저칼륨혈증 마비: 서로 다른 두 증례의 보고

정익진, 이해인, 유현준, 권희규, 이항재, 편성범

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Hypokalemic Paralysis: A Report of Two Different Cases

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Hypokalemic paralysis is a cause of acute paralysis that can be classified as primary (familial) or secondary according to its etiology. Routine electrodiagnostic examinations can be normal between attacks, potentially interfering with the diagnosis. We report two cases of hypokalemic paralysis with different etiologies. The first case involved secondary hypokalemic paralysis due to pharmacologic potassium shift, which was diagnosed by an electrodiagnostic study within the symptomatic period. The second case provides information on the diagnostic approach to primary hypokalemic periodic paralysis during the inter-attack period, as the diagnosis was made using the long exercise test. This case report highlights the need for a proper combination of routine electrodiagnostic studies and special techniques, such as the long exercise test, in patients suspected of hypokalemic paralysis to evaluate the disease state and exclude other possible causes of paralysis.

Keywords: Hypokalemic periodic paralysis; Electromyography; Long exercise test

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Introduction

Hypokalemic paralysis is characterized by symmetric muscle weakness due to low serum potassium levels, which is completely disappeared when the potassium levels become normalized. It can be classified into primary (familial) or secondary depending on the etiology. Primary hypokalemic paralysis, which is called hypokalemic periodic paralysis (HPP), is mostly caused by a gene mutation that codes calcium or sodium channel in skeletal muscle. It is quite rare, with an estimated prevalence of 1 in 100,000. Secondary hypokalemic paralysis can be caused by potassium ion loss through the gastrointestinal or renal system. It

can also be developed by an intracellular shift of potassium ion by pharmacologic causes such as insulin and beta-adrenergic agonists [1-3].

Although hypokalemic paralysis can be suspected with clinical features, electromyography (EMG) can be used to help to establish the diagnosis. During the attack of paralysis, compound muscle action potential (CMAP) amplitude declines and increased small polyphasic motor unit action potentials (MUAPs) with decreased interference pattern can be observed on the needle EMG. However, the routine electrodiagnostic examination can be normal between the attacks. Therefore, many provocative tests have been proposed. Among them, the long exercise test

(LET) has been regarded as the most useful and sensitive diagnostic test for HPP in the inter-attack state and is recommended by muscle channelopathies guidelines [4-6].

In this article, we reported two cases of hypokalemic paralyses. The first case is a secondary hypokalemic paralysis in diabetic ketoacidosis, and the second case is the HPP. The EMG study was performed during the paralytic attack in the first case, while it was performed between attacks in the second one. Therefore, each case presented distinct electrodiagnostic findings. We reported diagnostic approaches to hypokalemic paralysis according to symptoms and intended to emphasize the timely diagnosis of EMG study and utility of the LET.

Case Reports

Case 1

A 27-year-old male was admitted to the emergency department because of dyspnea. He had a medical history of diabetes. The initial arterial blood gas analysis was confirmed as metabolic acidosis of blood pH 7.09 (normal range, 7.35-7.45), bicarbonate 3.2 mmol/L (normal range, 22-26 mmol/L), and anion gap 28 (normal range, 14-18). The serum glucose level was 340 mg/dL (normal range, 70-100 mg/dL when fasting) and the HbA1C level was 10.6% (normal range, < 5.7%). The intravenous insulin supply was carried out under the diagnosis of diabetic ketoacidosis.

The muscle weakness of bilateral upper and lower extremities occurred, four days after the initiation of insulin therapy. On physical examination, the Medical Research Council (MRC) grades of proximal and distal extremities were grade 2/5 and 3/5, respectively. There was no sensory loss and the deep tendon reflexes were hypoactive. On the laboratory findings, the serum potassium level was 2.0 mmol/L (normal range, 3.5-5.0 mmol/L), which was 4.6 mmol/L at the time of admission. The thyrotropin level was 0.48 μ IU/mL (normal range, 0.4-4.0 μ IU/mL), and free T4 level was 1.17 ng/dL (normal range, 0.7-1.4 ng/dL); which is euthyroid state. The thyroid function test results excluded the possibility of thyrotoxic periodic paralysis.

The electrodiagnostic study was performed one day after the onset of muscle weakness. On the motor nerve conduction study (NCS), most of the CMAP responses showed prolonged latencies with decreased amplitudes (Table 1). On needle EMG, decreased insertional activities were noted in deltoid and brachioradialis muscles; and increased insertional activities were noted in the first dorsal interossei muscle. MUAPs were not observed in the deltoid muscle and showed reduced interference patterns in the biceps brachii, brachioradialis, and gastrocnemius muscles (Table 2). The patient denied any family history that could lead to muscle weakness. Along with the patient's medical history, laboratory testing, and EMG findings, we made the diagnosis of secondary hypokalemic paralysis due to insulin therapy. Oral potassium replacement therapy had started, and the serum potassi-

Table 1. Nerve Conduction Study Findings for Case 1

	Nerve, side	Stimulation site	Recording site	Latency (ms)	Amplitude	NCV (m/s)	F wave (ms)	Distance (cm)
Motor	Median, left	Wrist	APB	5.1*	1.8*	-	29.8	-
		Elbow	APB	9.8*	1.7*	47*	-	-
	Ulnar, left	Wrist	ADM	5.9*	3.5*	-	31.5*	-
		Below elbow	ADM	9.7*	3.4*	47*	-	-
		Above elbow	ADM	11.8*	3.2*	48*	-	-
	Tibial, left	Ankle	AH	5.3*	6.1	-	NR*	-
		Knee	AH	13.4*	4.1	40	-	-
	Peroneal, left	Ankle	EDB	5.9*	0.4*	-	NR*	-
		Fibular head	EDB	12.6*	0.4*	37*	-	-
		Knee	EDB	14.5*	0.4*	37*	-	-
Sensory	Median, left	Wrist	III digit	3.0/3.7	32	-	-	14
		Palm	III digit	1.0/2.0	52	-	-	7
	Ulnar, left	Wrist	V digit	2.8/3.4	31	-	-	14
	Sural, left	Calf	Ankle	3.2/4.0*	20	-	-	12
	Superficial peroneal, left	Calf	Ankle	2.6/3.3	13	-	-	12

Soleus Hoffman reflex: right side, NR; left side, NR.

Amplitudes are measured in millivolt (mV, motor) and microvolt (μ V, sensory); onset/peak latency used in sensory nerve conduction.

NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor hallucis; NR, no response; EDB, extensor digitorum brevis; -, not applicable.

*Abnormal value.

Table 2. Needle Electromyography Findings for Case 1

Side	Muscle	Insertional activity	Spontaneous activity	Motor unit action potentials	Interference pattern
Left	Deltoid	Decreased	-	-	Absent
	Biceps brachii	Normal	-	Normal	Reduced
	Brachioradialis	Decreased	-	Normal	Reduced
	First dorsal interossei	Increased	-	Normal	Normal
	Vastus medialis	Normal	-	Normal	Normal
	Tibialis anterior	Normal	-	Normal	Normal
	Gastrocnemius	Normal	-	Normal	Reduced

-, not applicable.

um level returned to normal of 4.0 mmol/L in one day with the full recovery of the muscle strength.

Case 2

A 63-year-old male visited the emergency department due to the sudden onset of motor weakness. The MRC grades of proximal and distal extremities were grade 2/5 and 3/5, respectively. The sensory examination was normal and deep tendon reflex was hypoactive. He has a family history of his son diagnosed with HPP. Routine laboratory study and arterial blood gas analysis were normal except for hypokalemia of 2.1 mmol/L. Oral potassium replacement was begun under the probable diagnosis of HPP, resulting the remission of muscle weakness with serum potassium level 4.5 mmol/L.

The electrodiagnostic study was performed one day after the recovery of motor strength. On the NCS, all the motor and sensory responses were within normal limits (Table 3). On needle EMG, polyphasic and small amplitude MUAPs with reduced interference patterns were noted in the deltoid and biceps brachii muscles, but there were no abnormal findings in other muscles examined (Table 4).

For accurate differential diagnosis, LET was performed. First, CMAPs recorded from the left abductor digiti minimi muscle were monitored every 30 seconds for 3.5 minutes before exercise to stabilize the baseline. Then, the patient was asked to contract the muscle as strong as possible for 5 minutes with monitoring CMAPs every 30 seconds. After the 5 minutes of exercise, the patient was asked to relax while CMAPs were recorded every 2 minutes for 40 minutes. During exercise, CMAP amplitude and area showed increment from baseline; 14.2% and 32.2%, respectively. Additionally, the prolonged gradual decline of CMAP amplitude and area was noted with the periods of rest; up to 34.8% and 57.5%, respectively (Fig. 1). The patient refused genetic testing for confirmatory diagnosis of HPP due to the cost of the test. However, based on the LET findings and the family history, we diagnosed the patients as HPP.

Discussion

Hypokalemic paralysis has heterogeneous etiologies with a final common clinical symptom which presents as an acute systematic weakness. An electrodiagnostic study is a valuable diagnostic tool and should be conducted to differentiate other possible causes of weakness [7]. In this article, we described two cases of hypokalemic paralysis; one is secondary hypokalemic paralysis, and the other is the HPP, a hereditary type. This case report is meaningful in that it provided a comprehensive review of hypokalemic paralysis that occurred after insulin treatment for diabetic ketoacidosis.

There are several reports about the mechanisms of muscle weakness due to hypokalemia. One of them is paradoxical depolarization. When hypokalemia is occurred, paradoxical depolarization is triggered and the resting membrane potential of muscle fiber is sustained at -60 mV, resulting in sodium channel inactivation. Another is hyperpolarization. Hypokalemia results in the hyperpolarization of the cell membrane potential, which leads to depolarization block of the muscle fiber membrane. The blockage of membrane depolarization decreases muscle fiber excitability, resulting in reducing CMAP amplitude and decreased insertional activity in EMG study. Also, increased insertional activities and spontaneous activities may be observed in the early attack of paralysis [8,9]. In the first case, most of the CMAP amplitudes were very small, and decreased insertional activities were observed. Especially, there were no MUAPs on the deltoid muscle. The prolongation of motor and sensory latencies and absent or prolonged F wave and H reflex was considered to be due to the early phase of diabetic polyneuropathy. This electrodiagnostic result was compatible with the prior reports of hypokalemic paralysis on its maximal period of paralytic attack [2].

In HPP, which has muscle channelopathies, underlying muscle fiber membrane instability exists. The LET reveals a progressive loss of muscle fiber excitability in the asymptomatic phase of the patient with HPP. It is known that there is an abnormal incre-

Table 3. Nerve Conduction Study Findings for Case 2

	Nerve, side	Stimulation site	Recording site	Latency (ms)	Amplitude	NCV (m/s)	F wave (ms)	Distance (cm)
Motor	Median, left	Wrist	APB	3.2	9.7	-	27.4	-
		Elbow	APB	7.7	9.2	54	-	-
	Ulnar, left	Wrist	ADM	2.7	10.4	-	28.7	-
		Below elbow	ADM	6.3	9.8	57	-	-
		Above elbow	ADM	8.3	9.2	50	-	-
	Tibial, left	Ankle	AH	5.3	16.4	-	48.6	-
		Knee	AH	12.8	10.8	51	-	-
Sensory	Median, left	Wrist	III digit	2.7/3.4	28	-	-	14
		Palm	III digit	1.3/2.0	39	-	-	7
	Sural, left	Calf	Ankle	3.4/4.0	11	-	-	14

Soleus Hoffman reflex: right side, 29.2 ms; left side, 29.6 ms.

Amplitudes are measured in millivolt (mV, motor) and microvolt (μ V, sensory); onset/peak latency used in sensory nerve conduction.

NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor hallucis; -, not applicable.

Table 4. Needle Electromyography Findings for Case 2

Side	Muscle	Insertional activity	Spontaneous activity	Motor unit action potentials	Interference pattern
Left	Deltoid	Normal	-	Polyphasic, small	Reduced
	Biceps brachii	Normal	-	Polyphasic, small	Reduced
	First dorsal interossei	Normal	-	Normal	Normal
	Vastus medialis	Normal	-	Normal	Normal
	Tibialis anterior	Normal	-	Normal	Normal
	Peroneus longus	Normal	-	Normal	Normal

-, not applicable.

Fig. 1. Long exercise test findings from the abductor digiti minimi muscle recording. (A) The compound muscle action potential (CMAP) amplitude showed a 14.2% increment and a 34.8% decrement during and after exercise, respectively. (B) The CMAP area showed a 32.2% increment and a 57.5% decrement during and after exercise, respectively.

ment of CMAP during the exercise period, followed by a prolonged gradual decrement during the post-exercise phase [5]. This increment and decrement of CMAP may appear in the normal population. However, based on recent research, 40% ampli-

tude or 50% area decrement with the peak-to-nadir method is suggested as optimal cutoff points for diagnosis [10]. In the second case, the CMAP area decreased to 57.5%, which corresponds to the suggested cutoff values. The LET takes consider-

able time and has an obstacle that is accompanied by discomfort due to repetitive stimulation to the same nerve. Therefore, the examiner should set stimulation intensity to the just supramaximal to minimize the patient's discomfort from stimuli. Since the genetic testing for HPP may require several weeks for results and the cost of analysis is prohibitively high, the importance of LET is once again highlighted.

The limitation of our report is that the completeness of the data has been compromised. First, we could not perform a follow-up EMG study due to the patient's refusal. Also, in the second case, we did not conduct peroneal nerve motor conduction study, and ulnar and superficial peroneal nerve sensory conduction studies. Considering that the patient's weakness was fully recovered at the time of the examination and the rest of the nerve conduction studies were within normal limits, the above conduction studies were thought to be less diagnostic but to increase the patient's discomfort. Another limitation was that we could not perform the genetic testing to exclude or confirm HPP in both cases. Although it is a very rare circumstance, in the first case, the possibility that underlying HPP may exacerbate hypokalemia due to insulin treatment cannot be completely excluded. Early diagnosis and management of hypokalemic paralysis is important since it can prevent life-threatening complications. However, periodic symptoms may resolve when patients visit a hospital, and the serum potassium level may be normal, which makes the diagnosis difficult. This case report highlights that the EMG study is a useful and sensitive diagnostic test for hypokalemic paralysis. A proper combination of routine EMG study and LET should be performed in patients suspected of hypokalemic paralysis to evaluate the disease state and exclude other possible causes of paralysis.

Conflict of Interest

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

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