

# Glucocorticoid Induced Hypokalemic Periodic Paralysis in Subclinical Hyperthyroidism: Case Report

## Glukokortikoid Kullanımına Bağlı Hipokalemik Periyodik Paralizi Gelişen Subklinik Hipertiroidizm Olgusu

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### Abstract

Thyrotoxic periodic paralysis (TPP), the most commonly seen disorder among Asian men, is characterized by abrupt onset of hypokalemia and paralysis. The underlying hyperthyroidism is often subtle, which causes difficulty in early diagnosis. Factors such as high-carbohydrate eating habit, excessive exercise, use of steroid, and stress can precipitate a TPP attack. We, hereby, present a young Turkish man who developed acute paralysis after receiving intravenously applied dexamethasone for weever fish poisoning. His serum potassium level was 2.3 mmol/l. Moreover, he had subclinical hyperthyroidism and elevated serum creatinephosphokinase (CPK: 609 U/L) and hypophosphatemia (p:1.8 mg/dl). He had neither a loss of renal (24 h urinary potassium: 19.9 mmol) nor gastrointestinal potassium. His muscle strength and serum potassium were fully recovered after a small amount of potassium replacement. The patient was diagnosed as Steroid induced TPP in subclinical hyperthyroidism and was treated with nonselective beta blockers to prevent the possible attacks. In conclusion, we deduced that Steroid induced TPP may develop even in the presence of subclinical hyperthyroidism. We want to share our experience on this issue to raise awareness.

**Keywords:** Hypokalemia, Periodic Paralysis, Steroid, Hyperthyroidism

### Özet

Tirotoksik periyodik paralizi (TPP) çoğunlukla asyalı genç erkeklerde görülen, ani başlayan, hipokalemi ve paralizi ile karakterize bir hastalıktır. Altta yatan hipertiroidizm sıklıkla belirgin olmayıp erken tanı koymak zordur. Aşırı karbonhidrat alımı, aşırı egzersiz, steroid kullanımı ve stress gibi etkenler TPP atağını tetikleyebilir. Biz, bu olguda balık sokması (weever fish) nedeni ile intravenöz deksametazon uygulandıktan sonra akut paralizi gelişen genç erkek hastayı sunduk. Hastanın serum potasyum düzeyi (2.3 mmol/l) ve fosfor düzeyi (1.8 mmol/l) düşük, keratin kinaz düzeyi (609 U/l) yüksekti. Hastada subklinik hipertiroidi saptandı. Renal (24 saat idrar potasyum düzeyi 19.9 mmol/l) ve gastrointestinal potasyum kaybı yoktu. Hastaya tirotoksik hipokalemik periyodik paralizi tanısı kondu. Tedavide akut atakları önlemek üzere nonselektif beta bloker başlandı. Olgumuzu; subklinik hipertiroidi varlığında bile steroid ile TPP atağının tetiklenebileceğine dair farkındalık sağlamak üzere sunmak istedik.

**Anahtar Kelimeler:** Hipokalemi, Periyodik Paralizi, Steroid, Hipertiroidizm

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### Introduction

Hypokalemic periodic paralysis (HPP) is a heterogeneous disease having characteristics of episodic muscle paralysis connected with hypokalemia during the period of the attacks due to the shift of potassium from plasma into muscle cells. HPP has both familial and non-familial forms. Familial form is inherited from an autosomal-dominant pattern. Nonfamilial HPP may occur in the presence of hyperthyroidism called as thyrotoxic periodic paralysis (TPP) or in the absence of hyperthyroidism called as spontaneous periodic paralysis (SPP) (1).

Thyrotoxic periodic paralysis (TPP) is a disease featured by acute and reversible episodes of muscle weakness coming from a massive shift of potassium into cells in the presence of high levels of thyroid hormone (2). TPP ingenerates more commonly in men at a ratio of 20:1 and 90% of patients are descended from the Asian (3). The condition

primarily has an effect on the lower extremities. The underlying hyperthyroidism is often subtle, which causes difficulty in early diagnosis. The thyrotoxic patients have an underlying tendency for muscle Na/K-ATPase over activity deteriorated by steroid use, catecholamines, insulin or excessive exercise (4). In this report, we describe a 30-year-old Turkish man suffering from a TPP attack after receiving dexamethazone. The potential mechanisms of glucocorticoid-induced TPP are discussed hereby.

### Case

A 30 year old Turkish man was admitted to the emergency department one hour after exposed to a weever fish sting in his right hand. He immediately suffered from abrupt onset of severe pain and right after his thumb became swollen and red. The patient was given intravenously an antihistamine, non-steroid anti-inflammatory drug and 8 mg dexamethazone. After a couple of hours the pain subsided but myalgia and fatigue occurred, which bring about weakness predominantly in both legs. He was referred to our hospital for a specialist's opinion. He was admitted to our hospital after 10 hours of weever fish sting exposure. His vital signs

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were as follow: body temperature 37°C, blood pressure 120/70 mmHg, pulse rate 88 beats/min, and respiratory rate 16 breaths/min. Electrocardiography revealed no abnormalities. The thyroid was not palpably enlarged. There was not any sign of exophthalmos. Neurological examination noticed flaccid paralysis in both lower extremities. Deep tendon reflexes were not

observed in lower extremities. The rest of the clinical examinations were unremarkable. At that time his serum potassium was 2.3 mmol/l (3.5-5.1mmol/l), free T4 was 12.7 pmol/L (12-22 pmol/L) and free T3 was 4.07 pmol/L (3.1-6.8 pmol/L), TSH was 0.13 mIU/L (0.27-4.2mIU/L). His laboratory studies are listed in Table 1.

**Table 1.** Laboratory data on first admission, pre-treatment, post-treatment.

First admission	Pre-treatment	Post-treatment
urea:28 mg/dl	urea:23 mg/dl	urea:25 mg/dl
creatinin:0.68 mg/dl	creatinin:0.61mg/dl	creatinin:0.7 mg/dl
Na:136 mg/dl	Na:141 mg/dl	Na:137 mg/dl
<b>K:3.0 mmol/l</b>	<b>K:2.3 mmol/l</b>	K:4.2 mmol/l
<b>glucose:223 mg/dl</b>	<b>glucose:142 mg/dl</b>	glucose:100 mg/dl
AST:20 u/L	<b>24 h urinary potassium: 19.9 mmol</b>	AST:19 u/L
ALT:19 u/L	<b>P: 1.8 mg/dl</b>	P:2.9 mg/dl
<b>CK:529 u/L</b>	<b>CK:609 u/L</b>	CK:205 u/L
wbc:12100	FT3:4.07pmol/L	wbc:7000
hgb:15.2 mg/dl	FT4:12.7 pmol/L	hgb:15.6
plt:166000	<b>TSH:0.13 mu/m</b>	plt:160000
	EMG: low-amplitude compound muscle action potential with no change after epinephrine.	

The patient fully recovered in 24 hours after the following treatment of the hypokalemia via intravenous potassium administration. He had subclinical hyperthyroidism, elevated serum creatine phosphokinase and hypophosphatemia at the same time. He did not have a family history on similar symptoms. He remembered that he had had other two mild attacks before. He had no renal or gastrointestinal potassium loss. In the light of these findings, we considered the diagnosis of the patient would be thyrotoxicperiodic paralysis. We started to give him propranolol to prevent attacks. Before he was discharged, his neuromuscular functions of the patient were fully recovered and also serial measurement of his serum potassium level remained within normal limits without oral potassium supplements during his stay in the hospital.

## Discussion

Patients with TPP are typically young adult males between the ages of 20–40. Attacks occur

intermittently and they are characterized by transient episodes of muscle weakness that range from mild weakness to flaccid paralysis. Proximal muscles are affected more than distal muscles and the attacks tend to involve the lower limbs first with progression to upper limbs. Episodes may last a few hours up to 72 h (2-4). Precipitating factors, including high carbohydrate loads, strenuous exercise, trauma, high-salt diet, emotional stress, exposure to cold, alcohol ingestion, menstruation, and use of drugs such as corticosteroids, have been reported with attacks of TPP. TPP occurs when the patient is thyrotoxic and it is abolished by a return to a euthyroid state (2-4).

Recent studies have provided interesting insights into the mechanism of hypokalemia. These studies have shown that mutations in the gene encoding Kir2.6, a skeletal muscle-specific Kir channel, are associated with TPP and they predispose these patients to acute paralytic attacks. Thyroid hormone upregulates the transcription of Kir2.6 through an upstream thyroid hormone

responsive element in the promoter region of channel gene (5,6).

The principle biochemical abnormality during a TPP attack is hypokalemia. Pathophysiologic details of this transcellular potassium shift into the cells are, however, not well understood. It is believed to be related to increase Na/K-ATPase pump activity in skeletal muscle due to direct stimulation by thyroid hormone,  $\beta$ -adrenergic hormones and insulin (2,4,7). Glucocorticoids may induce hypokalemia from a transcellular potassium shift caused by several mechanisms such as an increased Na<sup>+</sup> and steroid-induced hyperinsulinemia and hyperglycemia (7). Steroids can also cause muscle weakness rooting renal potassium loss and myopathy (7-9). In our patient, we assumed that the mechanism of TPP was that the thyroid hormone stimulated the skeletal muscle and in this way Na/K-ATPase enhanced the pump activity and glucocorticoids application caused the potassium shift by forming hyperinsulinemia and hyperglycemia. The patient suffered hypokalemia and weakness after glucocorticoid administration; therefore, the attack may be within the compass of TPP and/or glucocorticoid effects.

TPP can be difficult to diagnose because the hyperthyroidism may be mild and clinically manifest itself with only subtle symptoms and signs (2,4). The thyrotoxic symptoms may be absent at the time of attack of TPP in 10–25% of the patients. Most patients with TPP have only mildly elevated serum thyroid hormone levels and only about 10% of patients may have mild thyrotoxic symptoms. Using the Wayne's index, a reliable quantitative score of hyperthyroid severity, it was found that only 17% of TPP patients had toxic thyrotoxicosis (score > 19), supporting the notion that most TPP patients have equivocal symptoms (10). A high index of suspicion is needed for the diagnosis of TPP, especially in a young to middle aged male of Asian ethnicity who develops hypokalemia and paralysis. Biochemical hyperthyroidism with normal urinary potassium excretion clinches to diagnosis of TPP. Occurrence and severity of TPP do not depend on severity and etiology of thyrotoxicosis (10).

In the literature, we detected only one study in which the TPP development in subclinical hyperthyroidism has been observed so far. In Kalita's study, two-thirds of the patients with TPP had subclinical thyrotoxicosis/hyperthyroidism (11). Therefore, in our article, we describe a patient with subclinical hyperthyroidism who suffered from TPP after the use of glucocorticoid. To create awareness among physicians, we intend to share our experience about this issue in as much as this awareness may give the opportunity of an early diagnosis, appropriate treatment and the prevention of possible attacks.

The definitive treatment of TPP is to control the hyperthyroid state. Hypokalemia will eventually correct itself by shifting out of the intracellular compartment. Potassium replacement is used to hasten recovery and prevent cardiac arrhythmias. During replacement, the patient needs to be carefully monitored due to a possibility of rebound hyperkalemia. A nonselective  $\beta$ -blocker, propranolol, is considered to be a first-line agent in the treatment of acute TPP and in preventing attack (2-4,10).

In conclusion, TPP has to be always kept in mind while evaluating a case of hypokalemic paralysis. We reported an unusual case of TPP precipitated by the use of steroid. Acute paralysis, after the use of steroids, should raise a suspicion for TPP, especially in an Asian patient, even in the presence of subclinical hyperthyroidism.

**Informed Consent:** Written informed consent was obtained from patient who participated in this case (03.03.2015).

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