herpes zoster 3 years prior, presented with chronic tingling and itch-

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Table 1. Demographic Characteristics and Clinical Findings of Cases

Characteristic	Case 1	Case 2	Case 3
Sex/Age (y)	M/57	M/68	M/56
Chief complaint	Pain, allodynia, and hypoesthesia on the left T4 dermatome	Pain on the right gluteal area	Pain and itching sensation on the left upper back
Symptom duration (mo)	12	16	24
Previous treatment	Oral pain medication	Antiviral agent	Antiviral agent and oral gabapentin
Initial VAS	VAS 5	VAS 6	VAS 5
Treatment	Subcutaneous injection of 5DW on the left T4 dermatome	Subcutaneous injection of 5DW on the right gluteal area	Subcutaneous injection of 5DW on the left T5 dermatome
Follow-up VAS after the first injection	VAS 3	VAS 3	VAS 1
Follow-up VAS after the second injection	VAS 3	VAS 2	VAS 0
Follow-up VAS after the third injection	VAS 1	VAS 1	VAS 0

VAS, visual analog scale; 5DW, 5% dextrose in water.

ing pain on the left anterior and posterior chest that had persisted for 1 year. Despite receiving oral analgesics from a local clinic, he experienced no relief. At his initial visit, the patient rated his pain at 5 on a visual analog scale (VAS) and exhibited hypoesthesia to light touch and allodynia within the band-like pain area of the left T4 dermatome (Fig. 1A). Infrared thermography revealed a significantly reduced temperature in the affected left T4 dermatome compared to the contralateral side (Fig. 1B). The patient underwent an ultrasound-guided subcutaneous injection with 5DW totaling 15 cc in the left T4 dermatome (Fig. 1C). Two weeks after the injection, his VAS score decreased to 3, prompting a second 5DW injection of 18 cc. A third 5DW injection was performed 1 month later. At the 1-month follow-up after the third injection, the VAS score had decreased to 1, and there was a significant improvement in allodynia.

2) Case 2

A 68-year-old man, who had been previously diagnosed with and treated for herpes zoster 16 months earlier, presented with chronic pain in his right upper buttock. He rated his pain as a 6 on the VAS and reported no allodynia or sensory impairment. A change in cutaneous skin color was observed in the area of pain on the right upper gluteal region. The patient underwent an ultrasound-guided subcutaneous injection with 5DW, totaling 10 cc, in the right upper buttock. Subsequent injections of 5DW, each totaling 10 cc and then 12 cc, were administered at intervals of 1 to 2 weeks. Following the first, second, and third injections, the patient's VAS scores decreased to 3, 3, and 1, respectively. At the 1-month follow-up after the last injection, the patient's pain had nearly disappeared.

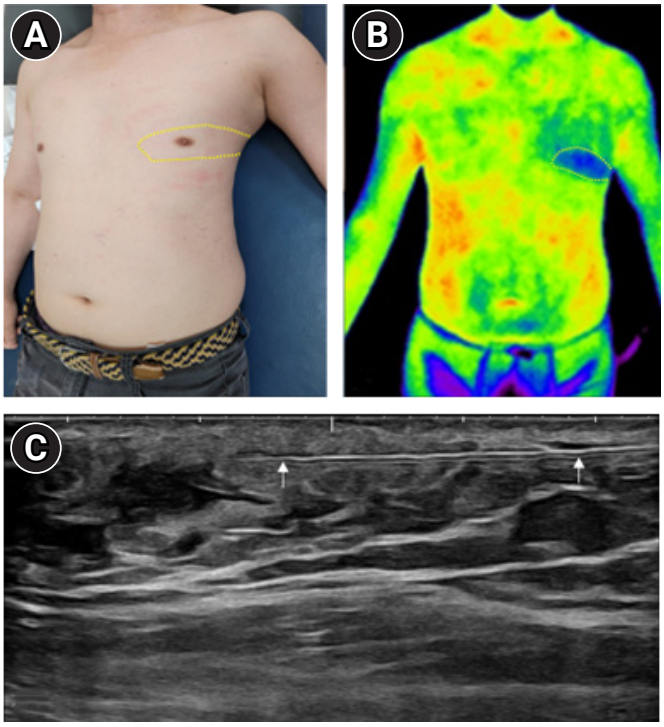

Fig. 1. Sensory changes in the left T4 dermatome (A) and low temperature in the left T4 dermatome (B) compared to the right side one infrared thermography in case 1. Ultrasound-guided subcutaneous injection with 5% dextrose in water on the left T4 dermatome was performed (C). White arrows indicate the needle just below the dermis.

3) Case 3

A 56-year-old man, previously diagnosed and treated for herpes zoster 2 years prior, reported chronic throbbing pain in his left upper back that worsened at night. He rated his pain as a 5 on the VAS, and although allodynia was present in the affected area,

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he retained sensation to light touch and pinprick. Cutaneous lesions were observed in the T5–6 dermatome on the left side of his back. Initially, the patient was prescribed a 2-week course of oral gabapentin, but his pain persisted. Subsequently, he received an ultrasound-guided subcutaneous injection of 5DW with a total volume of 5 cc at the left T5 dermatome. Three weeks after the injection, his VAS score decreased to 3, prompting a second injection of 5DW, this time with a total volume of 8 cc. Following the third 5DW injection (total 5 cc), the patient's pain and allodynia were completely resolved. Gabapentin was discontinued after the first injection, and the pain remained stably controlled without the need for gabapentin until the two additional injections were administered.

The study protocol received approval from the Institutional Review Board (IRB no. 2022AS0118).

Discussion

The pathophysiology of PHN can be partially attributed to the peripheral sensitization of primary afferent neurons. Fields et al. [6] suggested that for a subset of PHN patients who exhibit allodynia and relatively intact sensation, the pain mechanism may be characterized by an "irritable nociceptor." Pain signals are typically transmitted by unmyelinated C fibers and myelinated Aδ primary afferent neurons. When peripheral nerves are damaged, these neurons may develop pathological ectopic discharges, a reduced threshold for activation by thermal and mechanical stimuli, and an enhanced response to suprathreshold stimulation. These changes contribute to abnormal sensitization and the persistence of chronic neuropathic pain [7]. Experimentally, the *in vivo* injection of varicella-zoster virus into the footpads of rats has been shown to cause an upregulation of the $Na_v1.3$ and $Na_v1.8$ sodium channel subtypes [8]. This upregulation altered the sodium currents in afferent neurons, facilitating high-frequency ectopic firing that is implicated in neuropathic pain [9].

Various conventional treatments for PHN have been extensively studied and are clinically practiced. Antidepressants, anticonvulsants, opioids, and the lidocaine patch are supported by level A evidence, indicating their efficacy is backed by randomized controlled trials. However, a considerable number of patients find systemic therapy intolerable due to adverse effects, including dizziness, somnolence, and dry mouth.

PIT with 5DW for neuropathic pain was first introduced by Lyftogt [10] in 2007. Since then, it has been increasingly utilized to treat a range of peripheral entrapment neuropathies, with its effectiveness supported by a number of studies. For the most common peripheral entrapment neuropathies, carpal tunnel syndrome and ulnar neuropathies at the elbow, this technique has gained acceptance as a standard treatment, with its efficacy confirmed by randomized, double-blind studies. Furthermore, there have been case reports documenting the successful use of PIT with 5DW for various entrapment neuropathies, including radial nerve palsy, supinator syndrome, and meralgia paresthetica [5].

In our patients with PHN, ultrasound-guided subcutaneous injections using 5DW demonstrated efficacy in managing PHN. This was evidenced by a reduction in the VAS score, with initial scores ranging from 5 to 6 and final scores dropping to between 0 and 1. Notably, no minor or major complications were observed in any of the three cases.

Although the precise mechanism of 5DW remains unclear, several potential mechanisms have been proposed. The most widely accepted theory is that 5DW mitigates neurogenic inflammation by inhibiting the capsaicin receptor, TRPV-1, in peripheral nerves. TRPV-1 is a non-selective cation channel found in peripheral nociceptors and is implicated in the development of chronic allodynia and neuropathic pain [2]. Petersen et al. [3] observed that the topical application of capsaicin to the skin of patients with PHN significantly exacerbated pain and allodynia. This effect was particularly pronounced in patients with higher pain scores and preserved thermal sensation [3]. Additionally, mannitol, a sugar molecule structurally akin to dextrose, has been shown to alleviate capsaicin-induced pain when applied topically, according to a randomized controlled trial [4].

Building on previous studies that expected PIT with 5DW to have an effect on TRPV-1 in peripheral nerves, this study focused on TRPV-1 located at the nerve endings of peripheral sensory nerve fibers. TRPV-1 is predominantly found in unmyelinated C fibers and thinly myelinated Aδ fibers, which are responsible for transmitting pain and temperature sensations. The nerve endings of these fibers are situated in the epidermis and dermis. However, due to the considerable pain associated with dermal injections, this study opted for subcutaneous injections of a sufficient volume of 5DW just beneath the dermis. This approach was based on the expectation that the 5DW would disperse through the dermis.

In conclusion, ultrasound-guided subcutaneous injection with 5DW may be regarded as an effective and safe treatment alternative for patients experiencing persistent PHN that is unresponsive to conventional therapies.

Conflict of Interest

Dong Hwee Kim is an editor-in-chief 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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Glue-Sniffing Neuropathy: A Case Report

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Glue, a volatile substance that is illegal as a recreational drug, has been popularly used for decades, and it can serve as a stepping stone for harder drugs. Chronic exposure can lead to substantial damage to several organs, including central and peripheral nervous systems. Glue-sniffing neuropathy has been reported since the 1960s, but with a lower frequency in recent years. We report a 45-year-old man who sniffed glue and presented with symmetrical distal motor weakness and paresthesia. Based on the patient's inhalation history and initial electrodiagnostic study, we considered toxic neuropathy and demyelinating polyneuropathy in the differential diagnosis. He became chair-bound with repeating glue sniffing, and a following nerve conduction study showed the progression of motor-dominant polyneuropathies with markedly reduced amplitudes. An incomplete response to steroid therapy and recovery with inhalant cessation confirmed the diagnosis of glue-sniffing neuropathy. We conclude that glue, a neurotoxic volatile inhalant, produced glue-sniffing neuropathy with characteristic clinical and electrodiagnostic features.

Keywords: Glue; Glue-sniffing neuropathy; Toxic polyneuropathy

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Introduction

Illegal drug abuse has emerged as a key social issue, prompting the Korean Ministry of Justice to declare a "war on drugs" in an effort to eradicate the use, distribution, and trade of illegal substances [1]. Historically, even when drug-related crime was less prevalent in Korea, adolescents and young adults found glue to be an easily accessible inhalant [2,3]. The rise in glue inhalation has become a concerning social issue, potentially acting as a gateway to "harder" drugs. Until recently, relatively few Koreans have engaged in the long-term use of volatile inhalants, which can result in mild to severe organ system dysfunction [4]. We present the case of a patient who experienced extensive medical and social problems associated with glue inhalation, focusing primarily on polyneuropathic symptoms.

Case Report

A 45-year-old man with a history of hypertension presented with gait disturbance and bilateral lower limb motor weakness that had persisted for 2 months. He had been abusing inhalants, specifically glue, since his 20s and had been jailed multiple times. The patient had developed severe stress after being robbed, which led to a weight loss of 8 kg over 2 months. While taking prescribed antipsychotic medications, including chlordiazepoxide, lorazepam, and zolpidem, he also consumed alcohol and inhaled glue on a daily basis.

The patient had been unable to squat or stand without assistance for 2 months when he visited our department. On a manual muscle test conducted using the Medical Research Council scale, motor weakness was observed in the distal muscles of the bilateral lower extremities, including hip flexion (grade IV), knee flexion/extension (grade IV/IV), ankle dorsiflexion (grade II), ankle plantarflexion (grade III), and toe dorsiflexion (grade II).

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The bilateral upper extremities were less affected than the lower limbs. Muscle strength in the bilateral proximal upper limbs was intact, while finger flexion and extension displayed a grade of IV+. Light touch sensation, proprioception, and pain and temperature sensation were grossly intact. Deep tendon reflexes were absent in the bilateral knees and ankles.

Serologic test results revealed no definite abnormalities. The values were as follows: creatine kinase, 143 IU/L (normal range, 0 to 185); vitamin B1, 98.22 ng/mL (normal range, 66.5 to 200); vitamin B12, 594.8 pg/mL (normal range, 232 to 1,245); folic acid, 4.1 ng/mL (normal range, 4.6 to 18.7); and homocysteine, 11.3 μmol/L (normal range, 5.0 to 15.0).

Motor nerve conduction studies (NCS) revealed delayed onset latencies and mildly slowed motor velocities, along with conduction blocks in the bilateral median and ulnar nerves (Table 1). Sensory NCS indicated a slight sensory deficit, characterized by low amplitudes in the right median and bilateral ulnar nerves (Table 1). Needle electromyography demonstrated mild-to-moderate denervation potentials and reduced interference patterns in the right first dorsal interosseous, tibialis anterior, and vastus lateralis muscles. These electrodiagnostic findings are indicative of diffuse motor-dominant sensorimotor neuropathy with some demyelinating characteristics.

Intravenous pulses of 1 g methylprednisolone were administered over 5 days, resulting in a slight improvement of the bilateral lower limb weakness. Specifically, hip flexion improved to grade IV+, and ankle dorsiflexion increased to grade II/III. Upon discharge, the patient was prescribed a tapered dose of prednisolone, starting at 30 mg. However, he was unable to cease glue inhalation.

One month after his initial discharge, the patient's motor weakness had regressed to pre-treatment levels, and he reported aggravated symmetric distal paresthesia. During his second hospitalization, a follow-up electrodiagnostic study was conducted,

Table 1. Findings of the Initial Nerve Conduction Study

Nerve site	Onset latency (ms)		Amplitude (mV)		CV (m/sec)	
	Left	Right	Left	Right	Left	Right
Motor NCS						
Median						
Wrist	4.2*	4.1*	6.8	7.8	-	-
Elbow	9.6	9.3	3.2*	2.6*	41*	43*
Axilla	12.1	11.8	2.5*	2.3*	52	52
Ulnar						
Wrist	3.1*	3.1*	12.5	11.1	-	-
Below elbow	8.1	9.3	11.7	9.0	46*	37*
Above elbow	10.0	11.9	7.4*	6.9*	53	46
Axilla	11.9	13.8	7.3*	6.8*	58	63
Peroneal						
Ankle	6.0	6.6	1.8	2.0	-	-
Below fibula	14.9	16.0	1.0	1.0	37	35
Tibial						
Ankle	4.1	4.6	10.7	11.6	-	-
Knee	14.4	14.5	3.2	3.5	38	39
Sensory NCS						
Median						
Finger-wrist	3.3	3.0	9.2	6.5*	38	37
Palm-wrist	2.1	1.9	15.7	11.9	32	32
Wrist-elbow	3.5	3.3	25.4	26.1	54	54
Elbow-axilla	1.7	1.7	109.7	185.6	57	57
Ulnar						
Finger-wrist	2.1	2.7	2.4*	3.6*	37	23
Palm-wrist	1.3	1.4	13.7	11.5	37	33
Wrist-elbow	3.5	2.9	17.2	23.3	54	55
Elbow-axilla	1.8	2.3	51.8	52.0	56	54
Sural						
Calf	-	-	10.9	13.7	38	37

CV, conduction velocity; NCS, nerve conduction study.
*Abnormal value.

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revealing the progression of diffuse, motor-dominant sensorimotor neuropathy. Compared to the initial study, motor NCS showed greater delays in onset latencies and reduced amplitudes in the bilateral upper and lower extremities (Table 2). Sensory NCS of the distal upper and lower extremities could not be obtained (Table 2). The patient underwent a second round of intravenous methylprednisolone pulse therapy. For further management, he consented to be admitted to a hospital specializing in substance use disorders.

Despite attempts to discontinue inhalant use, the patient experienced a recurrently relapsing course in the outpatient setting, accompanied by worsening bilateral hand atrophy. Additionally, he was unable to walk unaided and required the use of a wheelchair. After the steroid dose was tapered to a minimal amount, specifically 10 mg of prednisolone, the patient was lost to follow-up in outpatient care.

About 1 year later, we received a letter from the patient, who informed us that he had surrendered to the police. During his incarceration, without access to the inhalant, he regained the ability to write and walk independently, as his distal muscle weakness improved.

The study received approval from the Institute Review Board of Ewha Womans University Mokdong Hospital (IRB no: 2023-08-024), and the requirement for written informed consent from the patient was waived due to the retrospective nature of the report.

Discussion

Glue sniffing can be broadly defined as the deliberate inhalation of volatile substances for the purpose of achieving a state of recreational intoxication. A commonly abused volatile substance, glue contains toluene and *n*-hexane [5]. It is readily available and relatively inexpensive, making it attractive to adolescents and young adults. The initial effects of glue inhalation include euphoria, excitation, dizziness, and mild headache, with rapid onset and short duration. With prolonged abuse, individuals may develop nausea, vomiting, dysarthria, gait disturbance, disorienta-

Table 2. Findings of the Follow-up Nerve Conduction Study

Nerve site	Onset latency (ms)		Amplitude (mV)		CV (m/sec)	
	Left	Right	Left	Right	Left	Right
Motor NCS						
Median						
Wrist	6.5*	6.2*	0.8*	0.9*	-	-
Elbow	11.8	14.1	0.4*	0.4*	42*	29*
Axilla	14.4	16.4	0.4*	0.4*	50*	52
Ulnar						
Wrist	4.5*	3.7*	3.2*	1.5*	-	-
Below elbow	9.9	9.5	2.1*	1.7*	43*	40*
Above elbow	12.3	13.3	2.3*	1.1*	42*	32*
Axilla	14.5	16.3	1.9*	1.2*	45*	40*
Peroneal						
Ankle	9.1*	7.8*	1.4*	1.3*	-	-
Below fibula	20.6	19.0	0.4	0.2	29*	29*
Tibial						
Ankle	6.3*	5.7*	3.2*	2.1*	-	-
Knee	16.3	16.9	0.6	0.5	36*	34*
Sensory NCS						
Median						
Finger-wrist	NR*	NR*	NR*	NR*	-	-
Wrist-elbow	3.4	3.7	15.4	20.5	49	49
Elbow-axilla	1.5	1.3	94.6	150.7	62	68
Ulnar						
Finger-wrist	NR*	NR*	NR*	NR*	-	-
Wrist-elbow	3.2	3.4	11.7*	14.1	48	47
Elbow-axilla	2.5	1.0	20.6	60.6	42	71
Sural						
Calf	NR*	NR*	NR*	NR*	-	-

CV, conduction velocity; NCS, nerve conduction study; NR, no response.
*Abnormal value.

tion, and delusion. Chronic abuse can lead to serious health issues such as myopathy, peripheral neuropathy, and encephalopathy, which are characterized by cognitive impairment, ataxia, seizures, and, in severe cases, coma or death [4,6].

Glue-sniffing neuropathy, also known as *n*-hexane neuropathy, has been well-established since the 1960s and is characterized by subacute onset and motor-dominant neuropathy [5,7]. However, the differential diagnosis should always include demyelinating polyneuropathies, such as chronic inflammatory demyelinating polyneuropathy (CIDP) [8,9]. In the present case, the initial manifestations were symmetric distal-dominant motor weakness with minimal sensory deficits. Given the clinical manifestations and the progressive, relapsing course, we considered CIDP, while bearing in mind the patient's history of inhalant use. The patient did not fully respond to steroid therapy, which is commonly used for immunosuppression. Follow-up NCS primarily indicated axonal injury, with less pronounced demyelinating features. Considering his history of inhalant abuse, we clinically diagnosed the patient with toxic polyneuropathy due to glue inhalation. His clinical course was consistent with subacute motor-dominant polyneuropathy, and the electrodiagnostic findings predominantly revealed sensorimotor neuropathies with delayed onset latency or mild conduction block. Moreover, his symptoms improved after he stopped inhaling the substance, which further supported the diagnosis.

The treatment for chronic inhalant abuse, as demonstrated with this patient, involves strict abstinence. No antidote is available for inhalant intoxication; however, counseling, psychiatric intervention, and appropriate social support can be beneficial.

In an era of increasingly prevalent illegal drug abuse in Korea, physicians must be cognizant of the various forms of substance abuse and their clinical manifestations. When evaluating patients with neuropathy, physicians should inquire about the patient's history of addiction and potentially consider toxic polyneuropathy in the differential diagnosis.

Conflict of Interest

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

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Colchicine-Induced Neuromyopathy with Myotonic Discharges in a Patient Using Concomitant Diuretics

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Colchicine is a widely used anti-inflammatory medication, but its neuromuscular adverse effects are under-recognized. One month ago, a 70-year-old woman presented to our clinic for an evaluation of general weakness. She had been taking colchicine and diuretics daily. The weakness, which began in both thighs and lower legs approximately 4 weeks before her visit, had progressively worsened. The patient also experienced mild paresthesia and hypoesthesia in both arms and legs. Her serum creatine kinase and aldolase levels were elevated, and nerve conduction studies indicated a motor-dominant sensorimotor polyneuropathy of the axonal type. Needle electromyography showed prominent fibrillation potentials, positive sharp waves, and myotonic discharges. Suspecting colchicine-induced neuromyopathy, we discontinued the colchicine and diuretics, after which her symptoms resolved.

Keywords: Colchicine; Neuromyopathy; Myotonic discharges

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Introduction

Colchicine is an anti-inflammatory medication used to treat various inflammatory conditions, such as familial Mediterranean fever and acute gouty arthritis [1]. Common side effects of colchicine include gastroenteritis, blood dyscrasias, and dermatitis. However, the neuromuscular adverse effects associated with colchicine are not well recognized [2]. Patients on concurrent medications or those with underlying renal insufficiency may face an elevated risk of experiencing neuromuscular complications from colchicine, which include chronic neuromyopathy and acute fulminant rhabdomyolysis. The characteristic neuromuscular complication induced by colchicine is neuromyopathy, which manifests as an elevated serum creatine kinase (CK) level, subacute weakness in the proximal lower extremities, and length-dependent sensory peripheral neuropathy, particularly when combined with renal impairment [3]. We report a case of colchicine-induced neuromyopathy with myotonic discharges in a patient using concomitant diuretics.

Case Report

One month ago, a 70-year-old woman presented to our clinic for an evaluation of general weakness. Her extensive medical history included hypertension, heart failure with pericardial effusion, hypothyroidism, and hyperuricemia. The weakness began in her thighs and lower legs approximately 4 weeks before her visit and had progressively worsened. She displayed mild myalgia along with slight paresthesia and hypoesthesia in both arms and legs. The patient did not indicate any cranial nerve deficits or issues with bladder or bowel function. However, she did report persistent diarrhea and poor oral intake over the prior 3 weeks. She had been taking colchicine at a dose of 1.2 mg daily for several months to manage hyperuricemia and pericardial effusion.

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Additionally, she had been on diuretics, including furosemide at 80 mg and spironolactone at 25 mg, for 2 months to address generalized edema and pleural effusion. Her medication regimen also included levothyroxine at 0.15 mg, aspirin at 100 mg, and allopurinol at 100 mg.

The initial physical examination revealed an arterial blood pressure of 133/69 mm Hg, a pulse rate of 98 beats per minute, a respiratory rate of 19 breaths per minute, and a body temperature of 36.6°C.

Laboratory test results indicated anemia, with a hemoglobin level of 8.2 g/dL (normal range, 13.5 to 17.5), and thrombocytopenia, with a platelet count of 55,000/μL (normal range, 150,000 to 400,000). Elevated liver enzymes were also noted, including alkaline phosphatase at 104 U/L (normal range, 7 to 45) and aspartate aminotransferase at 93 U/L (normal range, 8 to 43). Additionally, the patient's blood urea nitrogen level was elevated (33 mg/dL; normal range, 10 to 20), as was her creatinine level (1.8 mg/dL; normal range, 0.6 to 1.1). Her serum CK level was high, at 2,581 U/mL (normal range, 52 to 336), and her aldolase level was also high, at 9.4 U/mL (normal range, 1 to 7.5).

On neurological examination, the patient's cognitive functions and cranial nerves appeared normal. She exhibited both proximal and distal upper limb weakness (Medical Research Council [MRC] grade 3/5), severe weakness in hip flexion and ankle dorsiflexion (MRC grade 2/5), and diffuse weakness in the lower limbs (MRC grade 3/5). No clinical myotonia, muscle atrophy, or fasciculations were observed. Deep tendon reflexes were diffusely reduced in the upper limbs and absent in the legs. The patient was experiencing graded sensory loss, with pain and a cold sensation present up to the knees, reduced vibratory sensation at the ankles, and diminished joint position sensation in the toes. Our initial clinical diagnosis was Guillain-Barré syndrome. Motor nerve conduction studies revealed prolonged terminal latencies, low-amplitude compound muscle action potentials, and slow motor nerve conduction velocities in both median, ulnar, posterior tibial, and peroneal nerves, with asymmetrical involvement (Table 1). Sensory nerve conduction studies indicated low-amplitude action potentials and slightly slow conduction velocities in both median nerves (Table 2). These studies suggested a motor-dominant sensorimotor polyneuropathy of the axonal type. However, needle electromyography (EMG) demonstrated prominent fibrillation potentials, positive sharp waves, and myotonic discharges in the proximal and distal limb muscles (Table 3, Fig. 1). Analysis of motor unit action potentials revealed short duration and early recruitment in proximal muscles, but normal duration and reduced recruitment in distal muscles (Table 3). Cerebrospinal fluid studies and anti-ganglioside antibody tests for Guillain-Barré syndrome fell within normal ranges. Tests for anti-nuclear antibody, anti-double-stranded DNA (deoxyribonucleic acid) antibody, anti-Jo-1 antibody, anti-SCL-70 antibody, and anti-centromere antibody, which are used in the diagnosis of inflammatory myositis, were also within normal limits. Thyroid function tests and anti-thyroid peroxidase antibody titers were normal. Cytosine-thymine-guanine (CTG) repeat analysis of the dystrophia myotonica protein kinase (DMPK) gene, used in the diagnosis of myotonic dystrophy, was within the normal range as well. We suspected toxic or drug-induced neuromyopathy, as the electrophysiological findings could be attributed to the simultaneous occurrence of acute polyneuropathy and myopathy. The clinical, laboratory, and electrophysiological findings were consistent with colchicine-induced neuromyopathy exacerbated by diuretics in the context of renal insufficiency.

Table 1. Nerve Conduction Study (Initial): Motor Nerve Conduction Study

Site	Latency (ms)	Amplitude (mV)	Conduction velocity (m/sec)
Median motor left			
Wrist–APB	4.44*	5.4*	
Elbow–wrist	9.48	5.2*	43.7*
Axilla–elbow	10.9	5*	70.4
Median motor right			
Wrist–APB	4.27*	8.8	
Elbow–wrist	8.66	8.4	36.4*
Axilla–elbow	10.2	8.5	77.9
Ulnar motor left			
Wrist–ADM	3.15*	6.1*	
Below elbow–wrist	6.98	5.6*	40.5*
Above elbow–below elbow	9.23	5.2*	44.4
Axilla–above elbow	10.4	5.2*	72.6
Ulnar motor right			
Wrist–ADM	3.16*	9.9	
Below elbow–wrist	7.15	9.2	41.4*
Above elbow–below elbow	8.85	8.8	58.8
Axilla–above elbow	10.5	8.7	57.6
Tibial motor left			
Ankle–abductor halluces	7.99*	0.97*	
Popliteal fossa–ankle	17.7	0.68*	29.4*
Tibial motor right			
Ankle–abductor halluces	7.04*	4.6*	
Popliteal fossa–ankle	15.1	4.1*	35.4*
Peroneal motor left			
Ankle–EDB	4.99	0.43*	
Fibular head–ankle	12.8	0.31*	37.8*
Peroneal motor right			
Ankle–EDB	6.22*	0.29*	
Fibular head–ankle	13.1	0.13*	42.9

APB, abductor pollicis brevis; ADM, abductor digiti minimi; EDB, extensor digitorum brevis.
*Outside of normal range.

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Table 2. Nerve Conduction Study (Initial): Sensory Nerve Conduction Study

Site	Amplitude (μV)	Conduction velocity (m/sec)
Median sensory left		
Finger–wrist	8.3*	43.7
Palm–wrist	16.8	46.4*
Wrist–elbow	5*	47.1*
Elbow–axilla	10.7*	64.9
Median sensory right		
Finger–wrist	3.2*	42.7
Palm–wrist	8*	46.8*
Wrist–elbow	9.9*	56.6
Elbow–axilla	21.9	61.2
Ulnar sensory left		
Finger–wrist	10.3	54.6
Wrist–elbow	15.2	54.4
Elbow–axilla	14	87.2
Ulnar sensory right		
Finger–wrist	13.8	52
Wrist–elbow	18.3	62.1
Elbow–axilla	13.3	79.2
Peroneal superficial sensory left		
Calf–ankle	8.6	49.6
Peroneal superficial sensory right		
Calf–ankle	12.6	40.9

*Outside of normal range.

Upon admission, colchicine and diuretics were discontinued, and within 1 week, the patient's diarrhea, anemia with thrombocytopenia, and renal insufficiency resolved. After 2 months, she exhibited no weakness in the arms and only mild weakness in the lower limbs (MRC grade 4/5). Six months later, her nerve conduction study and serum CK levels were normal (Tables 4, 5).

Written informed consent by the patients was waived due to a retrospective nature of our study.

Discussion

By binding to tubulin, a crucial protein in mitosis, colchicine inhibits microtubule polymerization and prevents microtubule elongation [1]. Complications of colchicine treatment typically begin with gastrointestinal symptoms, such as abdominal pain, nausea, vomiting, and diarrhea, within 24 hours after the oral ingestion of large amounts [4]. In our patient, chronic diarrhea preceded the onset of neuromuscular symptoms. These gastrointestinal side effects should be managed to prevent dehydration, hypovolemic shock, and cardiovascular collapse. However, the present patient's continued use of diuretics exacerbated dehydra-

Table 3. Needle Electromyographic Findings (Initial)

Muscle	Insertion activity	Spontaneous activity			Analysis of MUPs		
		Fibrillation	PSW	Myotonic	Amp litude (K: 1 mV)	Duration	IP
Left vastus lateralis	Increased	–	++	+	1–2	Short	Early
Left tibialis anterior	Increased	+	+++	++	1–4	Normal	Reduced
Left triceps brachii	Increased	–	+	–	1–3	Short	Early
Left biceps brachii	Increased	+	++	+	1–2	Short	Early
Left first dorsal interosseous	Increased	–	++	–	1–5	Normal	Reduced
Left abductor pollicis brevis	Increased	+	++	+	1–5	Normal	Reduced

MUP, motor unit potential; PSW, positive sharp wave; IP, interference pattern.

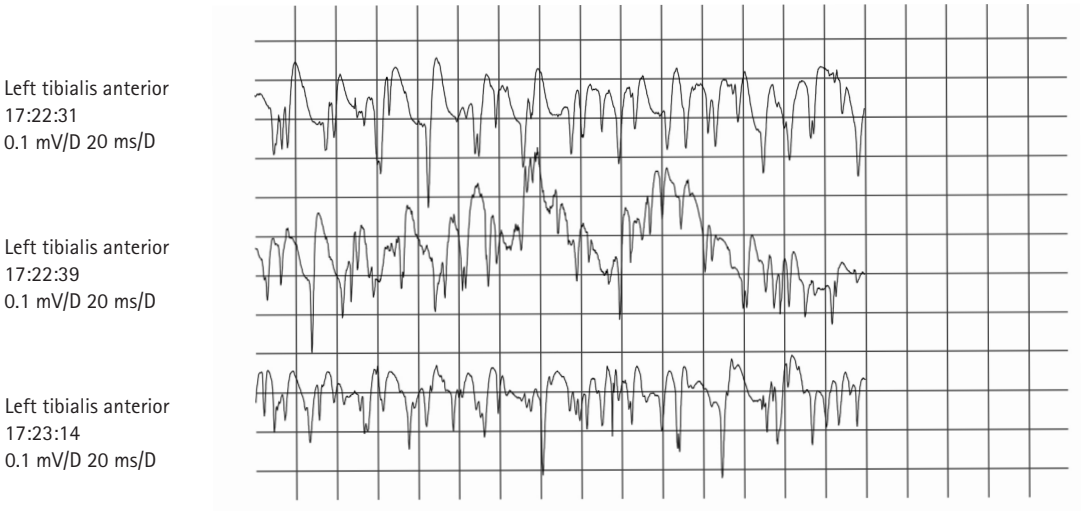

Fig. 1. Myotonic discharge in the left tibialis anterior muscle (mV/division).

Table 4. Nerve Conduction Study (6 Months After Discontinuation): Motor nerve conduction study

Site	Latency (ms)	Amplitude (mV)	Conduction velocity (m/sec)
Median motor left			
Wrist–APB	3.56	12.5	
Elbow–wrist	7.23	12.3	52.8
Axilla–elbow	9.17	12.2	67.3
Median motor right			
Wrist–APB	3.52	13.2	
Elbow–wrist	7.22	13.1	51.8
Axilla–elbow	8.66	12.9	76.5
Ulnar motor left			
Wrist–ADM	2.85	11.7	
Below elbow–wrist	6.45	11.5	53.4
Above elbow–below elbow	8.52	11.5	47.3
Axilla–above elbow	9.06	11.3	73.2
Ulnar motor right			
Wrist–ADM	2.95	10.2	
Below elbow–wrist	7.23	10.1	53.3
Above elbow–below elbow	8.75	10.1	58.9
Axilla–above elbow	10.3	9.8	53.8
Tibial motor left			
Ankle–abductor hallucis	4.15	10.5	
Popliteal fossa–ankle	12.6	6.8	42.6
Tibial motor right			
Ankle–abductor hallucis	3.85	12.3	
Popliteal fossa–ankle	12.2	8.5	42.5
Peroneal motor left			
Ankle–EDB	3.85	3.3	
Fibular head–ankle	10.6	3.1	40.6
Peroneal motor right			
Ankle–EDB	4.98	5.4	
Fibular head–ankle	10.7	5.1	41.5

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

Table 5. Nerve Conduction Study (6 Months After Discontinuation): Sensory Nerve Conduction Study

Site	Amplitude (μV)	Conduction velocity (m/sec)
Median sensory left		
Finger–wrist	11.5	48.7
Palm–wrist	17.8	51.5
Wrist–elbow	16.1	55.5
Elbow–axilla	15.3	52.1
Median sensory right		
Finger–wrist	9.8	45.2
Palm–wrist	10.2	53.3
Wrist–elbow	17.6	57.6
Elbow–axilla	22.3	61.1
Ulnar sensory left		
Finger–wrist	10.3	55.6
Wrist–elbow	17.3	63.2
Elbow–axilla	17	66.5
Ulnar sensory right		
Finger–wrist	9.8	54.3
Wrist–elbow	21.3	63.2
Elbow–axilla	14.3	76.2
Peroneal superficial sensory left		
Calf–ankle	7.8	52.2
Peroneal superficial sensory right		
Calf–ankle	11.2	41.2

tion and led to renal dysfunction. The mechanisms underlying colchicine-associated neuromuscular complications are not fully understood and are often overlooked. Nonetheless, colchicine-induced neuromyopathy is frequently observed in patients taking the standard dose, and certain conditions significantly increase the risk. These include impaired renal and hepatic function, as well as the concurrent use of medications that inhibit the cytochrome P450 3A4 isozyme (CYP3A4) and P-glycoprotein [5]. Patients who receive doses within the usual range may be relatively susceptible to this neuromuscular complication if they have chronic renal dysfunction or take diuretics [2]. Colchicine-induced neuromyopathy can also result from the coadministration of any medication metabolized by the CYP3A4 system [6]. Previous reports have indicated that numerous drugs, including clarithromycin, pravastatin, simvastatin, fluvastatin, atorvastatin, gemfibrozil, calcium channel blockers, and cyclosporine, can contribute to neuromyopathy when they interact with colchicine [7].

Our patient exhibited no neuromuscular issues while on colchicine monotherapy. However, the addition of diuretics led to renal insufficiency, which precipitated colchicine-induced neuromyopathy. Often, the primary clinical feature of this condition is painless proximal lower limb weakness; nevertheless, myalgia can sometimes be observed, as with our patient [8]. Additional manifestations, such as distal leg weakness, arm weakness, sensory abnormalities, and areflexia, have also been reported and were present in this case [8]. The course of colchicine-induced neuromyopathy is generally subacute, spanning 1 to 3 months, but the condition can present acutely in less than 4 weeks or chronically over more than 3 months [2]. While no respiratory or cardiac complications have been documented, dysphagia has been noted as an occasional symptom [2]. Laboratory tests typically reveal mild to marked elevation of CK levels [2]. Electrodiagnostic studies may suggest a sensorimotor axonal polyneuropathy and myopathic motor unit potentials with signs of membrane irritability, similar to findings observed with inflammatory myopathies [3]. Due to the predominant proximal weakness, elevated CK level, and irritable myopathy on EMG, polymyositis is frequently considered in the differential diagnosis for patients with colchicine-induced neuromyopathy. Although rare, the literature

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includes instances of colchicine-induced myopathy or neuromyopathy with myotonic discharges on EMG, yet without clinical myotonia [9]. In rare cases, colchicine alone has been implicated in peripheral neuropathy with electrical myotonia [10]. We contend that the presence of a myopathic pattern with myotonic discharges on EMG in patients taking colchicine is a noteworthy finding that may lead to unnecessary invasive muscle biopsy. Histologically, muscle tissue frequently exhibits vacuolar myopathy with increased acid phosphatase reactivity, which is particularly pronounced in proximal muscles [2]. The disruption of the microtubule-dependent cytoskeletal architecture is considered a potential pathogenic mechanism for colchicine-induced neuromyopathy [2]. A thorough patient history can help exclude neuromyopathy resulting from exposure to drugs or toxins such as alcohol, amiodarone, chloroquine, and vincristine.

Most patients who discontinue colchicine experience a complete reversal of symptoms [5]. Withdrawal from colchicine typically leads to a rapid improvement in the clinical and electrophysiological abnormalities associated with myopathy, although the resolution of neuropathy can take longer [3]. Colchicine-induced neuromyopathy should be considered in patients—particularly elderly individuals with renal insufficiency or those taking the drug in combination with other medications—who present with subacute weakness in the proximal lower extremities and distal sensory changes, even if electrophysiological studies indicate polyneuroradiculopathy and/or active myopathy with or without myotonic discharges. Early recognition of the characteristic features of colchicine-induced neuromyopathy can help avoid unnecessary muscle biopsies. Most cases involving clinical weakness and laboratory abnormalities can be resolved promptly with cessation of the medication.

Conflict of Interest

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

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CASE REPORT

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Successful Management of an Acute Dystonic Reaction Induced by an Anesthetic Agent

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Acute dystonic reactions (ADRs) are movement abnormalities characterized by involuntary muscle contractions that typically manifest after exposure to a triggering agent, such as a medication. The specific muscle groups affected determine the type of reaction. For instance, an oculogyric crisis primarily affects the ocular muscles, while oromandibular dystonia involves jaw opening and tongue protrusion. We present the rare case of a 68-year-old man with amyotrophic lateral sclerosis who was successfully treated for an ADR. The patient was admitted with loss of consciousness due to respiratory failure. Tracheostomy was promptly performed under sedation with multiple general anesthetic agents. Immediately after tracheostomy, the patient communicated via eye-blinking without any notable abnormalities, just as before the procedure. However, the following day, he became unresponsive to verbal cues and exhibited a decreased level of consciousness, accompanied by tongue dyskinesia, deviation of both eyes to the left, and loss of visual tracking. The patient's vital signs remained stable. Brain imaging and an electroencephalogram revealed no abnormalities. Treatment with midazolam produced initial improvement; however, due to a significant side effect of hypotension, the treatment was switched to oral diazepam. The patient's condition gradually improved, and the medication was eventually discontinued without further ADR episodes.

Keywords: Dystonic disorders; Amyotrophic lateral sclerosis; Anesthesia, general; Oculogyric crisis

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Introduction

Acute dystonic reactions (ADRs) are movement abnormalities characterized by involuntary muscle contractions that typically manifest after exposure to a triggering agent, such as a medication. The specific muscle groups affected determine the type of reaction. For example, an oculogyric crisis primarily affects the ocular muscles, leading to upward and outward deviations of the eyes, while oromandibular dystonia is characterized by jaw opening and tongue protrusion [1]. ADRs result from a dopaminergic-cholinergic imbalance in the basal ganglia [2]. Metoclopramide, a dopaminergic antagonist, is a common cause of ADRs [3]. Additionally, some case reports have indicated that propofol can induce ADRs, which in some instances may lead to life-threatening laryngeal spasms [4,5]. In this report, we present a case of an ADR accompanied by an oculogyric crisis that occurred following sedation with multiple general anesthetic agents for amyotrophic lateral sclerosis (ALS). The ADR was successfully managed with pharmacotherapy.

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Case Report

A 68-year-old man, diagnosed with ALS in 2020, was admitted to our hospital on March 7, 2023, due to a loss of consciousness. He exhibited respiratory failure that was attributed to the progression of ALS. Consequently, an arterial blood gas analysis was conducted, revealing a marked increase in carbon dioxide levels with a PCO_2 of 90.8 mm Hg. Endotracheal intubation was promptly performed, followed by the initiation of mechanical ventilation to ensure adequate respiratory support. The following day, on March 8, the patient underwent bedside tracheostomy while under general anesthesia in the intensive care unit (ICU).

Until 1:20 PM on March 9, the patient was still able to communicate by blinking his eyes, with no notable cognitive impairment, and his muscle strength remained at grade zero, consistent with his condition before tracheostomy. However, at approximately 1:30 PM, he became unresponsive to verbal cues and experienced a decrease in consciousness. This was accompanied by tongue dyskinesia and deviation of both eyes to the left, as well as a loss of visual tracking (Fig. 1, Supplementary Video 1). The patient's vital signs remained stable. Computed tomography and diffusion-weighted magnetic resonance imaging of the brain were performed to determine the underlying cause, but neither revealed any evidence of brain lesions, including acute stroke. An electroencephalogram also did not show any evidence of seizure activity. To our knowledge, the literature includes no reported cases of these symptoms appearing as a result of ALS progression.

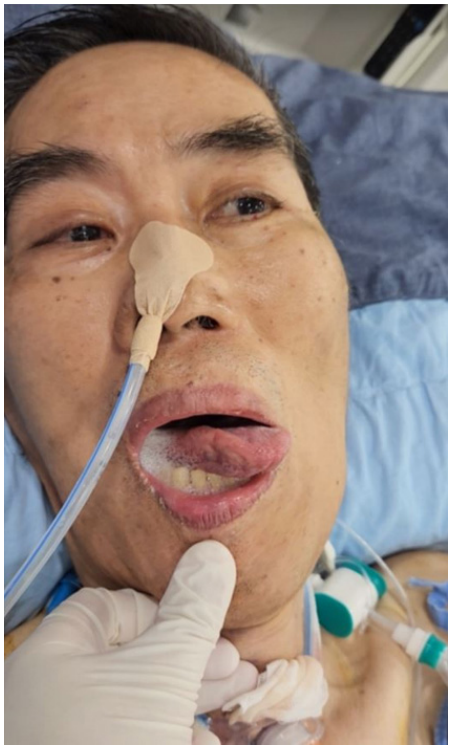

Fig. 1. The patient became unresponsive to verbal cues, exhibiting a decreased level of consciousness accompanied by tongue dyskinesia, deviation of both eyes, and loss of visual tracking.

Considering the patient's symptoms and circumstances at the time, the most plausible explanation is that an ADR occurred, manifesting as an oculogyric crisis following the administration of sedative medications (fentanyl and propofol).

On the first day of symptom onset, a 3-mg intravenous bolus of midazolam, a benzodiazepine, was administered with the goal of controlling the patient's symptoms. Thirty minutes after administration, the patient displayed an improvement in eye closure and sedation, as well as a positive response in tongue movement. One hour after receiving midazolam, the patient regained awareness and responded appropriately to one-step verbal commands. However, after 4 hours, he experienced a recurrence of impaired consciousness and tongue dyskinesia. This led to considerations regarding the pharmacokinetics of midazolam, which has a half-life of approximately 3 hours before its effectiveness significantly decreases. Due to its strong hypotensive effect, the repeated use of midazolam was limited. On the second day, oral administration of diazepam was initiated at a dose of 2 mg three times per day, while the administration of midazolam was discontinued. However, no notable improvements were observed in the patient's symptoms that day. On the third day, the patient consistently exhibited an alert mental state and responded appropriately to one-step verbal commands. Although limitations in smooth conversation persisted due to difficulties vocalizing after tracheostomy, the patient demonstrated appropriate responses to oral commands, including instructions to close his eyes and blink twice. His tongue dyskinesia was also reduced (Fig. 2, Supplementary Video 2). The patient's cognitive function remained unchanged from before the tracheostomy procedure, and the muscle strength in his limbs continued to receive a grade of zero. On day 15 after symptom onset, as the patient's symptoms gradually improved, the administration of diazepam was discontinued. No further ADR episodes or oculogyric crises occurred after the medication was stopped.

Written informed consent was obtained from the patient and his guardian.

Discussion

ADRs are known to occur due to cholinergic hyperactivity and

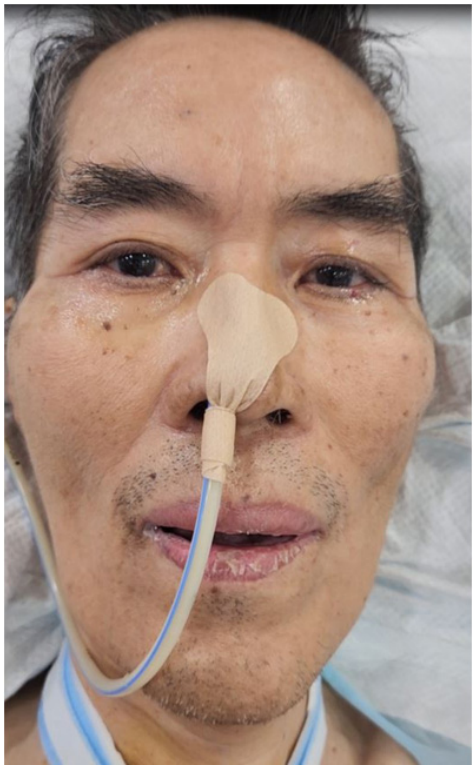

Fig. 2. The patient's symptoms were treated with oral diazepam, administered at a dose of 2 mg three times daily.

dopaminergic hypoactivity in the nigrostriatal pathway and are commonly induced by dopamine-blocking agents, such as both typical and atypical antipsychotics or antiemetics [2,3]. Reports have also described ADRs induced by anesthetic agents [4,5]. In the case presented here, mechanical ventilation was initiated 1 day before the onset of the patient's symptoms, with continuous use of fentanyl and dexmedetomidine for sedation. Therefore, 12 hours prior to the onset of symptoms, the patient had been administered fentanyl, dexmedetomidine, and propofol in connection with tracheostomy. While propofol has been widely reported as an anesthetic agent that can cause ADRs when used alone, the literature includes few reports of ADRs associated with the combination of fentanyl and dexmedetomidine, as our patient received [6]. The mechanism behind ADRs caused by these anesthetic agents may involve an imbalance between dopaminergic and cholinergic neurotransmission in the basal ganglia circuit, since a fine balance between dopamine and acetylcholine receptors is essential for neuromuscular coordination [4]. ADRs can manifest with a variety of clinical symptoms, including oculogyric crisis, oromandibular dystonia, and laryngeal dystonia [1,2]. Although laryngeal dystonia is only rarely reported to be caused by neuroleptics, it is potentially life-threatening [7,8]. Notably, dystonic reactions in the airways can be fatal in cases of neuromuscular disease. Consequently, the early diagnosis and treatment of ADRs are of paramount importance.

Treatment options for ADRs include the intravenous administration of benzodiazepines, such as diazepam and midazolam, or anticholinergic agents (e.g., benztropine). Antihistaminergic agents may also be considered in some cases [1,2]. In our case, we initially administered midazolam as the first-line of treatment and observed improvements in the patient's oculogyric crisis and tongue dyskinesia 30 minutes after administration. However, symptoms recurred 4 hours later, likely due to the diminishing effects of the drug after its 3-hour half-life. Nevertheless, the continued use of midazolam should be approached with caution due to its potential hypotensive effects.

In Thailand, a patient with severe myasthenia gravis experienced a reaction following the administration of multiple anesthetic agents and received treatment with intravenous diazepam [6]. In our case, diazepam was given orally, considering its hypotensive effects, and the patient's dystonic reactions quickly subsided. We attribute this outcome to diazepam's inhibition of the tonic release of dopamine, which in turn influences the balance between dopaminergic and cholinergic activity [9].

Importantly, patient conditions sometimes deteriorate, necessitating transfer to the ICU and the initiation of mechanical ventilation. Consequently, prompt implementation of brain imaging and electroencephalography is crucial for differential diagnosis, followed by the application of appropriate conservative measures and careful monitoring. In certain circumstances, immediate brain imaging may be difficult due to the patient's condition. It is advantageous to quickly determine whether clinical symptoms suggestive of ADR manifest after the initial administration of a sedative drug, even when brain imaging cannot be performed right away. In such instances, the intravenous administration of benzodiazepines may represent a suitable first-line option for symptom management. It is imperative to recognize that ADRs can result from the use of general anesthetic agents and may pose a threat to the patient's life. Therefore, prompt medical attention in an emergency department is strongly advised.

Conflict of Interest

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

Acknowledgements

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Supplementary materials

Further details on supplementary materials are presented online (available at https://doi.org/10.18214/jend.2023.00157).

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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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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.

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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.

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The title page should be uploaded online as a separate file and should describe the title of the article, full names of authors, institutional affiliation(s) with each author. English names should not be described in initials. All authors' ORCIDs should be described.

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Conclusions should avoid unqualified statements that are not adequately supported by the data and describe briefly novel findings of the study, according to the purpose of the study.

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If necessary, persons who have made contributions to the study, but who are not eligible for authorship may be named in this section. Their contribution must be specified, such as data collection, financial support, statistical analysis, or experimentation.

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