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Throtoxic Periodic Paralysis without Hypokalemia

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Thyrotoxic periodic paralysis (PP) is the most common acquired form of PP in Asian populations, and its cardinal and biochemical abnormality is hypokalemia. We describe a 39-year-old man who had acute bilateral limb motor weakness and paresthesia, and showed normokalemia during attack. Thyroid studies showed subclinical thyrotoxic Goiter. Control of the hyperthyroidism nearly eliminated his PP. Regardless of normokalemia, our patient might be a case of hypokalemic PP because of improvement from anti-thyroid medication.

Key Words: Periodic paralysis, normokalemia, hyperthyroidism

Periodic paralysis (PP), characterized by recurrent attacks of muscle weakness, is traditionally classified as hypokalemic, hyperkalemic, or normokalemic PP according to serum potassium levels measured during attacks.[1] Thyrotoxic hypokalemic PP is the most common acquired form in Asians, whereas familial PP is the most prevalent form in Caucasians.[2]

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Normokalemic PP, a variant of hyperkalemic PP due to mutation of the sodium channel gene (*SCN4A*), is a less well known and not a distinct disorder.[3] Although several reports have been issued on thyrotoxic normokalemic PP,[2,4,5] the mechanism of which has not been determined. Here, we present a patient of sporadic normokalemic PP associated with mild hyperthyroidism.

Case report

A previously healthy 39-year-old man suddenly experienced motor weakness of both upper and lower extremities, to the extent that he could not go upstairs or crouch the day before admission. His weakness developed without obvious provocation, such

Table 1. Nerve conduction study (NCS)

Nerve (Right)	Site	Attack → Normal	Provocation
Motor NCS			
Median nerve	Wrist-APB	11.7 → 11.1	-
	Elbow-APB	11.4 → 10.1	-
Ulnar nerve	Wrist-ADQ	12.2 → 15.5	-
	Elbow-ADQ	11.0 → 14.8	-
Peroneal nerve	Ankle-EDB	5.1 → 7.7	9.4
	FH-EDB	4.8 → 7.4	8.0
	PF-EDB	4.0 → 6.7	7.4
Posterior tibial nerve	Ankle-AHB	12.4 → 12.8	12.5
	PF-AHB	11.4 → 11.4	11.8
Sensory NCS			
Median nerve	Finger-Wrist	18.9 → 39.7	-
	Wrist-Elbow	53.7 → 59.6	-
Ulnar nerve	Finger-Wrist	15.6 → 24.4	-
	Wrist-Elbow	21.8 → 47.9	-
Sural nerve	LM-Calf	7.4 → 7.1	8.9

Values are mV (CMAP) or μV (SNAP). APB; abductor pollicis brevis, ADQ; adductor digiti quintii, EDB; extensor digitorum brevis, AHB; abductor hallucis brevis, PF; popliteal fossa, LM; lateral malleolus.

as, exercise, the consumption of excessive carbohydrates, or acute stress, although he had experienced flu-like symptoms (rhinorrhea, a non-productive cough, and a mild headache) two days prior to admission. He had not taken any medication, alcohol, or drugs, and had no family or previous history of PP. His vital signs included a blood pressure of 130/70 mmHg, a pulse rate of 80/min, a respiration rate of 20/min, and a skin temperature of 36.6℃. A physical examination revealed an enlarged thyroid gland. Motor power evaluations showed symmetric motor weakness of the lower extremities, which was graded as MRC (Medical Research Council) grade III in the proximal portions and MRC grade IV in the distal portions with hyporeflexia. He also complained of subjective paresthesia in upper and lower extremities.

On the first admission day, a nerve conduction study (NCS) (Medelec Synergy version 10, U.K.) during the attack showed unremarkable findings (Table 1). Laboratory findings checked during the attack showed an elevated creatine kinase level [537 IU/L (normal, 74~246)], and normal serum sodium and potassium levels of 145 (normal, 135~145) and 4.1 mmol/L (normal, 3.3~5.5), respectively. All other laboratory findings, including hepatic enzyme, calcium, and acetylcholine receptor antibody, were within normal limits. Cerebrospinal fluid analysis showed a normal finding including no white blood cell, and normal protein level [19 mg/dL (normal, 12~60)]. Under the tentative diagnosis of Guillain-Barré syndrome, intravenous gamma immunoglobulin therapy was started. On the day after admission (48 hours after symptom onset), he found a full restoration of his limb power on awakening, and a neurological examination confirmed normal muscle power in limbs. Four hours later, however, symmetric motor weakness of both lower extremities (MRC grade III in the proximal portion, MRC grade IV in the distal portion) and limb paresthesia developed again without any preceding events.

Serum electrolyte levels during this attack showed a sodium level of 142 mmol/L, and a potassium level of 3.5 mmol/L. The PP lasted for 2 hours and improved without potassium supplementation. Since such features are compatible with periodic paralysis

rather than Guillain-Barré syndrome, we have stopped further gamma immunoglobulin therapy. Serum thyroid function test revealed an elevated levels of T3 [2.63 ng/dL (normal; 0.6~1.81)], free T4 [2.68 ng/dL (normal; 0.89~1.76)], and a low level of thyroid stimulating hormone (TSH) [<0.08 ng/dL (normal; 0.35~5.50)]. Furthermore, serum anti-microsomal antibody was high [>260 IU/mL (normal; 25~30)], and TSH receptor antibody was elevated to 4.2 U/L (normal; ~1.5). Acetylcholine receptor binding antibody was 0.044 nmol/L (normal; ~0.2). An iodine-131 thyroid scan revealed diffusely increased uptake in an enlarged thyroid gland compatible with Grave's disease. However, He had shown no clinical symptoms related to hyperthyroidism, such as heat intolerance, weight loss, or palpitation.

On the 4th hospital day, he no longer complained of motor weakness. Follow up NCS showed relative increase in amplitudes of compound muscle action potentials (CMAPs) and sensory nerve action potentials (SNAPs) compared to the initial study (Table 1). Needle electromyography (EMG) from limb and paraspinal muscles also showed normal findings. Repetitive nerve stimulation test on the right abductor digiti quintii, deltoid, and nasalis muscles demonstrated no decrement of CMAP amplitude more than 20% at lower rate (5 Hz) stimulation.

The provocation test was performed on the 5th hospital days. A strenuous exercise[6] for 5 minutes (walking up and downstairs while gripping his hands) did not produce any symptom.[6] His serum electrolyte levels checked immediately after exercise were 145 mmol/L of sodium and 4.2 mmol/L of potassium. And a follow-up NCS demonstrated no reduction of CMAP or SNAP (Table 1) on either lower extremity. The long exercise test was performed on abductor digiti quintii by stimulating ulnar nerve at wrist with recording of CMAPs every minute for 40 minutes. The decrement was only slight and was 14.8% (decrements of >40% are classified as abnormal). Follow up EMG also produced unremarkable findings. He has been on anti-thyroid medication (propylthiouracil at 100 mg t.i.d.) since the 6th hospital day, and the PP has not recurred over 11 months follow up.

Discussion

In our patient, NCS and needle EMG were repeated by the same technician and physician respectively. It is noteworthy that our patient was not hypokalemic during attack of PP, which is quite unusual for thyrotoxic PP. We offer possible explanations for this 'normokalemia' as follows. First, a clinico-laboratory mix-up may have existed, and the normokalemic recovery may actually have preceded the PP. Second, a relatively mild degree of hyperthyroidism might have had a weak effect on serum potassium. In fact, thyrotoxicosis is known to affect potassium homeostasis by increasing Na^+-K^- pump expression and activity and by increasing beta-adrenergic hypersensitivity.[7] Finally, our patient may have had true normokalemic thyrotoxic PP. All previously reported cases of thyrotoxic normokalemic PP[2,4,5] have involved adult men, and in these studies, PP was not associated with provoking factors, such as, exercise, the consumption of excessive carbohydrate, trauma, acute stress, or alcohol ingestion, which is consistent with findings in our patient. Furthermore, they have stated that provocation did not induce paralysis in those with normokalemic thyrotoxic PP.[2,4,5]

In thyrotoxic hypokalemic PP, it is believed that an extracellular to intracellular potassium shift results from an adrenergic effect on Na^+/K^+ ATPase. Furthermore, β_2-receptor in skeletal muscle is believed to play an important role in this process.[8] In addition, a previous electrophysiological study in hypokalemic PP showed that CMAP amplitude is reversibly reduced by axonal hyperpolarization due to extracellular K^+ depletion.[9] SNAP was also found to be affected in a three case series of hypokalemic PP,[10] and it was suggested that the incomplete blood-nerve barrier of dorsal root ganglia might make sensory neurons particularly vulnerable to derangements associated with low serum potassium con-

centrations.[10] Although less significant, SNAP amplitude differences during ictal and the nonictal phases were also observed in our patient, which may have been related to his limb paresthesia.

Prolonged exercise testing is of value for identifying patients with PP.[6] Hypokalemic PP is characterized by a major decrement in CMAP (〉40%) after provocation testing. This decrement is defined as [(highest CMAP amplitude after exercise − smallest CMAP amplitude after exercise) / (highest CMAP amplitude after exercise)×100],[6] and the mean sensitivity of this test has been reported to be 63%.[10] Our patient showed only a small change in CMAP amplitude (*ca*. 14.8%) after provocation testing.

We describe a case of PP without hypokalemia in a patient with mild hyperthyroidism, and suggest that normokalemia in this patient could have resulted from a mild degree of hyperthyroidism or clinico-laboratory temporal mismatch. Although we could not exclude *SCN4A* mutation, it is most likely that our patient has thyrotoxic hypokalemic PP because of improvement from anti-thyroid medication.

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