Journal of Clinical Case Reports

Case Report Open Access

# Thyrotoxicosis Induced Periodic Paralysis with Severe Hypokalemia Causing Bradycardia and Cardiac Arrest: Case Report and Literature Review

**Haddad M* and Harris T**

*Department of Emergency Medicine, Hamad Medical Corporation, Doha, Qatar*

## Abstract

**Background:** Thyrotoxic periodic paralysis (TPP) is one of rare group of disorders called periodic paralysis. The usual presentation is lower limb weakness attributed to an intracellular shift of potassium. When the presentation is accompanied by increased thyroid hormone level the diagnosis of TPP can be made, and the treatment of acute attacks should be targeting hyperthyroidism with beta-blocker and antithyroid drugs, in addition to replacement of serum potassium with cautions. Cardiac arrhythmias are one of the possible complications that can occurs with tachyarrhythmias most commonly associated with TPP.

**Case presentation:** We report a case of an Asian male who presented with bilateral lower limb weakness, his venous blood gas showed sever hypokalaemia and quickly developed bradycardia followed by cardiac arrest. The patient later found to have thyrotoxicosis and diagnosed with TTP.

**Conclusion:** The diagnosis of TPP is often delayed due to similar presentation with familial periodic paralysis. The treating physician should have a low threshold for measuring the thyroid hormones. A patient with TPP can have variable arrhythmias with tachyarrhythmias being most common, but bradyarrhythmia can happen as with our case.

**Keywords:** Emergency department; Hypokalemia; Cardiac arrest; Hypokalemic thyrotoxic periodic paralysis; Familial periodic paralysis; ECG; Potassium supplementation

## Introduction

Thyrotoxic periodic paralysis (TPP) is one of three types of periodic paralysis, a rare group of disorders that can cause of sudden onset weakness (1). Death is rare (2). It resolves with treatment of the underlying thryrotoxicosis. Familial hypokalaemic periodic paralysis (FHPP) is an inherited condition characterized by ypokalaemia and limb weakness/paralysis. TPP is most commonly seen in Asian men (male: female ration 20:1) and occurs in approximately 2% of all thyrotoxic patients of Asian descent. Hypokalemia results from an intracellular shift of potassium induced by the thyroid hormone sensitization of Na+/K+–ATPase, rather than depletion of total body potassium (12). We report an unusual case of hypokalaemia cardiac arrest with successful resuscitation.

## Case Report

A 36 year old Filipino male presented with lower limb muscle weakness. He awoke to find he was not able to move his lower limbs, was weak in both arms and had abdominal cramps, loose stool and palpitations. He had eaten a rice-based meal the previous night. He reported a similar episode 3 years previously, which had resolved with intravenous potassium. He received no follow up or further investigation. He was not taking any medications. Examination revealed a GCS of 15, pulse 88, blood pressure 115/60. Examination of cardiovascular and respiratory systems were unremarkable. Cranial nerves II-XII were intact. Power was 3/5 upper limbs and 0/5 lower limbs with reduced tone and reflexes. A fine tremor in both hands was noted. Neck examination revealed no thyroid mass. A venous blood gas showed an unrecordable potassium level and the patient was transferred to the resuscitation area in the emergency department. Electrocardiogram shown in figure 1. A provisional diagnosis of familial hypokalaemic periodic paralysis (FHPP) was made. On arrival in the resuscitation area he was bradycardic and rapidly developed asystole. Immediate cardiopulmonary resuscitation resulted with return of spontaneous circulation with a heart rate of 25 beats per minute. 20 mmol of intravenous potassium was administered mg of IV magnesium. Investigations are reported in Tables 1-5.

## Clinical course

The patient returned to GCS 15 immediately post his brief period of cardiac arrest and his neurological examination had normalized around an hour later. A repeat blood gas posts the initial intravenous potassium bolus showed a potassium of 1.6 mmol/L. He received a further 120 mmol of oral potassium throughout his stay in divided doses. His potassium was normalized by around 11 hours post presentation. Thyroid function testing available on the evening of the same day showed profound hyperthyroidism, confirming the diagnosis of thyrotoxic periodic paralysis. He was observed for 24 hours and

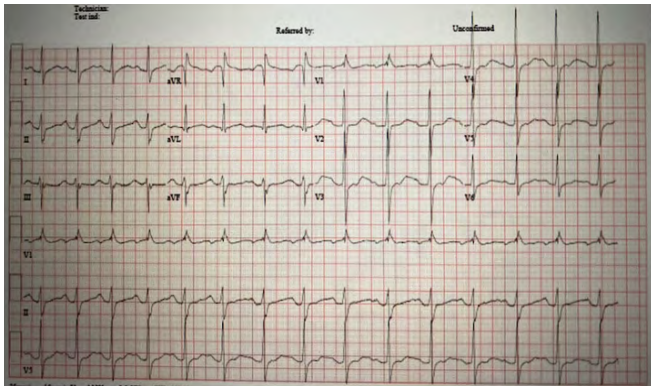

**Figure 1:** Electrocardiogram which shows features of hypokalemia.

***Corresponding author:** Haddad M, Department of Emergency Medicine, Hamad Medical Corporation, Doha, Qatar, Tel: +97466257009; E-mail: m.k.h93@icloud.com

**Received** January 24, 2020; **Accepted** March 19, 2020; **Published** March 26, 2020

**Citation:** Haddad M, Harris T (2020) Thyrotoxicosis Induced Periodic Paralysis with Severe Hypokalemia Causing Bradycardia and Cardiac Arrest: Case Report and Literature Review. J Clin Case Rep 10: 1331

| Variables | TPP | FHPP |
|---|---|---|
| Age at initial presentation | 20-40 | <20 |
| Sex distribution | Predominantly male | Equal |
| Genetic inheritance | Sporadic | Autosomal dominant |
| Ethnicity | Asian, American Indian/Hispanic, Caucasian | Caucasian, Asian |
| Family history | History of thyrotoxicosis | History of hypokalmeic paralysis |
| Clinical features of hyperthyroidism | Yes | No |

**Table 1:** Distinguishing features between TPP and FHPP.

| Serial VBG* | 04:26 am | 04:53 am | 06:48 am | 15:53 pm |
|---|---|---|---|---|
| PH | 7.37 | 7.37 | 7.39 | 7.44 |
| Na | 142 | 143 | 144 | 142 |
| K | Unrecordable | 1.6 | 1.8 | 5.5 |
| Other parameters | Normal | Normal | Normal | Normal |
| *Venous blood gas | | | | |

**Table 2:** Venous blood gas investigation.

| CBC* | 5:54 am |
|---|---|
| WBC | 7.9 |
| RBC | 5.6 |
| Hb | 14.7 |
| Platelet | 174 |
| *Complete blood count | |

**Table 3:** Complete blood count investigation.

| Serial BMP* | 05:54 am | 08:22 am | 18:30 pm |
|---|---|---|---|
| Urea | 4.6 | 3.7 | 2.5 |
| Creatinine | 64 | 55 | 55 |
| Sodium | 141 | 145 | 140 |
| Potassium | 1.5 | 2.2 | 4.6 |
| Chloride | 108 | 111 | 106 |
| Bicarbonate | 20 | 25 | 24 |
| Calcium core | 2.3 | 2.3 | 2.4 |
| Magnesium | 0.77 | | |
| *Basal Metabolic Panel | | | |

**Table 4:** Basal metabolic panel investigation.

| TFT, PTH** | |
|---|---|
| TSH | **<0,01** |
| FT4 | **56** |
| FT3 | **20.3** |
| PTH | 18.8 |
| *Thyroid function test<br>*Parathyroid hormone | |

**Table 5:** Hormonal profile investigation.

discharged on oral carbimazole and propranolol, with endocrinology follow up.

## Discussion

TPP and FHPP have distinct aetiologies. In TPP excess thyroid hormone, β-adrenergic catecholamines, and insulin all increase the Na+ to K+-ATPase pump activity in skeletal muscles, liver, kidneys and platelets [4].

A 1991 Chinese study exploring the mechanism of TPP measured the platelet Na+/K+–ATPase and *in vivo* sodium pump activities in healthy subjects and thyrotoxic subject with and without paralysis. They studied five groups of subjects:

- 21 healthy subjects, who denied taking any recreational or medical drugs.
- 23 thyrotoxic subjects with elevated T3, T4 and low TSH plasma concentration, who had not started on anti-thyroid treatment.
- 13 men with TPP who were admitted to the hospital with weakness or paralysis and studied within 48 hours of admission after correction of serum potassium level and muscle weakness but before starting beta-blockers and antithyroid drugs or both.
- Seven thyrotoxic subjects receiving treatment who were clinically and biochemically euthyroid.
- Six men who had episodes of TPP and who were receiving treatment and had clinically normal thyroid function.

The result showed that in thyrotoxic subjects the level of $Na^+/K^+$ ATPase (median 253 umol/h/g protein) was significantly higher than ($p<0.001$) that in healthy subject (134 umol/h/g protein) [3].

In subjects with TPP the platelet $Na^+/K^+$ ATPase activity (374 umol/h/g protein) was higher than that in healthy subjects ($p<0.001$) and patients with similarly severe thyrotoxicosis and no TPP ($p<0.01$). In patients with treated thyrotoxicosis with or without TPP the level of platelet $Na^+/K^+$ ATPase activity was similar (148 umol/h/g protein), and (131 umol/h/g protein) respectively. The authors concluded that $Na^+/K^+$ ATPase activity in patients with hyperthyroidism complicated

by TPP is higher in patients with uncomplicated hyperthyroidism, which may explain the mechanism causing hypokalemia [13-24]. In contrast to TPP, FHPP is an autosomal dominant disorder with the most common mutation involving a mutation in the gene that codes for the alpha-1 subunit of the dihydropyridine-sensitive calcium channel in skeletal muscle. How the calcium channel defect leads to episodic potassium movement into the cells and causes weakness is poorly understood [25,26].

Patients with TPP do not have the hereditary genetics causal of FHPP, but may also have a channelopathy, which in euthyroid state is not sufficient to create symptoms [7]. TPP occurs as a consequence of thyrotoxicosis and primarily affects the lower extremities [12]. Some individuals have only one episode, but recurrent episodes are more common [11]. The age of onset of the first attack ranges from 2 to 30 years old, with the duration of paralytic episodes averaging around 24 hours range from one to 72 hours) [11]. Common triggers include cessation of effort following strenuous exercise and carbohydrate-rich evening meals. Additional triggers can include cold, stress, excitement, fear, salt intake, prolonged immobility, use of corticosteroids or alcohol, and aesthetic procedures. The attacks of paralysis tend to occur during the night, as in the case presented here.

The diagnosis of TPP and FHPP are often delayed. An American retrospective chart review of 37 cases admitted with any type of hypokalemic periodic paralysis (30 with TPP, 6 FHPP, and one spontaneous periodic paralysis) reported that most patients underwent extensive diagnostic evaluation; including:

- Lumbar punctures;
- Electromyograms;
- Nerve conduction velocity studies;
- Head computed tomographic scan;
- Head
- Spine magnetic resonance imaging scans;
- Spine radiographs;
- Serum tests for human immunodeficiency virus,
- Microhemagglutination-Treponema pallidum assays,
- Fluorescent antinuclear antibody,
- Rheumatoid factor assays and
- Toxicologic screens.

When first seen in the emergency department, 8 patients were diagnosed as having familial or sporadic hypokalemic paralysis, 4 as having Guillain-Barré syndrome, 3 as having muscle weakness, one as having polymotor neuropathy, one as having acute muscular strain and one as having alcohol related myopathy. Only one patient had the correct initial diagnosis of TPP at admission to the hospital. Acute attack TPP should be distinguished from other causes of acute paralysis, such as FHPP, myasthenic crisis, Guillain-Barré syndrome, tick paralysis or botulism. In TPP proximal muscles are more severely affected than the distal muscles, and myalgia and stiffness are common. There is no involvement of the sensory system and mental function is intact. Usually cranial nerves, bulbar, ocular, and respiratory systems are spared. Deep tendon reflexes are usually lost but the anal and bladder sphincter tones are preserved. TPP is often misdiagnosed as familial hypokalemic periodic paralysis (FHPP) because of similarities in precipitating factors and the clinical pattern of paralysis. The neuromuscular presentations of both FHPP and TPP are identical and a low threshold to assess for hyperthyroidism is required. Early diagnosis aids in definitive management with nonselective beta-blockers and correction of hyperthyroidism. The absence of a family history of paralysis, male gender, presentation in the second to fourth decades of life, signs of thyrotoxicosis, laboratory abnormalities including mild hypophosphatemia and/or hypomagnesemia, and the electrocardiogram (ECG) changes described below suggest the diagnosis (Table 1).

Guillain-Barré syndrome is differentiated from TPP by its presentation of ascending paralysis and abnormal cerebrospinal fluid findings. Botulism is a toxin-mediated condition that presents as descending flaccid paralysis with the muscles of the head and neck are initially affected. In contrast to TPP, both Guillain-Barré syndrome and botulism can affect the respiratory system and lead to respiratory distress. Although neuromuscular disorders such as myasthenia gravis and Lambert-Eaton syndrome can present with extremity weakness, these are the result of an autoimmune reaction affecting the neuromuscular junction and do not typically present with electrolyte abnormalities. The usual clinical presentation of myasthenia gravis is muscle weakness which can affect any muscle group and is classically worse at the end of the day. Patients with Lambert-Eaton syndrome usually present with slowly progressive proximal muscle weakness and demostrate recovery of lost deep tendon reflexes or improvement in muscle strength with muscle activation. There are three possible life-threatening complications of FHPP and TPP:

- Hypokalemia leading to cardiac arrythmias.
- Weakness or paralysis of respiratory muscles leading to acute respiratory insufficiency.
- Inability to move that can lead to death if it occurs in a hostile environment (e.g. drowning) [11].

The ECG in TPP and FHPP may show the characteristic features of hypokalaemia, (ST depression, decrease in the amplitude of the T wave, an increase in the amplitude of U waves and prolonged PR interval). A range of arrhythmias may be associated with hypokalemia, including sinus bradycardia, premature atrial and ventricular beats, paroxysmal atrial or junctional tachycardia, atrioventricular block, ventricular tachycardia and ventricular fibrillation [8]. ECG features suggesting TPP include a relatively rapid heart rate, high amplitude QRS voltage and first-degree AV block [9]. The case presented here is unusual in that the presentation was bradycardia. In a retrospectively study of 19 patients with TPP the most frequent electrocardiographic changes observed are ST segment depression with T wave flattening, sinus tachycardia, and U waves, which are typical in hypokalemia and thyrotoxicosis [5]. During an acute episode of TPP the hypokalaemia slows re-polarisation and prolongs the refractory period, so predisposing to arrhythmias. The risk of arrythmias is further increased as ventricular re-polarisation is also lengthened in hyperthyroidism. Cardiac monitoring is necessary until hypokalaemia is corrected [10]. Treatment of TPP includes prevention of the cellular shift of potassium by using nonselective beta-blockade, correcting the underlying hyperthyroid state and replacing potassium. TPP ceases once a euthyroid state is achieved. The treatment of hypokalaemia is with intravenous or oral potassium guided by serum levels, with most clinicians using intravenous potassium below 2.5 mmol/L or in patients unable to be treated orally. Care is required in those cases with renal impairment. Administration of oral potassium should be accompanied with large volume of fluid (100-250 ml) of

water and be given with or after meals. Oral potassium supplements are available in tablet and liquid forms. The high bioavailability of the liquid forms (>85%) allows a peak serum levels to be reached within two hours of oral administration. Tablets and liquid forms are both well tolerated with similar dosing to intravenous regimes and their use is supported by clinical data [13]. Liquid formulations permit the rapid correction of hypokalemia and can be administered by a nasogastric tube.

One American study evaluated correction of potassium in an inpatient setting to evaluate the common practice of administering 10 mmol/L of potassium to increase the serum level by 0.1 mmol/L. The author reported that for every 10 mmol/L of potassium administration there was a mean increase in serum potassium of 0.13 mmol/L. Intravenous potassium increased the serum potassium level little more than oral potassium ( 0.14 per 10 mmol/L versus 0.12 per 10 mmol/L) administered, respectively. Therefore, oral potassium replacement offers similar effect to intravenous replacement in patient with normal gastrointestinal function [15]. Both FHPP and TPP involve potassium shifts as opposed to loss and there is little trial evidence to guide the value or dose of (intravenous or oral) potassium replacement. The current resuscitation guidelines recommends the incremental oral administration of 60 to 120 mmol/L of potassium chloride, for acute attack. Recovery takes minutes to hours. The presence of hypokalemia must be affirmed before starting therapy as potassium administration can worsen episodes due to hyperkalemic periodic paralysis [16]. Potassium administration during an acute episode can lead to rebound hyperkalemia as potassium moves back out of the cells and post treatment potassium levels should be monitored for 24 hours [17,18]. Potassium should not be administered in a dextrose containing solution as the resultant insulin response may cause intracellular shifts [19-26]. A retrospectively study of 19 patients with TPP evaluated clinical features, electrolyte changes, and outcomes of therapeutic interventions. All patients in the study had mild to severe hypokalemia (1.1-3.4 mmol/L) at presentation. Patients received 40 to 200 mmol (mean, 89 mmol) potassium chloride, with normalization of hypokalemia within 1.5 to 10.0 hours (mean, 4.8 hours) of presentation. There was no correlation between recovery time and potassium dose ($r$=0.17). Rebound hyperkalemia occurred in 42% of the 24 episodes in hospitalized patients with TPP, with a maximum serum K level of 6.6 mmol/L. This study demonstrated that in patients who received greater than 90 mmol/L of potassium in 24 hours, 80% developed rebound hyperkalemia. This can be prevented by giving 30 mmol/L of oral potassium every two hours until improvement begins, with a maximum dose of 90 mmol/L in 24 hours, with even slower rates suggested by some authors (<10 mmol/L/ per hour).

## Conclusion

TPP is common in Asian males and presents similarly to FHPP with weakness and hypokalemia. Treatment with potassium supplements may be similarly offered orally or intravenously but TPP also requires the underlying hyperthyroidism to be treated and β-blockers commenced. It has a higher incidence of cardiac arrythmias. Specific ECG features suggest the diagnosis, but clinicians should have a low threshold to measure thyroid function.

### References

1. Soule BR, Simone NL (2008) Hypokalemic periodic paralysis: A case report and review of the literature. Case J 1: 256.
2. Munir I, Mehmood T, Islam K, Soni L, McFarlane SI (2019) Thyrotoxic periodic paralysis with sensory deficits in young African American male: A case report and literature review. Am J Med Case Rep 7: 138.
3. Chan A, Shinde R, Chow CC, Cockram CS, Swaminathan R (1991) *In vivo* and *in vitro* sodium pump activity in subjects with thyrotoxic periodic paralysis. Bmj 303: 1096-1099.
4. Tella SH, Kommalapati A (2015) Thyrotoxic periodic paralysis: An underdiagnosed and under recognized condition. Cureus 7.
5. Manoukian MA, Foote JA, Crapo LM (1999) Clinical and metabolic features of thyrotoxic periodic paralysis in 24 episodes. Arch Int Med 159: 601-606.
6. Mease SJ, Faloon MJ, Dunn CJ, Changoor S, Sahai N, et al. (2019) Thyrotoxic periodic paralysis: A spine consultation. JAAOS Global Res Rev p. 3.
7. Kung AW (2006) Thyrotoxic periodic paralysis: A diagnostic challenge. J Clin Endocrinol Metabol 91: 2490-2495.
8. Kardalas E, Paschou SA, Anagnostis P, Muscogiuri G, Siasos G, et al. (2018) Hypokalemia: A clinical update. Endo Connect 7: 135-146.
9. Hsu YJ, Lin YF, Chau T, Lin SH, Liou JT, et al. (2003) Electrocardiographic manifestations in patients with thyrotoxic periodic paralysis. Am J Med Sci 326: 128-132.
10. Zumar-Sardar K, Waheed AF, Javed MA, Akhtar F, Bokhari SR (2019) Clinical and etiological spectrum of hypokalemic periodic paralysis in a tertiary care hospital in Pakistan. Cureus 11.
11. Ptacek LJ, Tawil R, Griggs RC, Engel AG, Layzer RB, et al. (1994) Dihydropyridine receptor mutations cause hypokalemic periodic paralysis. Cell 77: 863-868.
12. Grézard C, Rivard J, Robinson P, Leboucher G, Charpiat B (2019) Promoting oral potassium administration in a tertiary care hospital: An eleven-year study. Ann Pharmaceut Franc 77: 38-45.
13. Levene DL (1973) Potassium chloride: Absorption and excretion. Canadian Med Assoc J 108: 853.
14. Höck AD (2016) Clinical nephrology and renal care. p. 2.
15. Fontaine B, Lapie P, Plassart E, Tabti N, Nicole S, et al. (1996) Periodic paralysis and voltage-gated ion channels. Kidney Int 49: 9-18.
16. Ober KP (1992) Thyrotoxic periodic paralysis in the United States. Report of 7 cases and review of the literature. Med 71: 109-120.
17. Ko GT, Chow CC, Yeung VT, Chan HH, Li JK, et al. (1996) Thyrotoxic periodic paralysis in a Chinese population. Int J Med 89: 463-468.
18. Lin SH, Lin YF, Chen DT, Chu P, Hsu CW, et al. (2004) Laboratory tests to determine the cause of hypokalemia and paralysis. Arch Int Med 164: 1561-1566.
19. Loh K, Pinheiro L, Ng KS, Ks N (2005) Thyrotoxic periodic paralysis complicated by near-fatal ventricular arrhythmias. Singapore Med J 46: 88.
20. Griggs RC, Resnick J, Engel WK (1983) Intravenous treatment of hypokalemic periodic paralysis. Arch Neurol 40: 539-540.
21. Lu KC, Hsu YJ, Chiu JS, Hsu YD, Lin SH (2004) Effects of potassium supplementation on the recovery of thyrotoxic periodic paralysis. Am J Emerg Med 22: 544-547.
22. Pompeo A, Nepa A, Maddestra M, Feliziani V, Genovesi N (2007) Thyrotoxic hypokalemic periodic paralysis: An overlooked pathology in western countries. Eur J Int Med 18: 380-390.
23. Ryan DP, Da-Silva MR, Soong TW, Fontaine B, Donaldson MR, et al. (2010) Mutations in potassium channel Kir2. 6 cause susceptibility to thyrotoxic hypokalemic periodic paralysis. Cell 140: 88-98.
24. Sillén A, Sørensen T, Kantola I, Friis ML, Gustavson KH, et al. (1997) Identification of mutations in the *CACNL1A3* gene in 13 families of Scandinavian origin having hypokalemic periodic paralysis and evidence of a founder effect in Danish families. Am J Med Genet 69: 102-106.
25. Matthews E, Labrum R, Sweeney MG, Sud R, Haworth A, et al. (2009) Voltage sensor charge loss accounts for most cases of hypokalemic periodic paralysis. Neurol 72: 1544-1547.
26. Schalin-Jäntti C, Laine T, Valli-Jaakola K, Lönnqvist T, Kontula K, et al. (2005) Manifestation, management and molecular analysis of candidate genes in two rare cases of thyrotoxic hypokalemic periodic paralysis. Horm Res Paediat 63: 139-144.