

## CASE REPORT

# Thyrotoxic hypokalemic periodic paralysis in an African male: a case report

Dereje K. Belayneh<sup>1</sup> & Thomas Kellerth<sup>2</sup>

<sup>1</sup>International Cardiovascular Hospital, Addis Ababa, Ethiopia

<sup>2</sup>Department of Cardiology, Örebro University Hospital, Örebro, Sweden

### Correspondence

Dereje K. Belayneh, International Cardiovascular Hospital, Addis Ababa, Ethiopia. Tel: +25 1 011 442 4680; Fax: 0221126683/90; E-mail: dereketema@gmail.com

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### Key Clinical Message

Thyrotoxic hypokalemic periodic paralysis is a rare manifestation of thyrotoxicosis and is rarely reported in non-Asian populations. A 26-year-old Ethiopian male who presented with recurrent flaccid tetraparesis, hypokalemia, and hyperthyroidism is reported here. Thyroid function should be routinely checked in patients with acute or recurrent hypokalemic paralysis.

### Keywords

Hyperthyroidism, hypokalemia, paralysis, thyrotoxic hypokalemic periodic paralysis.

## Introduction

Hypokalemic periodic paralysis is characterized by diffuse muscle weakness associated with hypokalemia due to a transient shift of potassium into cells. It may occur spontaneously (sporadic hypokalemic periodic paralysis), as an autosomal dominant muscle disease (familial hypokalemic periodic paralysis), or as a rare manifestation of hyperthyroidism (thyrotoxic hypokalemic periodic paralysis, TPP). TPP must be distinguished from the sporadic and familial forms of hypokalemic periodic paralysis, since restoration to the euthyroid state in the former will result in complete remission of paralytic attacks [1].

TPP is more common in young Asian males than in Caucasians or Africans [2], and the condition may be overlooked, creating the potential for misdiagnosis in the latter populations. Failure to recognize and treat this condition appropriately may lead to potentially lethal cardiopulmonary complications.

## Case Presentation

In February 2011, this 26-year-old Ethiopian male awoke in the morning with bilateral paralysis of his extremities. When he presented to the emergency department 4 h later he exhibited partial recovery. He had no associated

swallowing or breathing difficulty, weakness of the facial muscles, sphincter disturbances, pain, sensory symptoms, or change in mental state. Two months earlier, he had undergone a similar episode, beginning after midnight, which resolved spontaneously within 3 h. He had been experiencing heart palpitations for several months, along with heat intolerance and failure to gain weight despite a good appetite. He had no other known prior medical or surgical illnesses. He denied alcohol abuse or illicit drug use and was not on any medications. No similar weakness or other remarkable diseases in the family was reported.

At presentation, his blood pressure was 120/80 mmHg and his heart rate was 114 beats/min. He had no thyromegaly, and his skin was warm and dry. He was fully oriented and cooperative. No gross cranial nerve deficits were noted. He demonstrated flaccid symmetrical proximal and distal weakness of the arms and legs (power: legs 3/5, arms 4/5). Knee and ankle deep tendon reflexes were depressed bilaterally (grade 1/4). Sensation was intact.

Blood tests showed serum  $K^+$ , 2.7 mmol/L (normal range: 3.6–5.5);  $Mg^{2+}$ , 1.8 mg/dL (normal range: 1.9–2.5); and creatine kinase-total, 223 IU/L (normal range: 38–174). Serum phosphate was not determined, but results of the remainder of the electrolyte panel, complete blood count, and blood chemistry were normal. Thyroid-stimulating hormone (TSH) was less than 0.0005 IU/mL

(normal range: 0.27–4.2), free triiodothyronine ( $T_3$ ) was 17.72 pg/dL (normal range: 2.02–4.43), and free thyroxine ( $T_4$ ) was 5.33 ng/dL (normal range: 0.93–1.71). The ECG showed sinus tachycardia at 120 beats/min, U waves fused with P waves, and inferior T-wave inversions (Fig. 1). Results of an electromyography and a nerve conduction study conducted the following day were within normal limits. Because of logistical constraints, a thyroid radioiodine uptake scan could not be done until  $\approx 6$  weeks later, during which time the patient had been receiving antithyroid medication. The results were reported normal.

## Treatment

Intravenous potassium chloride infusion was initiated within a half-hour of arrival at the hospital. After 30 min, serum  $K^+$  was reported to be 4.2 mmol/L, and the infusion was stopped. He completely recovered muscle strength within an hour of arriving at the hospital.

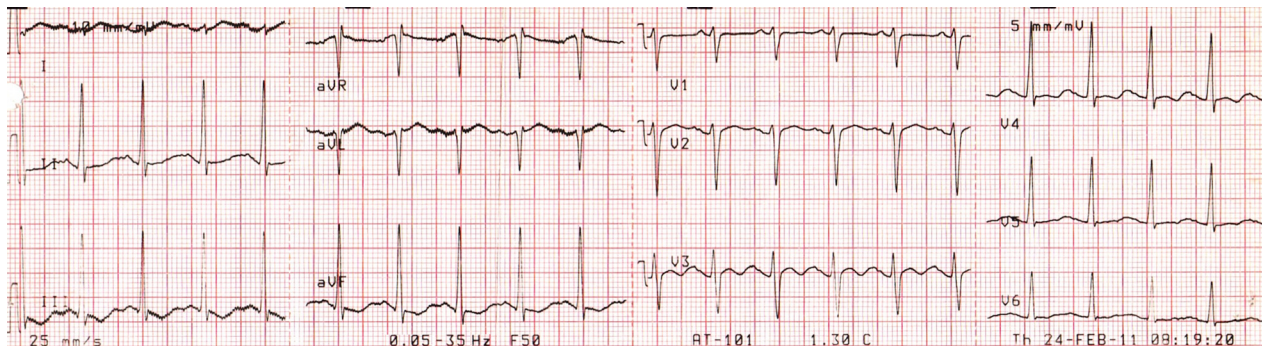
Serum potassium levels measured over the following 2 days ranged from 4.0 to 4.4 mmol/L. An ECG  $\approx 24$  h

after arrival (Fig. 2) showed sinus rhythm at 94 beats/min with distinct P waves, T wave inversions in the inferior leads, and small U waves in  $V_2$  and  $V_3$ . Treatment with oral propylthiouracil and propranolol was initiated, and he was discharged after 48 h in the hospital.

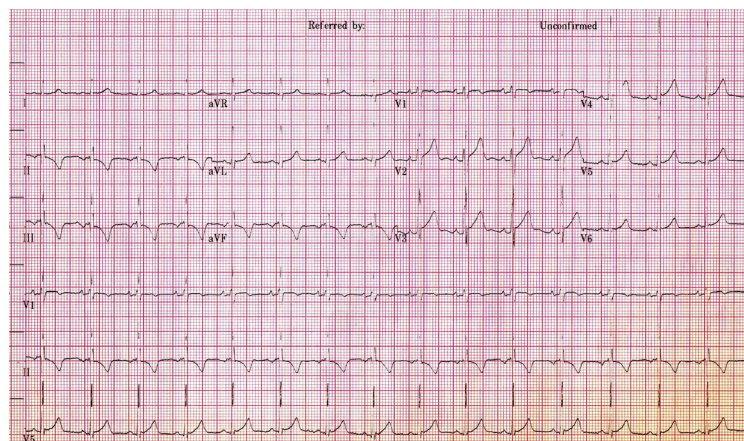
At an outpatient follow-up visit 6 weeks later, the patient was clinically and biochemically euthyroid. During follow-up over the ensuing 3 years, he has remained euthyroid, gained weight, and has experienced no recurrence of the paralysis.

## Discussion

TPP is primarily seen in young Asian males. The incidence reported in 1991 was 1.1% among hyperthyroid Japanese patients overall and 4.3% among hyperthyroid Japanese males [3]. It occurs in only 0.1–0.2% of North American hyperthyroid patients, mainly in Caucasians [1]. The disease is rare in blacks, with most cases having been reported in North America. A literature review revealed few cases reported in blacks of African ethnicity



**Figure 1.** Twelve lead electrocardiogram taken at the emergency department showing P waves partly hidden in the preceding U waves.



**Figure 2.** Twelve lead electrocardiogram taken a day after admission showing small U waves particularly in the precordial leads.

from Europe [2, 4–6]. Although thyrotoxicosis is most often seen in females, TPP disproportionately affects men at a ratio of 20:1 [7]. The usual age of presentation is in the second to fourth decades, consistent with the age distribution of thyrotoxicosis [8].

TPP is distinguished from the other forms of periodic paralyses in that the paralytic episodes occur in association with the hyperthyroid state and remit with restoration to the euthyroid state [1]. Grave's disease is the most common cause of hyperthyroidism in TPP, but thyrotoxicosis of any cause can trigger attacks in susceptible individuals [9].

It has been shown that  $\text{Na}^+/\text{K}^+$  ATPase activity is significantly higher in patients with TPP than in healthy subjects or thyrotoxic patients without periodic paralysis [10]. In addition, thyroid hormone sensitizes the cell to beta-adrenergic stimulation of  $\text{Na}^+/\text{K}^+$  ATPase [11]. Insulin resistance with compensatory hyperinsulinemia has also been suggested to play a role in the pathogenesis of TPP [10]. It is postulated that in TPP these mechanisms result in hypokalemia resulting from acute intracellular shift of potassium, subsequently leading to hyperpolarization of the skeletal muscle membrane and inexcitability of the muscle fibers.

Genetic abnormalities of voltage-gated skeletal muscle sodium, calcium, and potassium channels linked with familial periodic paralysis have not been identified in patients with TPP [12]. One study has identified a gene encoding an inwardly rectifying potassium (Kir) channel, Kir2.6, expressed in skeletal muscle and transcriptionally regulated by thyroid hormone. Loss-of-function mutations of this gene have been reported in up to 33% of Caucasian and Brazilian and 25% of Singaporean TPP patients, but in <1% of TPP patients from Hong Kong and Thailand, suggesting unique genetic contributions to TPP in populations of different ethnicities [13]. Some of these mutations alter the conductance properties of Kir2.6, resulting in alterations in skeletal muscle membrane excitability leading to paralysis.

Clinically, TPP is manifested by sudden onset of skeletal muscle paralysis that can range in severity from mild, transient, and self-limiting weakness of the extremities to severe tetraplegia with life-threatening respiratory failure and cardiac arrhythmia. There is more severe involvement of proximal than distal muscles [8]. The attacks of muscle weakness usually occur during the night or early morning hours [14]. They can also be precipitated by strenuous exercise or occur at rest after a large carbohydrate meal and can last from hours to days [15]. Deep tendon reflexes are usually markedly depressed or absent, but sensory function is generally preserved. Symptoms of hyperthyroidism, such as anxiety, weight loss, palpitations, and heat intolerance may be present but are often

subtle or absent [9]. Thus, thyroid function tests should be routinely conducted in patients exhibiting features of hypokalemic paralysis.

The degree of hypokalemia during attacks is variable; a study of 135 TPP patients showed initial potassium levels of  $2.17 \pm 0.4$  mmol/L [14]. Other laboratory findings include normal acid–base status, low urinary potassium excretion, mild hypomagnesaemia, hypophosphatemia associated with hypophosphaturia, and hypercalciuria [16]. Characteristically, thyroid function tests are consistent with hyperthyroidism with very low TSH and markedly elevated  $\text{T}_3$  and  $\text{T}_4$  values. Electrocardiographic changes strongly suggestive of TPP include those with typical features of hypokalemia and, in contrast to hypokalemia from other causes, sinus tachycardia. Other findings may include atrioventricular block, atrial fibrillation, asystole, and ventricular fibrillation [17].

Initial management of TPP relies on immediate and cautious potassium supplementation to prevent serious cardiopulmonary complications and to hasten the recovery of muscle function [1]. Since total body potassium is not depleted, close attention must be given to potassium replacement, as aggressive treatment can cause drastic rebound hyperkalemia [16]. Potassium supplements are not useful to prevent future attacks and should not be given [8]. Nonselective beta-adrenergic blockers (e.g., propranolol) can ameliorate and prevent recurrence of the paralytic attacks by reversing the adrenergic overstimulation of  $\text{Na}^+/\text{K}^+$  ATPase and thus blocking the intracellular sequestration of potassium [18].

Definitive treatment, resulting in complete remission of attacks, rests on management of the underlying thyrotoxicosis. Options for treatment to achieve a euthyroid state include antithyroid medications, thyroidectomy, or radioiodine therapy. Radiation thyroiditis with transient hyperthyroidism and recurrence of paralytic attacks following radioiodine therapy has been described [19]. This risk can be minimized by longer periods of initial treatment with antithyroid medications in order to deplete the thyroid hormone reserves.

## Conclusions

Thyrotoxic hypokalemic periodic paralysis (TPP) is an unusual complication of hyperthyroidism rarely seen in non-Asians, with the potential for misdiagnosis in other ethnic groups. Accordingly, there should be a high index of clinical suspicion for TPP, and thyroid function tests should be routinely conducted in patients with features of hypokalemic paralysis. Acute attacks of paralysis are managed with carefully administered potassium supplementation. Effective treatment of the underlying thyrotoxicosis prevents recurrence of the paralysis.

## Conflict of Interest

None declared.

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