SHORT REPORT

Thyrotoxic periodic paralysis: reports of seven patients presenting with weakness in an Asian emergency department

S Hiong Goh

Emerg Med J 2002;**19**:78–79

Objectives: This study was done to describe the features of thyrotoxic periodic paralysis in young Asian men.
Methods: Seven male patients were enlisted who presented to the emergency department over a period of three years with weakness and paralysis in the morning.
Results: Initial electrolyte studies revealed hypokalaemia in these patients, and later thyroid function tests confirmed thyrotoxicosis for all. Only two of these patients had clinical symptoms and signs of thyrotoxicosis, the others being asymptomatic.
Conclusions: Early morning paralysis can be the first manifestation of hyperthyroidism in Asian men, without the other more typical symptoms of weight loss, increased appetite, excitability, sweaty palms or goitre. Treatment to a euthyroid state will ameliorate the syndrome.

Hypokalaemic periodic paralysis is a dramatic presentation of hyperthyroidism in Asian men. Such patients wake up in the early hours morning with generalised weakness, flaccid paralysis and often have accompanying myalgia. This presentation may be unfamiliar to doctors in the West who are more likely to consider renal tubular acidosis or other familial periodic paralysis syndromes in their initial differential diagnoses.

Described here are seven patients with thyrotoxic periodic paralysis seen in our emergency department over a three year period.

PATIENTS AND METHODS

Over a period of three years, seven male patients were seen in our emergency department in the early hours of the morning with a dramatic onset of weakness and paralysis. Their ages ranged from 21 to 49 years (mean age =33.4). Four patients were Chinese, and three others were Filipino, Thai, and Malay respectively (see table 1). They had presented between the hours of 4 am to 7 am by ambulance to our emergency department.

All seven patients had gone to bed the night before asymptomatic. None of them had recent viral infections, or ingestion of canned foods. None of them had any past history or family history of renal disease known. All were also asked specifically for a history of thyroid disorders, but none had such problems before.

Physical examination of the patients revealed a similar pattern of proximal muscle weakness in all, affecting mainly the muscles of the back and the shoulder and pelvic girdles. Deep tendon reflexes were absent in all the patients. Four of the patients also had complaints of aching pains in the muscles of their back, shoulders and thighs. No sensory loss was found in all. All of them had intact cranial nerve functions, without dysphagia, stridor or loss of voice. There were also no cardiac arrhythmias on cardiac monitoring, and they did not have respiratory difficulties. No sphincter incontinence of both bowel and bladder were noted.

An examination for symptoms and signs of thyroid overactivity were also carried out in the patients. There were symptoms of weight loss and heat intolerance in patients 3 and 4, but the others had no history of weight loss, heat intolerance, sweaty palms or symptoms indicative of hyperthyroidism. No palpable goitre was found clinically in all patients, but patients 3 and 4 had mild exophthalmos and lid lag signs, indicative of Graves' disease.

All the patients were found to have hypokalaemia, ranging from 1.9 to 2.4 mmol/l, with a mean level of 2.07 mmol/l. There were no sodium or chloride abnormalities. Thyroid function tests confirmed thyrotoxicosis in all cases, with an increase of free thyroxine (T_4) levels and suppression of thyroid stimulating hormone levels.

All the patients were admitted to the hospital for further treatment. They were all discharged within a week with antithyroid medications, as well as with oral potassium tablets. In the subsequent weeks, patients 1, 2, 3, and 7 had recurrences of thyrotoxic periodic paralysis despite the use of oral potassium supplements (table 1). Most of these episodes

Table 1 Features of patients presenting with thyrotoxic periodic paralysis

	Age/sex/race	Initial serum potassium levels (mmol/l)	Free T4 (pmol/l)*	TSH (mU/l)†	Symptoms and signs of thyrotoxicosis	Recurrences	Aetiology of thyrotoxicosis
1	37/M/Filipino	2.0	53.84	<0.06	No	2 episodes within a month of diagnosis	Graves' disease
2	36/M/Malay	2.4	31.66	<0.06	No	1 episode within a month	Solitary toxic adenoma
3	27/M/Chinese	1.8	51.00	<0.06	Yes	1 episode within a month	Graves' disease
4	21/M/Chinese	2.0	34.88	<0.06	Yes	Nil	Graves' disease
5	35/M/Thai	2.1	26.49	<0.06	No	Nil	Unknown‡
6	49/M/Chinese	1.9	47.91	<0.06	No	Nil	Graves' disease
7	29/M/Chinese	2.3	69.06	<0.06	No	2 episodes, at 8 and 9 months after diagnosis	Graves' disease

*Reference range=10.30–31.00 pmol/l; †reference range=0.5 to 5.0 mU/l; ‡lost to follow up.

recurred within a month of the initial diagnosis but once they were rendered euthyroid, the episodes of periodic paralysis stopped. With patient 7, the recurrence occurred as late as nine months, but he was not compliant with his medications.

Subsequent studies revealed the cause of hyperthyroidism to be Graves' disease in five patients, and solitary toxic thyroid adenoma in one. One patient returned to Thailand for further treatment before a cause for the hyperthyroidism was established.

DISCUSSION

Thyrotoxic periodic paralysis has a predilection for afflicting Asian men, and less frequently women. It has been described in Japan,[1] Singapore,[2] China,[3] and also has been recognised in Thai, Filipino, Vietnamese, Korean, and Malay populations. Our patients (three Chinese, a Filipino, a Thai, and a Malay) were a good indication of how various Asian races are affected. Even so, the incidence is low, ranging from 1.8%[1] to 8.8%[4] in Japan, and 1.9% in China [3] for thyrotoxic patients. The incidence is even lower in female thyrotoxic patients, but there are no reliable figures.

The presentations of our patients are typical and in a Singaporean study,[2] 88.5% of patients experienced the onset of paralysis between 6 pm and 8 am. The flaccid paralysis involved predominantly the muscles of the back, and of the shoulder and pelvic girdles. Proximal muscles were more severely affected than the distal muscles. Myalgia and stiffness were well recognised complaints [3] and were present in four of our seven patients. There was no involvement of the sensory system, and mental function was intact in all. There was sparing of the cranial nerves, bulbar, ocular and respiratory muscles. Deep tendon reflexes were lost, but the anal sphincter tones were preserved, as were urinary continence. These findings differentiate thyrotoxic periodic paralysis from Guillain-Barre syndrome, myasthenia gravis, botulism and transverse myelitis.

The presence of hypokalaemia will often suggest the diagnosis of thyrotoxic periodic paralysis to the emergency physician practising in Asia rather than familial periodic paralysis, and raised thyroid function tests will serve to confirm it and exclude familial periodic paralysis. As a point of interest, for the same period surveyed, we saw only one patient with familial periodic paralysis.

In a previous study, McFadzean and Yeung [3] found that the manifestations of the hyperthyroid state preceded the episodes of paralysis by three months to nine years in 80% of affected subjects. This seems to suggest that the thyrotoxicosis was usually very obvious at the time of presentation. However, five of our seven patients had no clinical signs or symptoms of thyrotoxicosis in the emergency department, and the diagnosis was found on thyroid function testing. As such, we have to now regard that hypokalaemic periodic paralysis can be the initial manifestation of hyperthyroidism, which had, hitherto, remained clinically "silent".

The hypokalaemia that occurs is not attributable to a depletion of body potassium stores. Rather, it is attributable to an intracellular shift of body potassium stores that is catecholamine mediated.[5 6] Thyroid hormone increases the sodium-potassium-ATPase activity in skeletal muscle, liver, and kidney.[7–9] In hyperthyroidism, the resulting increase in inward shift of potassium thus causes periodic paralysis. Also, the diurnal variation in potassium movement where there is nocturnal potassium influx into skeletal muscle would explain the tendency for thyrotoxic periodic paralysis to occur at night.[10] Mcfadzean and Yeung have suggested that the severity of the hypokalaemia determines the severity of the weakness.[3] The tendency for it to occur more in men than women is as yet unexplained.

If left alone, the paralysis recovers over the next 36 hours as the potassium levels return to normal values as the potassium moves back out of the cells into the extracellular space. It can be hastened by potassium replacement, but as potassium is released from the cells into the circulation during the recovery phase of the paralytic attack, any aggressive potassium administration can cause a "rebound" hyperkalaemia, and there is less inclination now to replace potassium aggressively. The definitive treatment is achievement of a euthyroid state. Though Graves' disease is the commonest aetiology (as exemplified with five of our patients), thyrotoxic periodic paralysis can occur with hyperthyroidism from any cause.[3 11] The use of oral potassium supplements while awaiting the achievement of a euthyroid state has been popularly used in an attempt to avoid a recurrence of episodes of the periodic paralysis, but there has been no good evidence that it works,[2 3] and indeed three of our patients suffered relapses of thyrotoxic periodic paralysis while on this regimen. However, recently Birkhahn *et al*,[12] described a Malay patient with thyrotoxic periodic paralysis who was given parenteral propranolol in large doses to counteract the peripheral effects of the thyrotoxicosis (hypertension, tachycardia). This had the dramatic effect of also reversing the thyrotoxic periodic paralysis. As one of the proposed mechanisms of hypokalaemia in these patients is a catecholamine mediated intracellular influx of potassium, they believed that this mechanism may have been blocked by propranolol, thereby achieving faster resolution of symptoms without resorting to exogenous potassium. This may prove to be a more effective treatment regime in future.

CONCLUSION

Early morning weakness and paralysis with hypokalaemia should suggest thyrotoxic periodic paralysis to the emergency physician caring for Asian patients. It can be the first manifestation of thyrotoxicosis in male patients who are otherwise asymptomatic. The definitive treatment is to render the patient euthyroid. There is a high relapse rate for thyrotoxic periodic paralysis in the first month after starting treatment, while awaiting the euthyroid state. The prophylactic use of potassium supplements does not seem to be successful in preventing such relapses.

ACKNOWLEDGEMENTS

Funding: none.
Conflicts of interest: none.

REFERENCES

1 **Okinaka S**, Shizume K, Iino S, *et al*. The association of periodic paralysis and hyperthyroidism in Japan. *J Clin Endocrinol Metab* 1957;**17**:1454–9.
2 **Yeo PPB**, Lee KO, Cheah JS. Thyrotoxic periodic paralysis: a study of 51 patients. In: Proceedings of the Second Congress of the Association of Southeast Asian Nations (ASEAN) Federation of Endocrine Societies, 30 Nov–3 Dec,1983, Bangkok, Thailand.
3 **McFadzean AJS**, Yeung R. Periodic paralysis complicating thyrotoxicosis in Chinese. *BMJ* 1967;**1**:451–5.
4 **Satoyoshi E**, Murakami K, Kowa H, *et al*. Periodic paralysis in hyperthyroidism. *Neurology* 1963;**13**:746–52.
5 **Shizume K**, Shishiba Y, Sakuma M, *et al*. Studies of electrolyte metabolism in idiopathic and thyrotoxic periodic paralysis. I. Arteriovenous differences of electrolytes during induced paralysis. *Metabolism* 1996;**15**:138–44.
6 **Shizume K**, Shishiba Y, Sakuma M, *et al*. Studies of electrolyte metabolism in idiopathic and thyrotoxic periodic paralysis. II. Total exchangeable sodium and potassium. *Metabolism* 1996;**15**:138–44.
7 **Kjeldsen K**, Norgaard A, Gotzsche CO, *et al*. Effect of thyroid function on number of sodium-potassium pumps in human skeletal muscle. *Lancet* 1984;ii:8–10.
8 **Layzer RB**. Periodic paralysis and the sodium-potassium. *Ann Neurol* 1982;**11**:547–52.
9 **Chan A**, Shinde R, Chow CC, *et al*. In vivo and in vitro sodium pump activity in subjects with thyrotoxic periodic paralysis. *BMJ* 1991;**303**:1096–9.
10 **Charness ME**, Johns RJ. Hypokalemic periodic paralysis. *Johns Hopkins Med J* 1978;**143**:148–53.
11 **Norris FH Jr**, Clark EC, Biglieri EG. Studies in thyrotoxic periodic paralysis. *J Neurol Sci* 1972;**13**:431–42.
12 **Birkhahn RH**, Gaeta TJ, Melniker L. Thyrotoxic periodic paralysis and intravenous propranolol in the emergency setting. *J Emerg Med* 2000;**18**:199–202.