Hypokalemia and Thyrotoxicosis in a Patient with Quadriplegia

Nadear Elmahi, MD
Muhammad Noor, MD
Sunil Mehra, MD

Thyrotoxic periodic paralysis (TPP) is a rare condition that typically occurs in Asian men between ages 30 and 50 years. TPP is characterized by simultaneous thyrotoxicosis, weakness or paralysis,[1–4] and hypokalemia (plasma potassium levels usually < 3.0 mEq/L but can be normal[2,5]), although other associated electrolyte imbalances (eg, hypomagnesemia, hypophosphatemia) have also been reported.[5] Episodes of paralysis are typically benign, but rarely they affect the upper respiratory muscles, which can be fatal.[3,4] Early diagnosis is important to restore euthyroid condition, which will protect the patient from further episodes of paralysis. In this article, we report the case of a man who presented with a first episode of paralysis caused by hypokalemia associated with thyrotoxicosis. The clinical, biochemical, and electrocardiography findings as well as appropriate treatment for TPP are also discussed.

CASE PRESENTATION

Initial Presentation and History

A 27-year-old Hispanic man presented to the emergency department (ED) complaining of weakness in all 4 extremities and inability to walk. The night prior to presentation, the patient worked extra hours lifting heavy furniture. After work, he consumed a carbohydrate meal and went to bed. At 3:00 AM, he woke up to use the bathroom and discovered that he was unable to move his lower extremities and could only move his upper extremities from side to side. The patient denied numbness, tingling, blurred vision, slurred speech, headache, weight loss, sweating, loss of appetite, change in sleep patterns, tremors, urinary or fecal incontinence, and any previous episodes of weakness/paralysis of the extremities. The patient, however, indicated that he had experienced nervousness for 1 week prior to the admission with some palpitations. Otherwise, there was no significant past medical history and no family history of paralysis or thyroid disease. The patient was not taking any medications or using alcohol or drugs, and he denied allergies and smoking.

Physical Examination

In the ED, the patient was tachycardic and afebrile. His blood pressure was 130/64 mm Hg. Physical examination revealed an immobile patient secondary to flaccid quadriplegia. Skin was moist. Power was 0/5 in the right lower extremity, 1/5 in the left lower extremity, 2/5 in the right upper extremity, and 2/5 in the left upper extremity. The patient had hyporeflexia (+1 in all 4 extremities). No fasciculation was noted. Cranial nerves and sensory system were grossly intact. The thyroid gland was not enlarged, and there were no hand tremors or exophthalmos. S_1 and S_2 were heard, but there were no additional heart sounds, murmurs, or gallops. On auscultation, normal breath sounds were heard; there were no rales, rhonchi, or wheezes. Abdominal examination was negative.

Laboratory and Imaging Studies

Results from laboratory studies performed during the initial evaluation were significant for low serum potassium and magnesium levels (**Table 1**). Creatinine and blood urea nitrogen were within normal limits. Urinalysis was normal. An electrocardiogram (ECG) showed sinus tachycardia with right bundle branch block (RBBB) and ST depression in leads V_1, V_2, and V_3, with U waves overtaking the T waves and Q-U prolongation (**Figure 1**).

Hospital Course and Diagnosis

In the ED, the patient was administered 40 mEq/L

At the time of submission, Drs. Elmahi and Noor were residents at the Internal Medicine Department, New York Medical College (Brooklyn-Queens Division), St. John's Hospital–Queens, New York, NY. Dr. Elmahi is now a hospitalist at the Alamance Regional Medical Center, Burlington, NC. Dr. Noor is now a geriatric fellow in the Department of Medicine, Stony Brook University, Stony Brook, NY. Dr. Mehra is a clinical associate professor of medicine, New York Medical College, Valhalla, NY, and co-director of the Medical Intensive Care Unit, St. Vincent's Catholic Medical Center, New York, NY.

Table 1. Results of Initial Laboratory Studies for the Case Patient

Laboratory Tests	Result	Normal
Potassium (mEq/L)	1.7	3.5–5.0
Magnesium (mg/dL)	1.4	1.8–2.8
Phosphate (mg/dL)	2.5	2.2–4.8
Calcium (mg/dL)	9.2	8.5–10.8
Sodium (mEq/L)	140	135–146
Chloride (mEq/L)	104	95–110
Bicarbonate (mEq/L)	25	22–28
Hemoglobin (g/dL)	13.8	14.0–18.0
Hematocrit (%)	38.5	38–54
White blood cell count ($\times 10^3/\mu L$)	12.6	3.5–11.0
Platelet count ($\times 10^3/\mu L$)	177	150–450

of potassium chloride orally, 60 mEq/L of potassium chloride intravenously (IV), and 4 g of magnesium sulfate IV. He was then admitted with a working diagnosis of idiopathic hypokalemia. Four hours later, potassium levels were found to be 1.9 mEq/L, and the patient demonstrated slight improvement in motor function. Another 60 mEq/L of potassium chloride IV was administered, and the patient recovered completely from the quadriplegia within several hours. Repeat ECG performed after potassium administration showed only sinus tachycardia (**Figure 2**).

Additional laboratory studies that were ordered after admission and became available on hospital day 2 revealed: thyroid-stimulating hormone levels below 0.091 μIU/mL (normal, 0.35–5.5 μIU/mL) and free thyroxine levels at 21.1 μg/dL (normal, 4.5–11.0 μg/dL). Urine toxicology was negative. Analysis of urine electrolytes revealed: sodium, 125 mEq/L (normal, 40–220 mEq/L); potassium, 11 mEq/L (normal, 25–125 mEq/L); chloride, 184 mEq/L (normal, 30–250 mEq/L); and urine creatinine, 94.3 mg/dL (normal, 30–125 mg/dL). Plasma potassium levels were elevated at 5.4 mEq/L but corrected to 4.7 mEq/L without further treatment. Plasma magnesium levels also normalized after supplementation (2.0 mEq/L). Based on the patient's symptoms, laboratory findings (specifically, low levels of thyroid-stimulating hormone and hypokalemia), ECG abnormalities, and response to initial treatment, the patient was diagnosed with TPP.

On hospital day 2, results of repeat analysis of urine metabolites were as follows: sodium, 51 mEq/L; potassium, 43 mEq/L; chloride, 105 mEq/L; and creatinine, 84.2 mg/dL. The patient was given atenolol (50 mg orally once daily) to control for tachycardia. Propylthiouracil (100 mg orally 3 times daily) was started to manage the patient's thyrotoxicosis. The patient was discharged on the third day of hospitalization with a follow-up appointment at an endocrinology clinic. He was also scheduled for outpatient thyroid sonogram.

THYROTOXIC PERIODIC PARALYSIS

This patient's presentation is classic for TPP, which is a rare complication of thyrotoxicosis that primarily affects Asian men.[6] The patient presented with a first episode of paralysis with hypokalemia and high levels of thyroxine. The patient experienced hypomagnesemia as well, which also can occur in patients with TPP.[5] The primary differential consideration in patients with suspected TPP is familial hypokalemic periodic paralysis (HPP), although all other causes of paralysis (eg, motor neuron diseases) and hypokalemia should be considered in the differential diagnosis. Compared with familial HPP, TPP typically affects older men with hyperthyroidism who do not have a family history of periodic paralysis.[3] The case patient's age (27 years) and sex (male) as well as absence of a family history of paralysis made the diagnosis of TTP more favorable than familial HPP.

Epidemiology

TPP predominantly affects Asian men in the third to fifth decade of life[5]: 44 out of 45 affected Chinese patients in 1 study were male.[7] Another case report estimated that the risk of developing TPP is 15% to 20% in Chinese patients with hyperthyroidism.[4] A case review by Ober[3] suggested that the ethnic distribution of TPP in the continental United States was: white, 45%; Asian, 24%; Hispanic, 15.5%; black, 7%; Native American, 7%; and others, 1%.

Pathogenesis

The pathogenesis of TPP is not fully understood. The most accepted explanation is that the thyroid hormone increases activity of the Na^+-K^+ ATPase pump, resulting in increased cellular uptake of potassium.[6,8] In the setting of thyrotoxicosis, excess quantities of thyroid hormone may therefore increase the risk of paralytic episodes by increasing patients' susceptibility to the hypokalemic action of insulin.[3,7]

Multiple studies have been undertaken to determine whether mutations in calcium channel genes may be responsible for TPP given the high incidence in specific ethnic groups (eg, Chinese men).[1,9] In 1 study, only 1 of 16 patients with TPP was found to have an R83H mutation in the potassium (*KCNE3*) gene.[10] Other studies showed that Ca^+-ATPase and calcium uptake by the

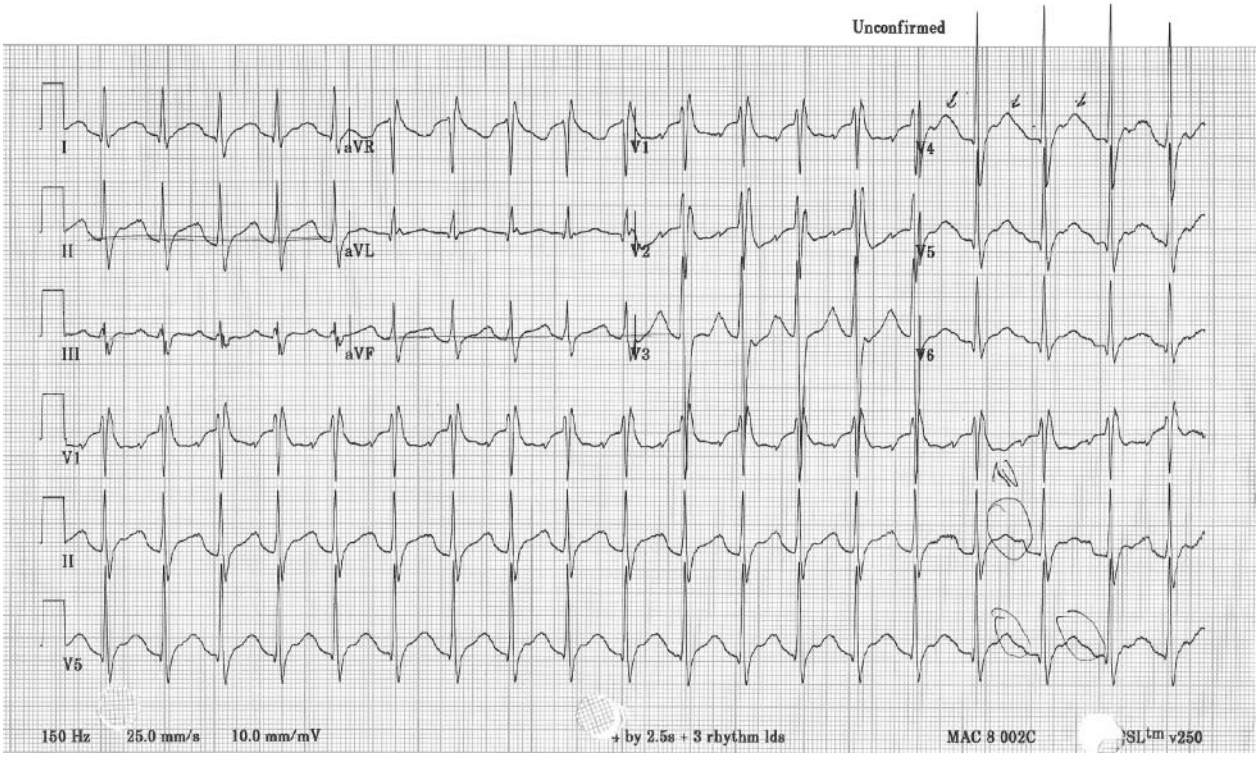

Figure 1. Electrocardiogram of the case patient demonstrating ST depression in leads V_1, V_2, and V_3 with U waves overtaking the T waves and Q-U prolongation (changes that are typical of hypokalemia) and sinus tachycardia with right bundle branch block.

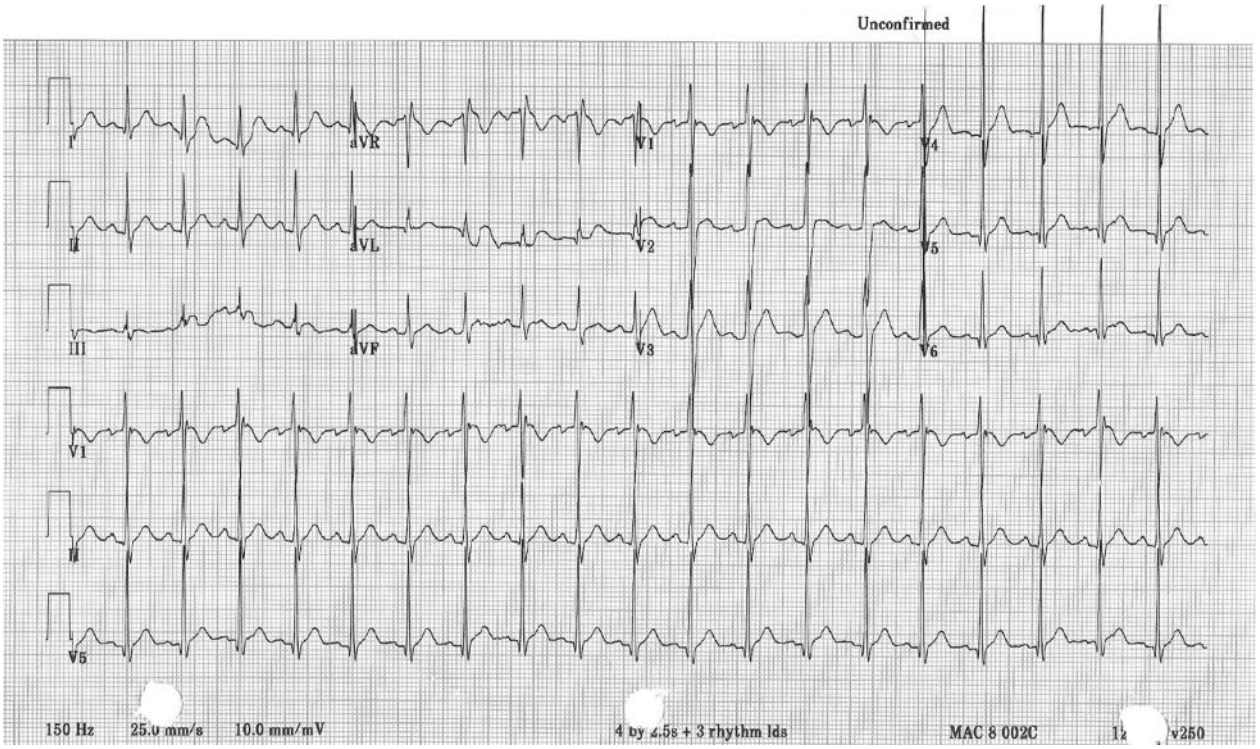

Figure 2. Repeat electrocardiogram of the case patient after potassium was administered, which reveals sinus tachycardia and resolution of right bundle branch block and ST depression.

Table 2. Causes of Hypokalemia

Gastrointestinal tract loss (eg, vomiting, diarrhea, fistula, gastrointestinal suctioning, use of laxatives, ureterosigmoidostomy)
Renal losses (Cushing's syndrome, hyperaldosteronism, Bartter syndrome, renal tubular acidosis, hypomagnesemia, leukemia)
Medications that can increase renal loss (eg, diuretics, penicillin, aminoglycosides)
Decreased potassium intake (as seen in anorexia nervosa or alcoholism)
Intracellular potassium shift with normal potassium pool in the body (eg, metabolic alkalosis, insulin overdose, HPP [eg, familial HPP or TPP], theophylline, barium and toluene intoxication)
Hereditary causes (eg, familial HPP, congenital androgenital syndrome, familial interstitial disease, Little's disease)
Idiopathic

HPP = hypokalemic periodic paralysis; TPP = thyrotoxic periodic paralysis.

sarcoplasmic reticulum decrease during the paralytic attack but revert to normal after the attack.[9,11] The authors assumed that the mutations in the calcium channels are not sufficient to produce symptoms during the euthyroid state.[1,9]

Diagnosis

In patients presenting with acute paralysis, distinguishing among the various etiologies is important as this will guide treatment. The differential diagnosis of acute paralysis includes quadriplegia caused by trauma, ischemia, inflammation or tumor, Guillain-Barré syndrome, periodic paralysis, myasthenia gravis, dissociative paralysis, and metabolic abnormalities, typically hypokalemia. Causes of hypokalemia (**Table 2**)[2] should also be considered during the initial evaluation.

Clinical features. Patients presenting with TPP usually report that the paralysis occurred during rest following exercise. In most of the reported cases, paralysis occurred after a few hours of sleep.[6] Other precipitating factors include stress and large carbohydrate meal,[2,5] which causes increased production of insulin and cellular potassium influx and subsequent hypokalemia.

In TPP, the degree of muscular involvement and severity of the attack can range widely.[5] The patient might experience aching or cramps in the affected muscles before the onset of acute paralysis.[5] Normally, the proximal muscles are more affected than the distal muscles.[1,12] Rare presentations of TPP with upper motor neuron findings have been reported.[13] Paralysis can be asymmetrical, and the muscles that were exercised will be more affected.[5,14] Rarely, attacks can be severe enough to affect the respiratory muscles and may be fatal.[3,4]

The case patient's presentation included nervousness and palpitations, findings consistent with hyperthyroidism. In a report of 45 Chinese patients, only 29% were known to have hyperthyroidism; 60% of these patients had clinical symptoms of thyrotoxicosis and 11% had subclinical disease.[5]

Laboratory studies. Laboratory findings are key for diagnosing TPP. The primary biochemical findings during the attack are elevated thyroid hormones and hypokalemia.[1–4] McFadzean and Yeung[5] found hypokalemia present in 100% of cases and hypophosphatemia in 80%; mild hypomagnesemia was also reported. Recent reports demonstrated that potassium levels may decrease during the attack but not always below the normal range.[3,4] Studies examining arteriovenous serum potassium and sodium changes during the attack suggested that the mechanism of potassium serum reduction is the entry of extracellular potassium into the intracellular space.[5,15] In rare cases, triiodothyronine may be elevated, while other thyroid function tests are within the normal range.[16]

Electrocardiogram. The ECG changes in hypokalemia begin with flattening of the T waves, followed by a U wave that may be associated with ST-T flattening or slight ST depression. Then, the ST depression becomes more marked and the U wave increases in amplitude until the U wave ultimately overtakes the T wave. At this point, distinguishing between the T wave and U wave may be almost impossible (Q-U prolongation).[17] However, ECG manifestations of hypokalemia and various arrhythmias are not always present in thyrotoxic patients.[7,13] The case patient had late changes of hypokalemia. The ECG revealed sinus tachycardia with RBBB and ST depression in leads V_1, V_2, and V_3 with U waves overtaking the T waves and Q-U prolongation (Figure 1). The sinus tachycardia was due to thyrotoxicosis, while the ST depression, U waves, and prolonged QU interval were caused by hypokalemia. To the authors' knowledge, no other case reports of TPP reported the presence of RBBB. With treatment, all of the ECG changes associated with hypokalemia and RBBB were corrected.

Light microscopy. In clinical practice, muscle biopsy is typically reserved for cases in which the diagnosis of TPP is uncertain. Light microscopy of muscle biopsy specimens from patients with TPP have shown some changes, including sarcolemmic nuclear proliferation, muscle fiber atrophy, fatty infiltrate, and vacuolations, although no changes were detected in one fourth of the patients.[18] Electron microscopy generally showed vacuolations (90%), mitochondrial abnormalities (100%), accumulation of glycogen granules (100%), myofibril interruption (50%), and T-system changes

(40%). These alterations do not correlate with the severity of the weakness.[18]

Treatment

In all patients with acute paralysis, the presence of hypokalemia should be confirmed before the start of treatment because some normokalemic or hyperkalemic paralytic conditions can worsen with the administration of potassium.[1,12] In hypokalemic patients, administration of 60 to 90 mEq/L of potassium chloride will normally abort the acute attack of paralysis within 15 to 20 minutes.[4] Doses of potassium above 90 mEq/L should be avoided because rebound hyperkalemia may occur as potassium moves out of the cells following the attack.[3,4,7,19] Unlike familial HPP and euthyroid paralysis, TPP is worsened by administration of acetazolamide.[20] It is not clear why this occurs, and further investigation is warranted. Correction of magnesium levels may also be necessary.[3] In some cases, the phosphate levels can be corrected without administering potassium supplements[3]; otherwise, phosphate levels should be corrected.

Prevention of hypokalemic episodes consists of restoring the euthyroid condition.[3–11] Nonselective β-blockers and thionamides are sufficient to correct thyroid hormone levels in most cases.[3,12] Other treatment modalities include potassium supplementation, potassium-sparing diuretics, a low carbohydrate diet, and carbonic anhydrase inhibitors.[3,21]

In the case patient, 40 mEq/L of oral and 60 mEq/L IV potassium chloride were initially given. Potassium increased to 1.9 mEq/L with slight improvement in motor function. With another 60 mEq/L of potassium chloride, the patient's motor function was restored. However, there was rebound hyperkalemia (5.4 mEq/L), which was corrected without treatment within a few hours. Rebound hyperkalemia was most likely due to excessive correction of potassium levels. The total amount of potassium chloride administered exceeded the recommended dose for the treatment of TPP because the patient was initially treated for idiopathic hypokalemia.

CONCLUSION

TPP is a rare condition that is most commonly reported in Asian men between the ages of 30 and 50 years; however, the precise sexual and racial predisposition remains unknown.[5] The case presented here involved a classic presentation of TPP in an epidemiologic group in which TPP is not commonly reported. This case illustrates the importance of considering TPP among the causes of acute paralysis, regardless of ethnic background. **HP**

REFERENCES

1. Fontaine B, Lapie P, Plassart E, et al. Periodic paralysis and voltage-gated ion channels [editorial]. Kidney Int 1996; 49:9–18.
2. Morovic-Vergles J, Ostric B, Skoro KM, Zelenika D. Thyrotoxic periodic paralysis: case report. Acta Clin Croat 2002; 41:99–102.
3. Ober KP. Thyrotoxic periodic paralysis in the United States. Report of 7 cases and review of the literature. Medicine (Baltimore) 1992;71:109–20.
4. Lin SH. Thyrotoxic periodic paralysis. Mayo Clin Proc 2005;80:99–105.
5. McFadzean AJ, Yeung R. Periodic paralysis complicating thyrotoxicosis in Chinese. Br Med J 1967;1:451–5.
6. Kemperman FA, Hoff HC, de Klerk G. [Hypokalemic periodic paralysis as the sole manifestation of hyperthyroidism.] [Article in Dutch.] Ned Tijdschr Geneeskd 1995;139:938–41.
7. Ko GT, Chow CC, Yeung VT, et al. Thyrotoxic periodic paralysis in a Chinese population. QJM 1996;89:463–8.
8. Chan A, Shinde R, Chow CC, et al. In vivo and in vitro sodium pump activity in subjects with thyrotoxic periodic paralysis [published erratum appears in BMJ 1992; 304:226]. BMJ 1991;303:1096–9.
9. Au KS, Yeung RT. Thyrotoxic periodic paralysis. Periodic variations in the muscle calcium pump activity. Arch Neurol 1972;26:543–6.
10. Dias Da Silva MR, Cerutti JM, Arnaldi LA, Maciel RM. A mutation in the *KCNE3* potassium channel gene is associated with susceptibility to thyrotoxic hypokalemic periodic paralysis. J Clin Endocrinol Metab 2002;87:4881–4.
11. Tricarico D, Servidei S, Tonali P, et al. Impairment of skeletal muscle adenosine triphosphate-sensitive K+ channels in patients with hypokalemic periodic paralysis. J Clin Invest 1999;103:675–82.
12. Rose BD, Post TW, editors. Clinical physiology of acid-base and electrolyte disorders. 5th ed. New York: McGraw-Hill; 2001:836–56.
13. Crane MG. Periodic paralysis associated with hyperthyroidism. Cardiologia 1960;92:285–8.
14. Kelley DE, Gharib H, Kennedy FP, et al. Thyrotoxic periodic paralysis. Report of 10 cases and review of electromyographic findings. Arch Intern Med 1989;149:2597–600.
15. Mehta SR, Verma A, Malhotra H, Mehta S. Normokalaemic periodic paralysis as the presenting manifestation of hyperthyroidism. J Assoc Physicians India 1990;38:296–7.
16. Sunohara N, Satoyoshi E. Triiodothyronine (T3) toxicosis with hypokalemic periodic paralysis. Eur Neurol 1984;23: 100–3.
17. Grauer K. 12-Lead ECGs: a "pocket brain" for easy interpretation. 2nd ed. St. Louis: Mosby; 2001.
18. Cheah JS, Tock EP, Kan SP. The light and electron microscopic changes in the skeletal muscles during paralysis in thyrotoxic periodic paralysis. Am J Med Sci 1975;269: 365–74.

19. Manoukian MA, Foote JA, Crapo LM. Clinical and metabolic features of thyrotoxic periodic paralysis in 24 episodes. Arch Intern Med 1999;159:601–6.
20. Shulkin D, Olson BR, Levey GS. Thyrotoxic periodic paralysis in a Latin-American taking acetazolamide. Am J Med Sci 1989;297:337–8.
21. Layzer RB. Periodic paralysis and the sodium-potassium pump. Ann Neurol 1982;11:547–52.

Copyright 2007 by Turner White Communications Inc., Wayne, PA. All rights reserved.