GITELMAN'S SYNDROME WITH SILENT THYROIDITIS

ATSUSHI SUZUKI, MASANORI YOSHIDA, YOSHITAKA MIURA and YUTAKA OISO

Department of Metabolic Diseases, Nagoya University Graduate School of Medicine,
Nagoya, Aichi 466-8550, Japan

Hypokalemic periodic paralysis is one of the most distinctive complications of hyperthyroidism and occurs in 8 to 34% of men and 0.2% of women with thyrotoxicosis in Asia.[1] It is also complicated by other diseases with potassium deficiency such as Bartter's syndrome, Cushing's syndrome, and Gitelman's syndrome. Generally, hypokalemic periodic paralysis with hyperthyroidism is diagnosed by assessing thyroid function and observing clinical manifestations of thyrotoxicosis.

A 34-year-old woman was admitted to a local hospital because of acute hypokalemic paralysis. She had never suffered from muscle weakness or paralysis before, and there was no family history of periodic paralysis or thyroid disease as far as she knew. Although diagnosed with Basedow's disease because of her diffuse goiter and undetectable thyroid stimulating hormone (TSH) level, she was prescribed potassium orally without any treatment for the disease. After 3 months, she was admitted to our hospital for sustained hypokalemia and muscle weakness. The patient experienced no hypertension or weight loss during her illness. On physical examination, she had a hard diffuse goiter of the thyroid gland without any other symptom or sign of thyroid illness. She exhibited both hypokalemia (serum potassium level, 2.9 mEq/l; normal range, 3.6–5.0 mEq/l) and hypomagnesaemia (serum magnesium level, 1.6 mg/dl; normal range 1.9–2.5 mg/dl); but she had no chronic dermatitis characterized by thickening with a purple-red hue often associated with chronic hypomagnesaemia. Urinary excretion of potassium was 30 mEq/day, and urinary Na/K ratio was 5.25. The level of urinary calcium excretion was low (0.024 g/g creatinine). Arterial pH was 7.469 and base excess was 4 mmol/l, suggesting metabolic alkalosis. Her plasma renin level was high (75.2 pg/ml; normal range 3.22–36.3 pg/ml), while her plasma aldosterone level was normal (65.8 pg/ml; 35.7-240 pg/ml), as were her adrenocorticotropic hormone and cortisol levels. A computed tomography study of the abdomen showed no evidence of adrenal tumor. In order to demonstrate the lack of a response of renal thiazide-sensitive Na-Cl cotransporter to thiazide, we examined the effect of the administration of 8 mg trichlormethiazide on chloride clearance (C_{Cl} = urinary chloride concentration × urine volume per min/serum chloride concentration). We found that chloride clearance was unchanged after thiazide administration (before, 1.30 ml/min; after 1.42 ml/min). On admission to our hospital, her TSH level was high (17.8 µU/ml; normal range, 0.56–3.91 µU/ml) with normal free triiodothyronine and free thyroxine levels. Anti-TSH receptor and anti-thyroid peroxidase antibodies were negative, but anti-thyroglobulin antibody was positive. An ultrasonographic study of the thyroid gland showed diffuse thyroid swelling with very low echogenecity. She was diagnosed as Gitelman's syndrome with silent thyroiditis,

Corresponding address: Atsushi Suzuki, MD PhD

Division of Endocrinology, Department of Internal Medicine, Fujita Health University School of Medicine,

1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan

Phone: +81-562-93-9242   Fax: +81-562-95-1879   E-mail: aslapin@fujita-hu.ac.jp

and was again administered potassium orally. However, muscle weakness and hypokalemia were observed when her serum TSH levels were periodically undetectable (Fig. 1). After she was given spironolactone in addition to potassium supplementation, her serum potassium level was elevated and the periodical muscle weakness disappeared.

Gitelman's syndrome has been described as a renal disorder characterized by hypokalemia, hypomagnesaemia, metabolic alkalosis, and hypocalciuria.[2] It is caused by inactivating mutations in the thiazide-sensitive Na-Cl cotransporter gene, and attenuated renal excretion in response to thiazide diuretics has been reported.[3,4] In comparison with Bartter's syndrome, the degree of volume contraction and the associated stimulation of the renin-angiotensin-aldosterone axis in Gitelman's syndrome are mild, and plasma aldosterone levels might remain within normal range as seen in her case.[5] She was first diagnosed as Basedow's disease in a local hospital because of periodic paralysis with a diffuse goiter, an undetectable serum TSH level, and hypokalemia. We subsequently found that her clinical features were compatible with silent thyroiditis and Gitelman's syndrome, though she declined genetic analysis. At its onset, silent thyroiditis often develops into thyrotoxicosis, but many patients exhibit changes in thyroid function, since the clinical course of silent thyroiditis conforms to the model for destruction-induced thyrotoxicosis. Thyrotoxic periodic paralysis can occur in any patient with a case of the thyrotoxicosis that may be clinically mild.[6] Total body potassium content in thyrotoxic periodic paralysis is normal, since its hypokalemia is the result of an intracellular shift of potassium. Thyrotoxic periodic
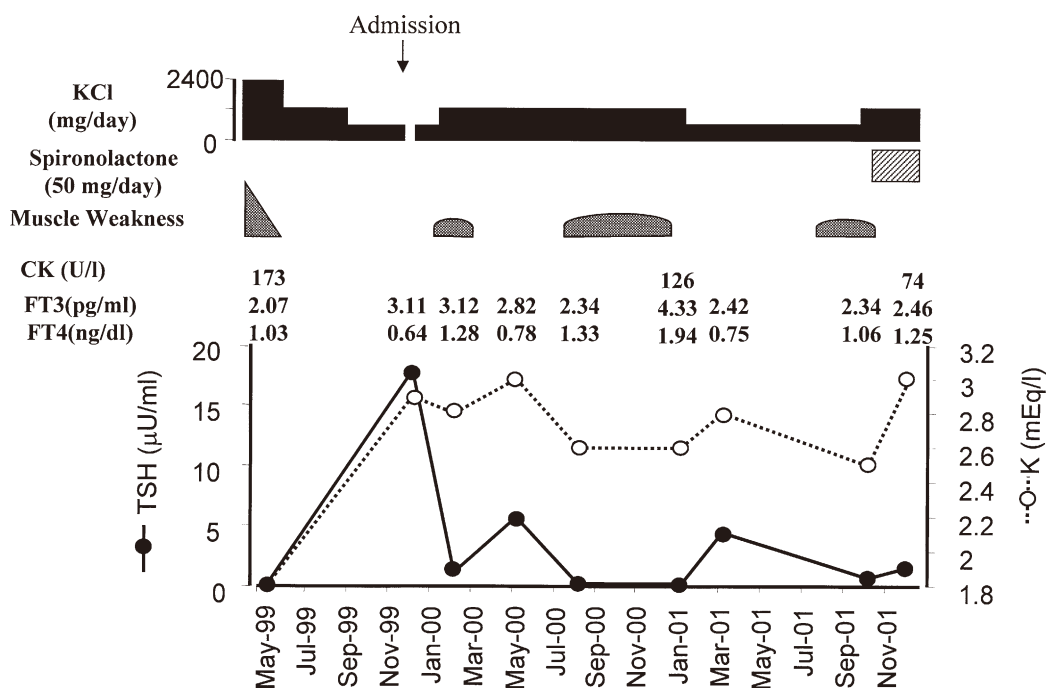

Fig. 1 Clinical course of the present case.
CK, creatine kinase (normal range, 20–170 U/l); K, potassium (normal range, 3.6–5.0 mEq/l); FT3, free triiodothyronine (normal range, 1.92–3.38 pg/ml); FT4, free thyroxine (normal range, 0.71–1.85 ng/dl); TSH, thyroid stimulating hormone (normal range, 0.56-3.91 µU/ml).

paralysis is most often associated with hypokalemia, but can occur at the onset when the serum potassium level is normal. Patients with non-thyroidal hypokalemic myopathy have a low total body store of potassium, and the severity of muscle weakness is correlated with the severity of hypokalemia. In our case, her serum potassium level and muscle weakness were correlated with a low serum TSH level, suggesting a negative correlation between her hypokalemia and serum thyroid hormone level. Thus, her episode seems to have been precipitated by thyrotoxicosis. After the administration of spironolactone, which can increase the total body potassium store, her muscle weakness and hypokalemia disappeared. Hypomagnesaemia can also affect myopathy, but the serum magnesium level in our case did not change when her muscle weakness occurred. Her serum creatine kinase level was high at the onset, and decreased to normal when her serum potassium level returned to normal, suggesting that potassium rather than magnesium played a pivotal role in the mechanism of her periodic myopathy.

In conclusion, given the great likelihood of misdiagnosis of cases like the present one, in which both thyrotoxicosis and Gitelman's syndrome coexist, the diagnosis of hypokalemic periodic paralysis should be made with extreme caution. The shift of potassium into the cells in thyrotoxicosis may precipitate hypokalemic myopathy caused by other diseases.

REFERENCES

1) Layzer, R.B. and Abrams, G.M.: Neuromuscular manifestations of endocrine disease. In Principles and Practice of Endocrinology and Metabolism, edited by Becker K.L., pp. 1912–1920 (2001), Lippincott Williams & Wilkins, Philadelphia, PA.
2) Gitelman, H.J., Graham, J.B. and Welt, L.G.: A new familial disorder characterized by hypokalemia and hypomagnesemia. *Trans. Assoc. Am. Physicians.*, 79, 221–223 (1966).
3) Simon, D.B., Nelson-Williams, C., Bia, M.J., Ellison, D., Karet, F.E., Molina, A. M., Vaara, I., Iwata, F., Cushner, H.M., Koolen, M., Gainza, F.J., Gitelman H.J. and Lifton, R.P.: Gitelman's variant of Bartter's syndrome, inherited hypokalaemic alkalosis, is caused by mutations in the thiazide-sensitive Na-Cl cotransporter. *Nat. Genet.*, 12, 24–30 (1996).
4) Coloussi, G., Rombola, G., Brunati, C. and De Ferrare, M.E.: Abnormal reabsorption of Na^+/Cl^- by the thiazide-inhibitable transporter of the distal convoluted tubule in Gitelman's syndrome. *Am. J. Nephrol.*, 17, 103–111 (1997).
5) Guay-Woodford, L.M.: Bartter syndrome: unraveling the pathophysiologic enigma. *Am. J. Med.,* 105, 151–161 (1998).
6) Scheinman, S.J. and Moses, A.M.: The kidneys and electrolyte metabolism in thyrotoxicosis. In Werner & Ingbar's The Thyroid: a fundamental and clinical text, edited by Braverman, L.E. and Utiger, R.D., pp. 617–621 (2000), Lippincott Williams & Wilkins, Philadelphia, PA.