CASE REPORT

Thyrotoxic periodic paralysis as an initial presentation of Graves' disease in a Saudi patient

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SUMMARY

Thyrotoxic periodic paralysis (TPP) is a well-known complication of hyperthyroidism, characterised by recurrent flaccid paralysis with hypokalaemia. To date, only five cases of this rare disorder have been reported in Saudi Arabia. Here, we report an additional case involving a 25-year-old Saudi man who presented with lower limb paralysis and severe hypokalaemia. Clinically, he showed symptoms and signs suggestive of Graves' disease, which was confirmed by laboratory investigations. Carbimazole, a beta-blocker and potassium replacement were administered, resulting in dramatic improvement of the TPP. This case emphasises the importance of considering TPP in patients with acute muscle weakness and the importance of promptly initiating treatment and preventing relapse of TPP.

BACKGROUND

Thyrotoxic periodic paralysis (TPP) is defined as the occurrence of attacks of acute flaccid paralysis and low serum potassium concentration in the presence of hyperthyroidism, as confirmed by thyroid function tests.¹ Between the attacks, the patients show complete recovery. Typically, there is no effect on the sensory system.² TPP most commonly occurs in Asian men aged 20–40 years,³ with an incidence among Asians of approximately 2%. On the other hand, in Western countries, the incidence has been reported as 0.1%–0.2%; however, because of immigration, it has become a familiar manifestation of hyperthyroidism even in these countries.² Similarly, TPP is a highly rare thyrotoxic manifestation in Saudi Arabia, with only five previous cases reported. Here, we report a rare case involving a Saudi patient who presented with TPP as a first manifestation of Graves' disease.

CASE PRESENTATION

A 25-year-old Saudi man presented to the emergency department of Prince Sultan Military Medical City in May 2016, complaining of bilateral lower limb paralysis for 6 hours after awaking from sleep. He had experienced a similar episode 3 weeks earlier, which had improved spontaneously. He had a history of unintentional weight loss of 20 kg over the last 2 years. His family had noticed that he had become increasingly nervous, with protruding eyes, over the last 6 months. He had no history of palpitation, heat intolerance or diarrhoea. There was no history of heavy physical exertion or recent

infection and no history of recent alcohol or carbohydrate-rich food consumption.

INVESTIGATIONS

On examination, the patient was conscious with normal mental function. The hands were moist, with no clubbing or swelling of the digits. His pulse was 111 beats/min, regular with good volume; his blood pressure was 130/82 mm Hg; he was afebrile; and his oxygen saturation was 100% on room air. A fine tremor was observed, along with exophthalmos without lid lag or conjunctival congestion. The thyroid was not enlarged, and no bruit was noted. The respiratory, cardiovascular and abdominal examinations were unremarkable. Neurological examination showed intact cranial nerves, upper limb wasting of the proximal muscles, normal sensation and tone, and brisk reflexes. Examination of the lower limbs showed no muscle wasting, intact sensation, a Medical Research Council scale of muscle power of 0/5, flaccid tone and tender muscles. The ankle and knee reflexes were diminished, while the plantar reflexes were equivocal. No pretibial myxoedema was observed.

ECG showed sinus tachycardia, prolonged QT interval (corrected QT interval 677 ms; normal <440 ms) and decreased T wave amplitude (figure 1).

The diagnosis of Graves' disease with TPP was established based on the laboratory results (table 1).

DIFFERENTIAL DIAGNOSIS

In addition to TPP, the differential diagnoses of acute lower limb paralysis included the following:

- ▶ familial periodic paralysis
- ▶ Guillain-Barré syndrome
- ▶ polymyositis
- ▶ myasthenia gravis
- ▶ acute intermittent porphyria
- ▶ severe hypokalaemia
- ▶ sagittal sinus thrombosis
- ▶ transverse myelitis.

TREATMENT

After the diagnosis of Graves' disease with TPP was established, the patient was admitted to the intensive care unit of our hospital, where he was kept under ECG monitoring and a central line was inserted. An immediate correction of potassium through the central line was started to prevent life-threatening arrhythmia. Potassium chloride infusion (60 mmol in 250 mL 0.9% normal saline) over 2 hours was

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Figure 1 ECG on arrival to the emergency department showed sinus tachycardia, decreased T wave amplitude and prolongation of the QT interval (corrected QT interval 677 ms).

administered along with carbimazole 15 mg orally and propranolol 10 mg orally every 8 hours. The serum potassium level was measured every 2 hours; if it was <4 mmol/L, 20 mmol of potassium chloride in 250 mL 0.9% normal saline infusion was administered over 2 hours. Twenty-four hours from admission, the serum potassium reached 5.4 mmol/L and the creatine kinase (CK) and magnesium levels improved to normal. In addition, the lower limb muscle tenderness disappeared, with improvement of muscle power to a Medical Research Council scale score of 5/5.

OUTCOME AND FOLLOW-UP

Repeat ECG showed resolution of the previous ECG findings (figure 2). The patient was kept for observation for another 24 hours and was subsequently discharged home on carbimazole 15 mg orally and propranolol 10 mg orally every 8 hours. The long-term treatment goals included achieving a euthyroid state as well as preventing the recurrence of TPP. Accordingly, the patient was scheduled for a follow-up appointment at the endocrine clinic in our institute.

Table 1 Laboratory investigations

Laboratory parameter	Results	Normal range
Potassium (mmol/L)	1.8	3.2–5.0
Sodium (mmol/L)	141	135–145
Inorganic phosphate (mmol/L)	1.34	0.81–1.45
Magnesium (mmol/L)	0.6	0.74–1.00
Corrected calcium (mmol/L)	2.2	2.06–2.44
Urea (mmol/L)	2.7	2.0–6.7
Creatinine (μ mol/L)	47	45–84
Creatine kinase (U/L)	554	30–170
Thyroid-stimulating hormone (μ IU/mL)	<0.005	0.270–4.200
Free T4 (pmol/L)	68.3	12–22
Thyroid-stimulating hormone receptor antibody (IU/L)	37.22	0.00–1.75

DISCUSSION

TPP is a rare, fatal complication of thyrotoxicosis.² It may occur secondary to any cause of hyperthyroidism.⁴ However, Graves' disease is the underlying cause of approximately 96% of TPP cases.⁵

TPP is characterised by transient, recurrent episodic attacks of flaccid paralysis involving predominantly the lower limbs. These episodes are not associated with sensory or higher mental function abnormalities.^{4,6} Precipitating factors are identifiable in 34%–50% of cases and include upper respiratory tract infection, heavy physical activity, warm weather, alcohol ingestion and high-carbohydrate diets.^{5,7} Although 70% of TPP cases reportedly occur during the seasons of summer and fall, our patient experienced the attacks during spring.⁵ In addition, although most patients with TPP have high systolic blood pressure, our patient was normotensive during the hospital course.⁶

Our patient had sinus tachycardia, decreased T wave amplitude and prolonged QT interval, as evidenced by ECG. Reportedly, 83% of TPP cases are accompanied by ECG changes, including tachycardia, ST–T changes, U waves, first-degree heart block, prolongation of the QT interval, multiple atrial ectopics and atrial flutter.³ These ECG changes, especially prolongation of the QT interval, put the patients at high risk for developing life-threatening arrhythmia such as torsade de pointes and ventricular arrhythmia.^{8–10}

The hypokalaemia accompanying TPP is caused by an intracellular shift of potassium without a total potassium deficit.⁵ Skeletal muscle is the main pool of potassium in the body; the inward and outward movements of potassium are regulated by Na^+/K^+ adenosine triphosphatase (ATPase) and potassium channels, respectively.¹¹ Thyroid hormones and their stimulatory effects on the adrenergic response can enhance the Na^+/K^+ ATPase activity, causing influx of potassium intracellularly, without a total potassium deficit.^{2,5,11} To maintain the extracellular potassium homeostasis, this influx is supposed to be accompanied by an efflux of potassium via the potassium channels in the skeletal muscles. However, in patients with TPP, it is considered that this potassium efflux mechanism is defective, thereby leading to

Figure 2 ECG 10 hours after starting potassium replacement, propranolol and carbimazole treatment showed improvement of the T wave amplitude and QT interval (corrected QT interval 415 ms).

persistent hypokalaemia and eventually flaccid paralysis.^{5 11} This defect of the potassium efflux mechanism could explain why only 2% of hyperthyroid patients develop TPP. Thus, during paralysis, hypokalaemia is always present, and the severity of hypokalaemia correlates with the severity of the weakness experienced by the patient.⁴ Considering the hormonal effects on Na^+/K^+ ATPase, the concept of using non-selective beta-blockers to prevent paralytic attacks in patients with hyperthyroidism was established. In addition, androgens have been shown to stimulate and increase the expression of Na^+/K^+ ATPase^{2 5}; this androgenic effect could explain the high male-to-female ratio of TPP (20:1),³ despite the fact that hyperthyroidism affects females more commonly than males.⁴

Beside hypokalaemia, the magnesium level in our patient was also low, and he showed increased CK levels, findings that are common in patients with TPP.^{2 4} This mild elevation of CK could explain the lower limb tenderness, which resolved with potassium replacement.¹²

An estimated 67%–83% of TPP cases do not have previously diagnosed hyperthyroidism, and 50% have recurrent attacks of paralysis before the diagnosis of TPP is established.^{3 5} Moreover, 50%–83% of patients with TPP have no symptoms or signs of hyperthyroidism at the time of TPP diagnosis,^{5 7} and about 81% of patients with Graves' disease have no previous history of thyroid disease, with TPP being the first presenting manifestation of thyrotoxicosis.¹³ In some cases, TPP may also be complicated by life-threatening ventricular arrhythmia and rhabdomyolysis.^{8–10}

To our best knowledge, this is only the sixth reported case of TPP in Saudi Arabia.⁸

During the attack of paralysis, the potassium level should be corrected immediately to prevent life-threatening arrhythmia in similar patients. This correction should be made in small doses to avoid the risk of rebound hyperkalaemia. However, potassium supplementation does not have an effect on preventing recurrence of TPP.⁴ Conversely, as mentioned above, non-selective beta-blockers diminish the activity of Na^+/K^+ ATPase and can thus be used both at the time of the attack and to prevent further attacks. In addition, antihyperthyroid treatment should

be commenced to achieve a euthyroid state, which is the only way to achieve complete remission of TPP.^{2–4 8} In the reported cases, all patients with Graves' disease complicated by TPP who underwent total thyroidectomy achieved permanent recovery of TPP. However, non-surgical modalities, namely, anti-thyroid drugs and radioactive iodine, are associated with relapse rates of TPP in patients with Graves' disease of 50% and 43%, respectively.¹³

In conclusion, TPP is a well-known complication of hyperthyroidism. Because of the potential life-threatening sequelae of this disease, a high suspicion is needed for the diagnosis, and prompt and adequate treatment is required. Most patients with TPP are unaware of their hyperthyroidism, and recurrent attacks of TPP often occur before the correct diagnosis can be established. Replacement of potassium should be performed judiciously, under careful monitoring, to avoid the risk of rebound hyperkalaemia. Non-selective beta-blockers are effective for both the immediate treatment, as well as for the prevention of TPP. However, the only way to ensure complete remission of TPP is to achieve a euthyroid state by antihyperthyroidism treatment.

Learning points

- ▶ Although thyrotoxic periodic paralysis (TPP) is rare in Saudi Arabia, it should be included in the differential diagnosis of patients with lower limb weakness, even in patients without known hyperthyroidism.
- ▶ TPP recognition and immediate treatment are crucial to avoid life-threatening complications.
- ▶ There is no total body potassium deficit in patients with TPP; hence, potassium replacement should be performed cautiously and under careful observation.
- ▶ Achievement of a euthyroid state is the only way to ensure complete remission of TPP.

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 Garg RK, Malhotra HS, Verma R, *et al*. Etiological spectrum of hypokalemic paralysis: a retrospective analysis of 29 patients. *Ann Indian Acad Neurol* 2013;16:365–70.
- 2 Aggarwal R, Chugh P. Thyrotoxic periodic paralysis: a short clinical review. *J Res Med Sci* 2015;3:539–42.
- 3 Abbas MT, Khan FY, Errayes M, *et al*. Thyrotoxic periodic paralysis admitted to the medical department in Qatar. *Neth J Med* 2008;66:384–8.
- 4 Pothiwala P, Levine SN. Thyrotoxic periodic paralysis: a review. *J Intensive Care Med* 2010;25:71–7.
- 5 Chang CC, Cheng CJ, Sung CC, *et al*. A 10-year analysis of thyrotoxic periodic paralysis in 135 patients: focus on symptomatology and precipitants. *Eur J Endocrinol* 2013;169:529–36.
- 6 Lu KC, Hsu YJ, Chiu JS, *et al*. Effects of potassium supplementation on the recovery of thyrotoxic periodic paralysis. *Am J Emerg Med* 2004;22:544–7.
- 7 Wi JK, Lee HJ, Kim EY, *et al*. Etiology of hypokalemic paralysis in Korea: data from a single center. *Electrolyte Blood Press* 2012;10:18–25.
- 8 Hakami O, Ahmad MM, Al Johani N. A case of nonfatal ventricular arrhythmia due to thyrotoxic periodic paralysis in a saudi patient as an initial presentation of Graves' disease. *Clin Med Insights Case Rep* 2016;9:5–9.
- 9 Loh KC, Pinheiro L, Ng KS, Ks N. Thyrotoxic periodic paralysis complicated by near-fatal ventricular arrhythmias. *Singapore Med J* 2005;46:88–9.
- 10 Chang KY, Lee SH, Park HS, *et al*. Severe hypokalemia and thyrotoxic paralysis from painless thyroiditis complicated by life-threatening polymorphic ventricular tachycardia and rhabdomyolysis. *Intern Med* 2014;53:1805–8.
- 11 Lin SH, Huang CL. Mechanism of thyrotoxic periodic paralysis. *J Am Soc Nephrol* 2012;23:985–8.
- 12 Glancy DL, Subramaniam PN, Rodriguez JF, *et al*. Lower extremity paralysis. *Am J Cardiol* 2016;118:1609–10.
- 13 Chang RY, Lang BH, Chan AC, *et al*. Evaluating the efficacy of primary treatment for Graves' disease complicated by thyrotoxic periodic paralysis. *Int J Endocrinol* 2014;2014:1–6.

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