Case Report

Thyrotoxic Periodic Paralysis Complicated with Primary Aldosteronism

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A 35-year-old man presented with acute onset of bilateral lower extremity weakness after ingesting a large amount of carbohydrates. Laboratory investigation revealed severe hypokalemia (1.9 mEq/l) and hyperthyroidism. The patient also exhibited primary aldosteronism due to a left adrenal adenoma. As a diagnostic tool, paralysis with hypokalemia (2.8 mEq/l) was induced with a glucose infusion. After treatment with methimazole, there were no further episodes of paralysis and subsequent induction of paralysis with glucose was impossible, though primary aldosteronism persisted. These findings indicate that hyperthyroidism played a major role in the development of periodic paralysis, while primary aldosteronism apparently increased the patient's vulnerability to paralytic attacks.

Key words: Paralytic attack, Hypokalemia, Hyperthyroidism, Adrenal tumor

Periodic hypokalemic paralysis is not a rare complication of thyrotoxicosis in Asia. Hypersecretion of aldosterone has been suggested to be an underlying mechanism. In hyperthyroidism, volume depletion and hyperfunction of the sympathetic nervous system stimulate the renin-angiotensin system, which in turn increases aldosterone secretion and results in potassium depletion (1, 2).

Here, we report a case of periodic thyrotoxic paralysis in which primary aldosteronism, due to an aldosterone producing adenoma, preceded the occurrence of thyrotoxicosis. The attacks of paralysis subsided following treatment of the hyperthyroidism. The association of primary aldosteronism with thyrotoxicosis is very rare but it is important to elucidate the significance of potassium deficiency as an underlying mechanism in thyrotoxic paralysis.

CASE REPORT

A 35-year-old man visited a local physician in May 1986 with an acute onset of bilateral lower ex-

trémity weakness and myalgia. The previous evening he had ingested a large amount of carbohydrates. On awakening in the morning, he was unable to walk. Blood chemistry tests showed severe hypokalemia (1.9 mEq/l). He was treated with intravenous potassium chloride and the paresis gradually resolved. He repeatedly experienced similar episodes after ingesting midnight snacks and was admitted to our hospital on Oct. 10, 1986. Past history disclosed hypertension of 150/110 mmHg with a duration of at least 2 yr, severe weight loss (18 kg) and excessive sweating over the past 3 months. He was not taking diuretics or other medication. There was no family history of thyroid or neurologic disease.

On physical examination, blood pressure was 168/108 mmHg, pulse rate, 110 beats/min and regular, and temperature, 36.4°C. The thyroid gland was diffusely enlarged. There was no pretibial edema. Neurological examination disclosed intact cranial nerves, no paresis of the four extremities, no muscular atrophy and no sensory impairment.

Laboratory studies revealed serum sodium of 144

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mEq/l, chloride 104 mEq/l, potassium 3.2 mEq/l, calcium 9.2 mg/dl, phosphorus 3.8 mg/dl, glucose 90 mg/dl, blood urea nitrogen 15.5 mg/dl, creatinine 0.8 mg/dl and alkaline phosphatase 10.5 K.A. (N 1.6 to 10.4). Serum levels of creatine phosphokinase (CPK), aldolase (ALD), lactate dehydrogenase (LDH), aspartate aminotransferase (GOT) and alanine aminotransferase (GPT) were all within normal limits. Arterial blood gas analysis showed pH 7.47, P_{CO_2} 41.3 mmHg, P_{O_2} 107 mmHg and HCO_3^- 30.1 mEq/l. An electrocardiogram revealed sinus tachycardia with the presence of U waves. Thyroid function tests were as follows: triiodothyronine (T_3) 1.96 ng/ml (N 0.8 to 1.8), thyroxine (T_4) 13.4 μ g/dl (N 4.5 to 13.0), free- T_4 2.48 ng/dl (N 0.78 to 2.12) and thyroid stimulating hormone (TSH) 0.01 μ U/ml (N 0.34 to 3.5). ^{123}I -thyroid scintigraphy showed a diffuse uptake in an enlarged thyroid gland (Fig. 1). The 24-h radioactive iodine uptake was 77% (N 15 to 45%), indicating primary hyperthyroidism.

Primary aldosteronism was also suspected due to a suppressed plasma renin activity of 0.29 ng/ml/h (N 0.5 to 2.0) and a high plasma aldosterone concentration (PAC) of 282 pg/ml (N 47 to 131). A left adrenal mass was confirmed by computerized tomography (Fig. 2). Adrenal scintigraphy showed a high uptake of ^{131}I -aldosterol in the mass. Adrenal venography revealed a round tumor with

Fig. 1. ^{123}I thyroid scintigraphy.

displacement and stretching of the veins in an arcuate fashion around the surface (Fig. 3). Blood sampling from the adrenal vein demonstrated an approximately 12-fold increase in PAC on the left side compared with the right (lt. 4,856; rt. 384 pg/ml). He was diagnosed as having primary aldosteronism due to a left adrenal adenoma.

After admission the patient had episodes of hypokalemic paralysis. Induction of paralysis with glucose infusion (300 ml of 50% glucose for 1 h) was attempted. Grasping power began to decrease gradually with the decrease of the serum potassium level at the end of the first hour of the glucose infusion. Paralysis with hypokalemia (2.8 mEq/l) occurred in the fourth hour and then slowly returned

Fig. 2. Computerized tomography of the abdomen demonstrating a left adrenal tumor (arrows).

Fig. 3. Adrenal venography showing a round tumor with displacement and stretching of the veins in an arcuate fashion around the surface.

to the basal level (Fig. 4). Thyroid function was normalized forty days after the oral administration of an antithyroid drug (methimazole, 40 mg/day). The patient experienced no further attacks of paralysis even though primary aldosteronism persisted. No paralysis was induced on a subsequent attempt with the same maneuver. Grasping power was relatively unchanged, and paralysis was no longer induced even when a high PAC and hypokalemia was present (2.9 mEq/l at 4th h) (Fig. 4). After control of the serum potassium level and blood pressure was obtained by oral administration of potassium chloride and spironolactone, the left adrenal tumor (35×30×20 mm) was extirpated. Histological examination demonstrated mixed cell adenoma composed of clear cells and compact cells. After the operation, PAC decreased to 22.1 pg/ml with a

normal serum potassium level of 4.2 mEq/l and a blood pressure of 110/60 mmHg. The patient is now taking only methimazole (5 mg/day).

DISCUSSION

Hyperthyroidism and primary aldosteronism are both common causes of periodic hypokalemic paralysis. The incidence of periodic paralysis in Japan ranges from 1.9% to 6.2% in patients with hyperthyroidism (3, 4) and 20.4% in patients with primary aldosteronism (5). The present case was very unusual in that hyperthyroidism and primary aldosteronism occurred simultaneously. It is important, in such a case, with respect to pathophysiologic mechanisms, to determine which disease is of primary importance in precipitating the hypokalemic periodic paralysis. This patient had developed diastolic hypertension two yr before the initial paralytic attack. It is therefore probable that the primary aldosteronism preceded the occurrence of hyperthyroidism. However, the attacks of periodic paralysis in this patient approximately coincided with the onset of hyperthyroidism. Once euthyroidism was established, the attacks no longer occurred, indicating that paralysis was dependent on the thyrotoxic state.

To identify the mechanism of hypokalemic paralysis, we attempted to induce it by the standard provocative maneuver, both before and after methimazole treatment. In a hyperthyroidic state, induction of paralysis was successful with a glucose infusion. However, once euthyroidism was established, paralysis could not be induced. Before the start of methimazole treatment, serial measurements of the change in grasping power corresponded roughly with the change in the serum potassium level. When a euthyroid state was achieved, even in the presence of primary aldosteronism, a glucose load failed to decrease grasping power although it decreased the serum potassium level to the extent similar to that observed in a hyperthyroid state. These findings suggest that prolonged potassium depletion or hypokalemia per se, caused by primary aldosteronism, were not sufficient to induce paralysis in this case. The metabolic consequences of thyrotoxicosis in combination with the above, prepared the muscle to become susceptible periodic paralysis.

Regarding the occurrence of paralytic attacks,

Fig. 4. Serial changes in grasping power, serum potassium, immunoreactive insulin (IRI) and plasma aldosterone concentration (PAC) during glucose infusion before (●—●) and during (○- - -○) methimazole treatment.

prior studies of thyrotoxic periodic paralysis support the hypothesis that extracellular fluid with potassium rapidly enters into muscle cells, depleting extracellular potassium and resulting in a relative decrease of the intracellular potassium level and a failure of depolarization (6, 7). The exact mechanism of this shift is not known, but the direct effect of thyroid hormone in stimulating membrane Na-K-ATPase activity (8, 9), and/or the indirect effect of thyroid hormone in stimulating insulin hypersecretion (10), may be involved in the intracellular potassium shift. Additionally, since thyroid hormone increases the sensitivity of beta-receptors, thereby augmenting catecholamine-mediated cellular potassium uptake, it may also be a cause of thyrotoxic paralysis (11, 12). In our case, even though changes in intracellular potassium levels were not investigated, repeated episodes of hypokalemic paralysis after the ingestion of midnight snacks and a persistent increase of insulin after glucose infusion might support the insulin hypersecretion theory.

In *in vitro* studies of thyrotoxic rats fed a potassium depleted diet, Shishiba et al (13), showed that insulin causes an abrupt decrease in muscle membrane potential. In muscle from thyrotoxic animals fed a diet containing normal amounts of potassium, the same maneuver failed to induce depression of the membrane potential (13). Potassium depletion is responsible for muscle weakness and fatigue, affecting intracellular and extracellular potassium ion concentration in muscle tissue and resulting in an abnormality in the membrane potential. In this case, hypokalemia resulting from primary aldosteronism might, therefore, be the underlying cause in inducing the paralytic attack. A similar situation was reported in a case of hyperthyroidism associated with Bartter's syndrome (14).

A similar patient who presented with a paralysis attack complicated with both primary aldosteronism and thyrotoxicosis was reported by Hamaguchi et al (15). In that case, the paralysis attack was obviously due to primary aldosteronism as the paralysis attack continued after a euthyroid state was established. Serum enzymes including CPK, GOT, GPT and LDH, which are considered to originate from muscle tissue, were markedly elevated during paralysis and returned to normal levels with the com-

plete disappearance of paralysis after potassium administration. They speculated that continuous hypersecretion of aldosterone from the tumor increased renal distal tubular reabsorption of intratubular sodium and secretion of both potassium and hydrogen ions, with a progressive depletion of body potassium, inducing muscle necrosis and hypokalemic myopathy. This may explain the paralysis attacks caused by primary aldosteronism. In contrast, the present case exhibited normal serum levels of muscle originating enzymes during the paralysis attack. In addition, the physical examination did not support muscle necrosis or myopathy. In the present case, if the body potassium depletion had been marked as in the case of Hamaguchi et al (15), primary aldosteronism might have played the primary role in the development of periodic paralysis.

In conclusion, both thyroid and adrenal function should be comprehensively investigated in periodic paralysis, since cases such as the one reported here may occasionally be seen.

REFERENCES

- 1) Takeda R, Morimoto S, Uchida K, Miyamori I. Changes in plasma renin activity and plasma aldosterone in the induced paralytic attack of thyrotoxic periodic paralysis. *Acta Endocrinol* **82**: 715, 1976.
- 2) Haruyama K, Yamazaki M, Toki T, Fukuchi S. Aldosterone secretion and metabolism in hyperthyroidism. *Folia Endocrinol Jpn* **57**: 1496, 1981.
- 3) Okinaka S, Shizume K, Iino S, et al. The association of periodic paralysis and hyperthyroidism in Japan. *J Clin Endocrinol Metab* **17**: 1454, 1957.
- 4) Satoyoshi E, Murakami K, Kowa H, et al. Periodic paralysis in hyperthyroidism. *Neurology* **13**: 746, 1963.
- 5) Takeda R, Miyamori I, Yasuhara S. Clinical periodic paralysis: From the viewpoint of endocrinology. *Jpn J Med (Jpn)* **3238**: 13, 1986.
- 6) Norris FH, Clark EC, Bigliere EG. Studies in thyrotoxic periodic paralysis. *J Neurol Sci* **13**: 431, 1971.
- 7) Feely J. Potassium shift in thyrotoxic periodic paralysis. *Postgrad Med J* **57**: 238, 1981.
- 8) Asano Y, Liberman UA, Edelman IS. Thyroid thermogenesis: Relationships between Na^+ -dependent respiration and $\text{Na}^+ + \text{K}^+$ -adenosine triphosphatase activity in rat skeletal muscle. *J Clin Invest* **57**: 368, 1976.
- 9) Shishiba Y, Ozawa Y, Takaishi M, Eguchi N, Shimizu T. Potassium deficiency enhances the effect of thyroid hormone on Na-, K-ATPase in liver and kidney. *Endocrinol Jpn* **27**: 329, 1980.
- 10) Shishiba Y, Shimizu T, Saito K, Shizume K. Elevated

- immunoreactive insulin concentration during spontaneous attacks in thyrotoxic paralysis. *Metabolism* **21**: 285, 1972.
- 11) Sharma VK, Banerjee SP. β -Adrenergic receptors in rat skeletal muscle. Effects of thyroidectomy. *Biochim Biophys Acta* **539**: 538, 1978.
 - 12) Scarpace PJ, Abrass IB. Thyroid hormone regulation of rat heart, lymphocyte and lung β -adrenergic receptor. *Endocrinology* **108**: 1007, 1981.
 - 13) Shishiba Y, Shimizu T, Ozawa Y. Pathogenesis of thyrotoxic periodic paralysis. in: *Thyroid Research VIII*, Stockigt JR, Nagataki S, Eds. Australian Acad Sci, Camberra, 1980, p.577.
 - 14) Hashizume K, Kobayashi M, Hiramatsu K, Katakura M, Ichikawa K, Kotani M. A case of hyperthyroidism associated with Bartter's syndrome. *Int Med (Jpn)* **54**: 1193, 1984.
 - 15) Hamaguchi K, Sakai F, Ishihara N, Ebata K, Nakagawa S. Quadriparesis in primary aldosteronism: Hypokalemic necrotizing myopathy. *Clin Neurol (Jpn)* **13**: 705, 1973.
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