

Hypokalemic thyrotoxic periodic paralysis: a case series

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ABSTRACT

Hypokalemic periodic paralysis is a rare and dramatic complication of hyperthyroidism. This series summarizes the clinical and metabolic features of 10 patients who presented to the Western and Sunshine hospitals in Melbourne, Australia, between 1997 and 2002 with thyrotoxic periodic paralysis (TPP). TPP classically presents with proximal lower-limb weakness in the setting of a low potassium level and biochemical evidence of thyrotoxicosis: low thyroid-stimulating hormone levels along with elevated free thyroxine (FT₄) or free triiodothyronine (FT₃). The challenge for emergency physicians is to recognize the association with thyroid disease, since features of hyperthyroidism may not be apparent on history and examination. Acute treatment with potassium supplements and long-term management is aimed at achieving an euthyroid state. Thyrotoxic periodic paralysis is more common in Asian populations; however, increasing immigration from Asia will lead to higher TPP prevalence in Western countries.

Key words: hypokalemic periodic paralysis; thyrotoxicosis; thyrotoxic periodic paralysis

RÉSUMÉ

La paralysie périodique hypokaliémique est une complication rare et dramatique de l'hyperthyroïdie. Cette série d'articles résume le tableau clinique et métabolique de dix patients reçus au Western Hospital et au Sunshine Hospital à Melbourne, en Australie entre 1997 et 2002 pour une paralysie périodique thyrotoxicque (PPT). La PPT se manifeste typiquement par une faiblesse proximale des extrémités inférieures dans le contexte d'un faible taux de potassium et de signes biochimiques de thyrotoxicose : faibles taux de thyroestimuline et taux élevés de thyroxine (T₄) libre ou de triiodothyronine (T₃) libre. Le défi pour le médecin d'urgence est d'identifier l'association avec l'atteinte de la thyroïde, puisque les caractéristiques de l'hyperthyroïdie peuvent ne pas être apparentes lors de l'anamnèse et de l'examen. Un traitement actif à l'aide de suppléments de potassium et la prise en charge à long terme visent à atteindre un statut euthyroïdien. La paralysie périodique thyrotoxicque est plus courante parmi la population asiatique; cependant, une immigration croissante en provenance de l'Asie conduira à une augmentation de la prévalence de la PPT dans les pays occidentaux.

Case reports

Over a 5-year period, 9 men and 1 woman presented to the emergency departments of Western Hospital and Sunshine Hospital in Melbourne, Australia. Six of the patients were

Vietnamese, and the remaining 4 were Filipino, Korean, Laotian and Caucasian. Their ages ranged from 18 to 58 years (mean 34).

In 9 of the 10 patients, the onset of lower-limb paraplegia occurred at night, between 10:00pm and 6:00am. Prior

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to their paralysis, 3 patients described a physically demanding day at work, 2 reported symptoms of a viral upper respiratory tract infection, 1 had eaten a large meal, another had undergone general anesthesia for circumcision 2 days earlier and 1 had been on an alcohol binge.

All 10 patients described symmetrical, proximal lower-limb weakness. Deep tendon reflexes were diminished in 1 patient, increased in another and normal in 8. None of these patients had sensory findings, cranial nerve abnormalities, ocular signs or respiratory muscle involvement. The most common hyperthyroid findings were a goiter in 4 patients, tachycardia in 4 patients, a thyroid bruit in 2, hyperreflexia in 2, and tremor in 1.

Five patients had a pre-existing diagnosis of hyperthyroidism, and the remainder were diagnosed during their index admission, based on clinical features and biochemical confirmation in 9 cases (low thyroid-stimulating hormone [TSH] levels along with elevated free thyroxine [FT_4] or free triiodothyronine [FT_3]). One patient was biochemically euthyroid. The most common hyperthyroid symptoms were weight loss, tremor, palpitations, heat intolerance, diarrhea and increased appetite. Eight of the 10 were diagnosed with Grave's disease, and 2 had thyrotoxicosis of uncertain etiology.

All patients were hypokalemic, with potassium levels ranging from 1.6 to 2.4 mmol/L (normal 3.5–5.5 mmol/L) (Table 1). Five had decreased phosphate (PO_4) levels, 4 had decreased magnesium (Mg), and 2 had decreased calcium (Ca). Eight patients had electrocardiograms and all were abnormal — 4 showed U waves, and 4 showed sinus tachycardia (ST) depression with T-wave flattening.

Discussion

This study and others show that thyrotoxic periodic paralysis (TPP) is a disease of young Asian males. TPP is 10 times more common in Asian than in non-Asian countries,¹ and although thyrotoxicosis most often affects females, TPP has been reported in 0.11% of Japanese women (v. 4.3%–8.2% of Japanese men) and in 0.17% of Chinese women (v. 12.9% of Chinese men).²

In this series, 90% of patients experienced symptom onset between 10:00pm and 6:00am. These findings are similar to those of Yeo and colleagues, who reported that 88.5% of TPP patients in a Singapore series had symptom onset between 6:00pm and 8:00am.³ Previous authors have identified precipitating factors such as ingestion of a high carbohydrate food load, strenuous physical activity followed by a rest, surgery, and insulin use, and many of these factors were apparent in this case series.

Symmetric proximal lower-limb muscle weakness is characteristic of TPP, but asymmetric involvement may occur. The absence of ocular and respiratory involvement differentiates TPP from myasthenia gravis and Guillain-Barré Syndrome (GBS); however, respiratory involvement is rarely an early finding in GBS. Sensation is preserved in TPP, and deep-tendon reflexes are usually depressed, although the majority of patients in this study had normal deep-tendon reflexes. In cases of proximal muscle weakness, emergency physicians should also consider proximal myopathy, spinal cord lesions, electrolyte abnormalities (including diuretic abuse), primary hypoaldosteronism, and alcoholism in the differential diagnoses. It is im-

Table 1. Features of patients with hypokalemic periodic paralysis

Gender / age / race	Serum potassium levels (mmol/L)*	TSH levels (mU/L)†	Free T_4 / T_3 levels (pmol/L)‡	Initial serum Ca / PO_4 / Mg levels (mmol/L)§	Hyperthyroidism		Etiology of hyperthyroidism
					Symptoms	Signs	
M / 32 / Vietnamese	2.1	<0.02	36.0 / 13.5	2.25 / 0.90 / 0.73	No	Yes	Grave's disease
M / 38 / Vietnamese	2.4	<0.04	33.2 / 11.5	2.31 / 0.96 / 0.75	Yes	Yes	Grave's disease
M / 33 / Vietnamese	1.7	<0.02	54.0 / 13.8	2.29 / 0.67 / 0.69	Yes	Yes	Grave's disease
M / 42 / Vietnamese	1.6	<0.04	32.4 / 12.0	2.23 / 0.33 / 0.68	Yes	Yes	Grave's disease
M / 23 / Vietnamese	1.8	<0.02	111.3 / 32.4	2.22 / 0.68 / 0.55	Yes	Yes	Not known
M / 36 / Vietnamese	1.9	<0.04	36.0 / 10.8	2.09 / 1.58 / 0.83	Yes	Yes	Grave's disease
M / 18 / Caucasian	1.8	<0.04	47.9 / 27.5	2.41 / 0.68 / 0.61	No	Yes	Grave's disease
M / 24 / Korean	1.7	<0.04	45.1 / 20.0	2.31 / 0.85 / 0.79	Yes	Yes	Grave's disease
F / 34 / Filipino	2.2	<0.04	28.6 / 11.5	1.97 / 0.79 / 0.83	Yes	Yes	Not known
M / 58 / Laotian	2.0	2.40	12.8 / 3.5	2.23 / 0.98 / 0.92	No	No	Grave's disease

TSH = thyroid-stimulating hormone; T_4 = thyroxine; T_3 = triiodothyronine; Ca = calcium; PO_4 = phosphate; Mg = magnesium

*Normal range 3.5–5.5 mmol / L; †Normal range 0.1–4.0 mU / L; ‡Normal range FT_4 9.0–26.0 pmol / L, FT_3 2.2–5.4; §Normal range calcium 2.10–2.60 mmol / L, phosphate 0.80–1.50 mmol / L, magnesium 0.70–1.30 mmol / L

portant to remember that hysteria and other psychological conditions may present as muscle weakness.

Although any thyroid disorder may be associated with TPP, Grave's disease is the most common.⁴ The Asian literature suggests that thyrotoxicosis is usually obvious at presentation, whereas Western authors tend to emphasize the subtlety of hyperthyroid symptoms.⁴ In this series, 7 patients had obvious hyperthyroid symptoms, but among the others it was only after directed questioning and thyroid function testing that the diagnosis of hyperthyroidism was made. This may reflect an unfamiliarity with the condition and the subtlety of symptoms. TPP can also be the first presentation of hyperthyroidism in an otherwise asymptomatic person.⁵

Hypokalemia in TPP is related to intracellular shifting rather than a total body potassium deficiency.⁶ Hypophosphatemia and mild hypomagnesemia are also common findings, but are not consistent features of TPP.² The precise pathophysiology underlying TPP is not completely clear. A genetic component has been postulated, given its propensity for Asian men. A number of factors such as increased activity of the sodium (Na^+), potassium (K^+) adenosine triphosphatase (ATPase), increased responsiveness to β -adrenergic stimulation, disturbance in intracellular calcium (Ca^+) shifts in muscle, hypophosphatemia and exaggerated insulin response to carbohydrate loading may be responsible.^{4,7} The most common ECG findings include U waves, ST depression and T-wave flattening and sinus tachycardia. Sinus arrest and ventricular fibrillation are uncommon but potentially lethal.

Without treatment, TPP victims will spontaneously recover muscle strength over a period of 36 hours as K^+ shifts out of cells into the extracellular space. Potassium supplementation will prevent cardiac arrhythmias and hasten recovery during the acute paralysis; however, potassium does not consistently prevent recurrent attacks.⁵ Although there are no randomized trials addressing the value of potassium supplementation, one author suggests administering 27 mEq of oral potassium chloride every 2 hours for 6 hours or until muscle power begins to recover, then every 4 hours.³ Two patients in the current study suffered rebound hyperkalemia, which is a potential hazard associated with aggressive potassium treatment during acute paralysis.²

The definitive treatment for TPP is control of the hyperthyroid state. Once patients are euthyroid, episodes of paralysis generally cease.⁴ Avoiding high carbohydrate meals is recommended, and propranolol may reduce the likelihood of relapse until the euthyroid state is achieved.⁸ In this study, 1 patient who had previously been treated successfully with radioactive iodine for Grave's disease proved an exception to the rule. Despite being clinically

and biochemically euthyroid on admission, he presented with hypokalemic periodic paralysis responsive to potassium. One other case reported described periodic paralysis that persisted in the euthyroid and hypothyroid state, and resolved following thyroid replacement.⁹ Therefore, when faced with an euthyroid patient who has hypokalemic periodic paralysis, it is appropriate to ask about previously treated hyperthyroidism.

Conclusion

TPP is a rare complication of hyperthyroidism. The diagnosis is most likely in young Asian men presenting with hypokalemia, early morning weakness and proximal lower extremity paralysis. Potassium should be administered in the acute setting to hasten recovery and prevent cardiac arrhythmias, but achievement of the euthyroid state is the definitive treatment.

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References

1. Kelley DE, Gharib H, Kennedy FP, Duda RJ, McManis PG. Thyrotoxic periodic paralysis: report of 10 cases and review of electromyographic findings. *Arch Intern Med* 1989;149:2597-600.
2. Manoukian MA, Foote JA, Crapo LM. Clinical and metabolic features of thyrotoxic periodic paralysis in 24 episodes. *Arch Intern Med* 1999;159:601-6.
3. Yeo PPB, Leo KO, Cheah JJ. Thyrotoxic periodic paralysis: a study of 51 patients. Proceedings of the Second Congress of the Association of Southeast Asian Nations (ASEAN) Federation of Endocrine Societies. Bangkok, Thailand; 1983.
4. Ober KP. Thyrotoxic periodic paralysis in the United States: report of 7 cases, a review of the literature. *Medicine* 1992; 71:109-20.
5. Goh SH. Thyrotoxic periodic paralysis: reports of 7 patients presenting with weakness in an Asian emergency department. *Emerg Med* 2002;19:78-9.
6. Shizume K, Shisiba M, Sakuma M, Yamauchi H, Nakao K, Okinaka S. Studies of electrolyte metabolism in idiopathic and thyrotoxic periodic paralysis: total exchangeable sodium and potassium. *Metabolism* 1966;15:145-52.
7. Braverman LE, Utiger RD, editors. *Werner and Ingbar's The thyroid: a fundamental and clinical text*. 8th ed. Lippincott Williams and Wilkins; 2000.
8. Conway MJ, Seibel JA, Eaton RP. Thyrotoxic periodic paralysis: improvement with beta blockade. *Ann Intern Med* 1974; 81:332-6.
9. Gandara DR, Fariss BL. Persistence of periodic paralysis following treatment of thyrotoxicosis: case report. *Military Med* 1979;144:337-8.

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