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Thyrotoxic Periodic Paralysis Is Not Correlated With the Severity of Hyperthyroidism and Can Be Seen with All Forms of Hyperthyroidism

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SUMMARY

Background

Thyrotoxic periodic paralysis (TPP) is characterized by acute and severe generalized weakness due to a shift of potassium into the intracellular space without loss of total body potassium content (1). The disease is best documented in patients of Asian origin who have hyperthyroidism, can occur with any kind of hyperthyroidism, and has to be differentiated from other causes of hypokalemic paralysis. Several factors have been reported to precipitate these crises, the best known being a carbohydrate load and strenuous exercise. This study from Taiwan is a prospective investigation extending from 2002 to 2012. It includes probably the largest group of patients observed over time in a single center.

Methods

Over a period of 10 years, 135 patients with TPP (130 men, 5 women) were studied in a prospective manner. The selection criteria were strict, excluding any other possible causes for an abrupt decrease in serum potassium. Thyroid function was evaluated not only by the classical biochemical and ultrasound criteria but also by clinical assessment using the Wayne Index. Special attention was given to possible precipitating factors (carbohydrate load, strenuous exercise, upper respiratory tract infection (URI), steroids, catecholamines, etc.). In 55 patients, it was possible to provoke an attack of hypokalemia with a glucose load (2 g per kilogram of body weight).

Results

The attacks occurred mainly in the morning and during summer and fall. Hyperthyroidism was confirmed by increased serum FT_4 and FT_3 levels and a serum TSH of <0.03 mU/L. Patients with Graves' disease accounted for 96% of the cases, but the attacks were also seen in patients with subacute thyroiditis and multinodular toxic goiter and even in patients using weight-reducing agents containing thyroid hormones. There was no correlation between TPP and the severity of hyperthyroidism. Only 24% of the patients were diagnosed with hyperthyroidism before the attack; the others were diagnosed at the moment of TPP. There were no familial cases. As expected, carbohydrate overload was present in 34% of the cases, being the best identifiable precipitating factor. Exercise as another precipitating cause accounted for only 7% of cases and URI for 8%. In 55 patients, the role of carbohydrate overload could be checked with intentional hyperglycemia which was induced not earlier than 24 hours after a spontaneous attack. Hypokalemia was seen in only 10 (18%) of 55 patients, but it was severe—the mean nadir of serum potassium was 2.5 mmol/L. To prevent further attacks, correction of hyperthyroidism was obviously crucial, and in the meantime the patient received beta-adrenergic blockers and oral potassium chloride supplements (8 to 16 mmol/day).

Conclusions

Thyrotoxic periodic paralysis is seen mainly in the Asian population. Even though it is associated with

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hyperthyroidism, there is no correlation between the occurrence of the crisis and the severity of hyperthyroidism. Some patients even had no clinical symptoms of hyperthyroidism according to the Wayne Index. A carbohydrate overload can certainly precipitate thyrotoxic periodic paralysis but only in a minority of cases was induced hyperglycemia sufficient to cause an attack. The same is true for exercise-induced TPP. The treatment is symptomatic (potassium supplements and beta blockers), but more importantly hyperthyroidism must be treated rapidly.

ANALYSIS AND COMMENTARY

This report originates from Taiwan, yet it is now established that TPP is not limited to Asian populations with thyrotoxicosis (2). Latin American patients and even Caucasians and black patients with thyrotoxicosis have presented with attacks of TPP. The shift of serum potassium to the intracellular space is the hallmark of the disease. Rarely, the decrease in serum potassium is modest. Therefore, in the presence of unexplained muscle weakness in Graves' disease with TPP has to be considered. The pathophysiology is unclear. Recent progress indicates the presence of several mutations in at least one potassium channel gene, Kir2.x (3), and the term endocrine channelopathy is occasionally used to describe TPP. The well-known T_3-dependent Na+–K+–ATPase could also play an important role (4). it is interesting that among the many precipitating factors of TPP, increased insulin sensitivity has been reported (5). Insulin favors the shift of potassium into the intracellular space. Finally, TPP should not be confused with periodic hypokalemic paralysis in patients without increased thyroid hormone levels.

References

1. Lin SH. Thyrotoxic periodic paralysis. Mayo Clin Proc 2005;80:99-105.
2. Maciel RM, Lindsey SC, Dias da Silva MR. Novel etiopathophysiological aspects of thyrotoxic periodic paralysis. Nat Rev Endocrinol 2011;7:657-67.
3. Puwanant A, Ruff RL. INa and IKir are reduced in Type 1 hypokalemic and thyrotoxic periodic paralysis. Muscle Nerve 2010;42:315-27.
4. Chan A, Shinde R, Chow CC, Cockram CS, Swaminathan R. Hyperinsulinaemia and Na+, K(+)-ATPase activity in thyrotoxic periodic paralysis. Clin Endocrinol (Oxf) 1994;41:213-6.
5. Soonthornpun S, Setasuban W, Thamprasit A. Insulin resistance in subjects with a history of thyrotoxic periodic paralysis (TPP). Clin Endocrinol (Oxf) 2009;70:794-7.