CASE REPORT

Thyrotoxic hypokalaemic periodic paralysis: a rare presentation of Graves' disease in a Hispanic patient

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SUMMARY

A 26-year-old Hispanic man with no significant medical history presented to our emergency room with gradual onset weakness of his lower extremities. He was haemodynamically stable and examination revealed loss of motor function in his lower limbs up to the level of hips. Laboratory data revealed hypokalaemia. The patient was started on potassium supplementation and he recovered his muscle strength. Differential diagnosis included familial hypokalaemic periodic paralysis and thyrotoxic periodic paralysis (TPP). Further investigations revealed a low thyroid-stimulating hormone and high free thyroxine levels. Radio iodine 123 scan revealed an enhanced homogeneous uptake in the thyroid suggesting Graves' disease. Thyroid stimulating antibodies were also found to be elevated. The patient was started on methimazole and propranolol and he never had another attack of TPP even at 1 year follow-up.

BACKGROUND

Thyrotoxic periodic paralysis (TPP) is a rare manifestation of Graves' disease which manifests as acute episodic attacks of weakness associated with hypokalaemia. It is commonly reported in Asians, rarely in Hispanics. We present the case of a young Hispanic individual who presented with acute paraplegia and was diagnosed with TPP secondary to Graves' disease. Patients with TPP typically present to the emergency room with recurrent episodes of lower limb weakness and hypokalaemia and are sometimes misdiagnosed with familial hypokalaemic periodic paralysis in the emergency room. We would also like to stress on the importance of obtaining a thyroid stimulating hormone (TSH) level early in the course of the disease as recurrent attacks can be prevented with the appropriate antithyroid therapy with methimazole or propranolol.

CASE PRESENTATION

A 26-year-old Hispanic man with no significant medical history presented to the emergency room with gradual onset weakness of lower extremities of a 6 h duration. He denied any weight loss, heat intolerance, anxiety, palpitations, tremors, diarrhoea or increased perspiration. He was not on any medications at home. He denied smoking, alcohol or illicit drug abuse or any family history of episodic weakness or paralysis. Blood pressure was 124/82 mm Hg, heart rate 84/min, respiratory rate 18/min, temperature 98.4°F and body mass index was 22 kg/sq.m.

Neurological examination revealed a power of 1/5 in the lower extremities and 3/5 in the upper extremities. Sensations to fine and crude touch were intact. Deep tendon reflexes were diminished. Rest of the physical examination was unremarkable and did not reveal any thyromegaly, ophthalmopathy or dermopathy.

INVESTIGATIONS

Laboratory data revealed a low serum potassium level of 1.8 mEq/L (reference range 3.5–5.4) and a TSH level of 0.02 mIU/L (reference range 0.34–5.6).

Urine drug screen was negative for illicit drugs. ECG revealed prominent U waves. The patient was diagnosed with TPP. He was started on intravenous potassium supplementation and recovered his muscle strength within 6 h.

Further investigations revealed an elevated thyroglobulin level of 48.8 ng/mL (reference range 1.3–38.1), T4 2.32 ng/dL (reference range 0.6–1.6) and T3 8.9 pg/dL (reference range 2.5–3.9). TSH receptor antibody level was 5.78 IU/L (reference range <1.75), antithyroid peroxidase 621.2 IU/mL (reference range 0–9) and thyroid-stimulating Ig 156.

The laboratory data is summarised in [table 1](#).

Radio iodine 123 scan of the thyroid showed elevated homogeneous uptake of radiotracer (41% at 4 h and 61% at 24 h) suggesting Graves' disease ([figure 1](#)).

OUTCOME AND FOLLOW-UP

The patient was started on propranolol and methimazole. He made a good clinical recovery in the hospital and was discharged home on methimazole and propranolol. Three-month follow-up after discharge revealed a normal TSH level. The patient was clinically and biochemically euthyroid at 1 year follow-up and never had any episodes of paraplegia.

DISCUSSION

TPP is a very rare but potentially lethal manifestation of hyperthyroidism characterised by acute self-limiting attacks of muscle weakness, that closely resembles familial hypokalaemic periodic paralysis (FHPP).

Epidemiology

It is more common in Asians compared with other ethnic groups such as Hispanics, Caucasians or African-Americans.¹ The incidence on TPP in thyrotoxic patients in North America was found to be 0.1–0.2%.² TPP occurs predominantly in men; the

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Table 1 Summary of laboratory investigations

Laboratory test	Patient value	Reference range
Haemoglobin	14	13–15 g/dL
RBC	5	4.6–6.8×106/ μ L
WCC	7	3.6–10.3×103/ μ L
Platelets	74	140–420×103/ μ L
Sodium	135	135–145 mmol/L
Potassium	1.8**	3.7–5.1 mmol/L
Chloride	102	96–110 mmol/L
Bicarbonate	25	22–32 mmol/L
Total protein	6.2	6–8.4 g/dL
Albumin	3.3	3.5–5 g/dL
Blood urea	15	6–24 mg/dL
Creatinine	1	0.6–1.3 mg/dL
Alkaline phosphatase	75	43–138 U/L
Aspartate transaminase	30	10–40 IU/L
Alanine transaminase	68	12–78 IU/L
Total bilirubin	0.8	<1.5 mg/dL
Prothrombin time/INR	1.19	
Lipase	30	73–393 U/L
TSH	0.02**	0.34–5.6 mIU/L
Troponin	<0.01	<0.49
Free T4	2.23**	0.6–1.6 ng/dL
Free T3	8.9**	2.5–3.9 pg/dL
Thyroid stimulating immunoglobulin	158**	<130
Thyroglobulin	48.8**	1.3–38.1 ng/dL
Anti-TPO	621.2**	0–9 IU/mL
TSH receptor Ab	5.78**	<1.7 IU/L

INR, International Normalised Ratio; RBC, red blood cells; TPO, thyroid peroxidase; TSH, thyroid stimulating hormone; WCC, white cell count.

male–female ratio is approximately 20:1.³ The usual age at presentation is 20–40 years.³

Aetiology

TPP has been reported with Graves' disease, toxic nodular goitre, iodine-induced thyrotoxicosis, excessive thyroxine use, solitary toxic thyroid adenoma, lymphocytic thyroiditis and thyrotropin-secreting pituitary adenomas.³

Pathogenesis

TPP is almost always associated with hypokalaemia. In a study of 135 patients the mean K⁺ level was found to be 2.17 mEq/L.⁴

Figure 1 Radio iodine uptake scan showing increased homogeneous uptake of iodine 123 at 24 h.

The underlying pathology seems to be excessive entry of potassium into the myocytes and subsequent hyperpolarisation of the cell membrane leading to paralysis. Thyroxine directly stimulates the Na⁺ K⁺ ATPase pump by enhancing transcription and directly leading to increased transport of potassium into the cells. The Na⁺ K⁺ ATPase pump activity on skeletal muscles is increased in patients with thyrotoxicosis and paralysis compared to patients who are thyrotoxic without paralysis.^{5 6} Hyperthyroidism can also lead to a hyperadrenal state.⁷ Increased epinephrine release from the adrenal gland can stimulate the β -2 receptors on skeletal muscles and increase K⁺ uptake into the myocytes;⁸ but the whole body stores of potassium remain normal.⁹ Insulin resistance and hyperinsulinaemia are also suspected to be involved in the pathogenesis.¹⁰ A recent Chinese study revealed that patients with TPP had higher total and free testosterone levels than patients with Graves' disease without TPP.¹¹

Genetics

Genetic studies indicate that TPP might be a channelopathy such as FHPP. Mutations of the voltage-dependent calcium channel (Ca(v)1.1 (R528H, R1239H and R1239G)), sodium channel (Na(v)1.4 (R669H, R672G and R672H)) and potassium channel (K(v)3.4 (R83H)) identified in patients with FHPP have not been found in patients with TPP.³ These results suggest that, despite clinical similarities between TPP and FPP the underlying genetic factors seem to be different. The presence of different HLA antigen subtypes in certain populations, such as HLA-DRw8 in Japanese persons, HLA-A2, Bw22, Aw19 and B17 in Singapore Chinese, and B5 and Bw46 in Hong Kong Chinese, may make such persons susceptible to TPP.¹² Mutations of the inward rectifying potassium channel, Kir2.6 were found in 33% of patients with TPP.¹³ The defect in the rectifying current seems to decrease the ability of the cell to correct the hyperpolarised state leading to paralysis.

Clinical features

TPP only affects the skeletal muscles. Episodes of paralysis are usually periodic and self-limiting. The triggering factors include exercise, trauma, high carbohydrate diet, emotional stress or cold exposure. The attacks may be preceded by muscle aches, cramps or stiffness. The attacks are more common early in the morning¹ and the duration can last from a few hours to a few days. The attack of paralysis typically starts in the proximal muscles of the lower limbs. The paralysis can also ascend and lead to flaccid quadriplegia.² Respiratory muscles can also be involved in severe cases.¹⁴ Sensory system and mental status are usually unaffected. Hypokalaemia can lead to typical ECG abnormalities such as ST depression, T wave inversion and prominent U wave.¹⁵ It can lead to cardiac tachyarrhythmias such as ventricular tachycardia and fibrillation.

Management

Acute management of TPP involves potassium supplementation. Patients who received potassium supplementation recovered their muscle strength sooner compared with patients who received normal saline (6.3 vs 13.5 h¹⁶). Intravenous supplementation of potassium leads to shorter recovery time compared with oral supplementation.¹⁷ As the body potassium stores are not depleted, potassium supplementation can sometimes lead to rebound hyperkalaemia after the acute episode has resolved. Intravenous propranolol has been shown to be effective in patients who are refractory to potassium supplementation.^{18 19} Magnesium levels should be checked and supplemented if low. Definitive control of hyperthyroidism completely abolishes the attacks of TPP and

includes antithyroid medications such as propranolol or methimazole, surgical thyroidectomy and radioiodine therapy. Propranolol has been shown to prevent recurrent attacks of TPP by decreasing the peripheral conversion of T4 to T3 and by its antagonist effect β -adrenergic receptors. Potassium supplementation has not been shown to prevent any future attacks. Patients should be advised to avoid any precipitating factors.

Learning points

- ▶ Thyrotoxic periodic paralysis (TPP) is a rare manifestation of Graves' disease.
- ▶ TPP should be considered in the differential diagnosis of patients presenting to the emergency room with acute onset of paralysis or periodic paralysis even in patients not of Asian heritage.
- ▶ Thyroid-stimulating hormone should be a part of the initial workup in the emergency room along with electrolytes.
- ▶ Prompt replacement of potassium will lead to recovery.
- ▶ Intravenous propranolol should be used in refractory cases.
- ▶ Correcting the underlying hyperthyroid state prevents future attacks.

Competing interests None.

Patient consent Obtained.

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