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Thyrotoxic periodic paralysis: Report of a rare case and literature review

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Abstract

Thyrotoxic hypokalemic periodic paralysis (TPP) is a rare condition characterized by the triad of acute hypokalemia without total body potassium deficit, episodic muscle paralysis, and thyrotoxicosis. Hypokalemia in TPP results from an intracellular shift of potassium induced by the thyroid hormone sensitization of Na^+/K^+–ATPase rather than depletion of total body potassium. TPP is most commonly found in the East Asian population, with an incidence of approximately 2% in patients with thyrotoxicosis of any cause; however, with globalization and immigration, TPP is no longer limited to certain geographic areas. TPP is commonly misdiagnosed in western countries because of its similarities to familial periodic paralysis. Although thyrotoxicosis is more common in women, episodes of TPP occur more often in men. Early diagnosis not only aids in definitive management with nonselective beta-blockers and correction of hyperthyroidism, but also prevents the risk of rebound hyperkalemia due to excessive potassium replacement. Physician should their patients how to avoid precipitating factors like heavy exercise, high-carbohydrate meals and alcohol consumption that usually occur during holidays or weekends.

Keywords

thyrotoxic periodic paralysis; TPP; FPP; hypokalemia; hyperthyroidism; rebound hyperkalemia

Epidemiology

Thyrotoxic periodic paralysis (TPP) is a rare condition, the first case of non-specific periodic paralysis was described in 1882 and a relation with hyperthyroidism was identified in 1902 [1]. The pathogenesis of TPP has remained largely mysterious for decades since the discovery of the first case [2]. Approximately 2% of patients with thyrotoxicosis in China and Japan reportedly have TPP [3]. It has been recognized also in Thai, Filipino, Vietnamese, Korean, and Malaysian populations. In the United States, the incidence of TPP in the non-Asian population is approximately one tenth (0.1%-0.2%) that found in Asian countries [3]. Physicians should remember that Asian and Hispanic patients with thyrotoxicosis are particularly susceptible to periodic paralysis. It is also important to remember that, although hypokalemia is common during the acute paralytic episode, the between-attacks' levels of plasma potassium and total body potassium remain within normal limits [4].

TPP occurs predominantly in men; the male-female ratio is approximately 20:1 commonly in 3rd-4th decade without family history presence. The racial differences and male predominance in TPP are

intriguing. 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. Genetic mutations in the control of Na^+, K^+-adenosine triphosphatase (ATPase) activity, which controls the exchange of intracellular potassium with extracellular sodium within the same HLA antigen subtype, may explain ethnic differences [3].

Despite a higher incidence of thyrotoxicosis in women, the male predominance may reflect the action of androgen on Na^+, K^+-ATPase activity. Thyrotoxic periodic paralysis occurs most commonly during the summer and autumn. Increased consumption of sweet drinks, outdoor activities and exercise, emotional stress, and increased potassium loss in sweat are possible explanations for the seasonal pattern, or during holidays and weekends, so a careful history should be taken when we are facing such medical emergency.

Etiology

Thyrotoxic periodic paralysis TPP can occur in association with any of the cause of hyperthyroidism as following:

Graves' disease (most common)
Toxic nodular goiter
Iodine-induced thyrotoxicosis
Excessive thyroxine use
Solitary toxic thyroid adenoma
Lymphocytic thyroiditis
Thyrotropin-secreting pituitary adenoma
Amiodarone-induced thyrotoxicosis [3]

Case Report

A 34 y o Filipino male presented to me in ER department with a muscle weakness from lower abdomen down to his feet that started this early morning. Weakness was so progressive and severe that he couldn't stand up or walk to bathroom. Also less weakness in right upper limb. He denied had such problem before and taking medications, except he drinks and smokes occasionally, otherwise he feels healthy. Furthermore, no recent history of Hypertension, D.M, diarrhea, vomiting, dysuria nor cough.

On physical examination, he was lying on bed, oriented, not distressed, no goiter, regular heart rate, and decreased muscle strength and tendon reflexes in both lower extremities. He had no exophthalmos or sensory or cranial nerve deficits. His vital signs: BP= 141/90 mmHg, HR= 88 bpm, Temp. = 37C, SpO2= 98% in R/A.

Initial laboratory results on admission came back and showed: Potassium level was 2.7mmol/L (normal range, 3.5-5mmol/L), serum phosphorus level was 4.0 mg/dL (normal range, 2.7-4.5 mg/dL), and his serum magnesium level was 1.6 mg/dL (normal range, 1.7-2.6 mg/dL), calcium 2.33 mmol/L (normal range, 2-2.6 mmol/L), Vit. B12= 641 (200-900 pg/l), Cortisol= 1.83 (4.30-22.40ug/dl).

TSH<0.005 IU/ml (normal range, 0.34-5.60 IU/mL),T3= 32 (3.10-6.80 pmol/l), T4= 90 (12-22 pmol/l). Others like: CBC, Blood sugar, RFT, Cardiac enzymes, CPK, Urine test were all within normal limits. His electrocardiogram also was normal, so an initial diagnosis of TPP was made. He was given

40 mEq of intravenous potassium chloride in the emergency department and was then started on a normal saline infusion with 20 mEq/L of potassium till morning with careful monitoring of his potassium level every 2 hours to avoid rebound hyperkalemia. Gradually his muscle weakness started to improve, and on his second day he was able to walk to bathroom; where his serum potassium level increased to 4.8 mEq/L. He was given carbimazole 20 mg once daily and discharged with complete resolution of symptoms and well educated about the TPP and given an appointment to follow up with our endocrinologist in future.

Differential Diagnosis of hypokalemic paralysis PP:

1- Transcellular shift:

- Drugs (Diuretics, tolotics, theophylline toxicity, chloroquine toxicity, insulin overdose)
- TPP
- Familial periodic paralysis
- Barium poisoning
- Primary hyperaldosteronism
- Pseudohyperaldosteronism: licorice ingestion

2- Renal loss of potassium:

- Barret's syndrome
- Gitelman's syndrome
- Renal tubular acidosis, Other; nephrotic syndrome, acute tubular necrosis, diabetic ketoacidosis

3- Gastrointestinal loss of potassium:

- Infectious diarrhea; Salmonella enteritis, Strongyloides enteritis, and Yersinia enterocolitis, short bowel syndrome [6] .

Bulbar, respiratory, and ocular muscles are usually spared in TPP [5] .Clinically we should exclude other similar symptomatic presentations as in:

1. Gullain-Barré syndrome, 30% affect respiratory muscle
2. Myasthenic crisis
3. Acute myelopathy(e.g.; transverse myelitis)
4. Acute spinal cord compression
5. Tick paralysis
6. Botulism [6]

Discussion

TPP is a rare disorder with an incidence of 2% among Asians with hyperthyroidisms as compared to just 0.1-0.2% in non-Asians with hyperthyroidism [5]. The age of onset is usually in the third decade of life. The high incidence of this disorder in Asians and the association with the presence of HLA-DRw8 suggests that the basic defect may be genetically determined, but the precise pathogenesis of TPP remains unclear [8]. It is predominantly in men, TPP characterized by the triad of acute hypokalemia without total body potassium deficit, episodic muscle paralysis, and thyrotoxicosis. Although bulbar, respiratory, and ocular muscles are usually spared in TPP, patients with TPP may require intensive care unit (ICU) admission. A majority of our patients were admitted to the ICU due to electrocardiogram (EKG) changes and severe hypokalemia. It is thought that thyroid hormone increases sodium-potassium ATPase activity, which drives potassium into cells, creating muscle membrane hyperpolarization. Thus,

whole-body potassium stores are not depleted, just temporarily driven intra-cellularly (Figure: 1), (Figure: 2). Management of TPP requires urgent potassium administration, nonselective beta-blockers and correction of hyperthyroidism. Thus the danger may result from the management is rebound hyperkalemia and should be avoided in first 24 hours.

Grave's disease is the most common cause of hyperthyroidism in all the patients [5]. Features of hyperthyroidism may precede the onset of PP by months or even years [7], also noted at same time in 43%-60% of patients or following development of PP. Duration of symptoms can range from minutes to days. Attacks of TPP tend to occur during night and at rest after eating carbohydrate-rich meals, vigorous exercise, alcohol intake, exposure to cold, corticosteroid therapy, emotional stress and infections. It is also postulated that male hormones increase Na^+/K^+-ATPase activity, and that this explains why males are at a higher risk of TPP despite thyroid disease being more common in females [7].

Figures

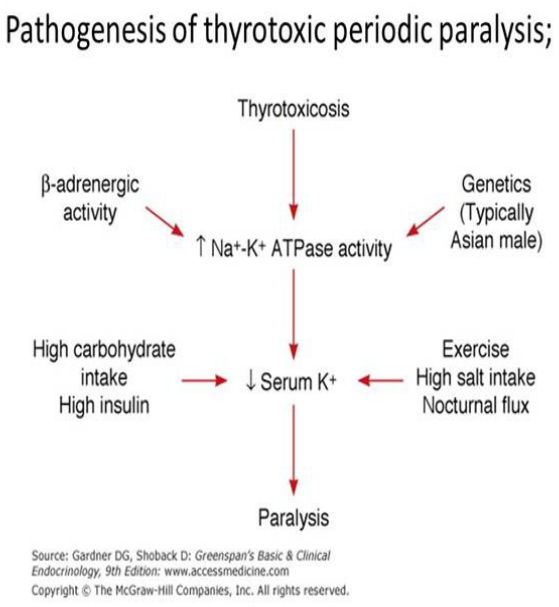

Figure 1

Thyrotoxic periodic paralysis

	Thyrotoxic periodic paralysis
Diagnosis and associated features	Paralytic attack that is associated with hypokalemia and hyperthyroidism (low TSH with high T4 or high T3)
Mechanism	Thyroid hormone increases tissue responsiveness to beta-adrenergic stimulation → Increases Na-K ATPase activity on the skeletal muscle membrane → Drive potassium into cells → Hyperpolarization of the muscle membrane → Paralyses
Etiology	Thyrotoxicosis Possible inherited predisposition
Age at onset	>20 years
Attack duration	Hours to days
Epidemiology	Highest incidence in Asians, men > women
Precipitants	Rest after strenuous exercise High-carbohydrate load Stress
Preventive treatment	Euthyroid state Propranolol

Figure 2

Conclusion

Because of TPP is a rare medical case and it has subtle signs and symptoms of hyperthyroidism, doctors should be highly suspicious of TPP in order to administer potassium urgently with non-selective B- blockers with caution to avoid fatal rebound hyperthyroidism. Also patients need to be educated about the precipitating factors, like; strenuous exercise, high- carbohydrate meals and alcohol consumption among Asian population, especially in Middle East such as in Oman. Also I would like encourage that all ER facilities should offer urgent thyroid function tests to save life of our patients by reaching definitive diagnosis of TPP as soon as possible.

References

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