

A Case of Myotonic Dystrophy with Electrolyte Imbalance

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Type 1 myotonic dystrophy (DM1) is an autosomal-dominant inherited disorder with a multisystem involvement, caused by an abnormal expansion of the CTG sequence of the dystrophic myotonia protein kinase (DMPK) gene. DM1 is a variable multisystem disorder with muscular and nonmuscular abnormalities. Increasingly, endocrine abnormalities, such as gonadal, pancreatic, and adrenal dysfunction are being reported. But, Electrolytes imbalance is a very rare condition in patients with DM1 yet. Herein we present a 42-yr-old Korean male of DM1 with abnormally elevated serum sodium and potassium. The patient had minimum volume of maximally concentrated urine without water loss. It was only cured by normal saline hydration. The cause of hypernatremia was considered by primary hypodipsia. Hyperkalemic conditions such as renal failure, pseudohyperkalemia, cortisol deficiency and hyperkalemic periodic paralysis were excluded. Further endocrine evaluation suggested selective hyperreninemic hypoaldosteronism as a cause of hyperkalemia.

Key Words: Myotonic Dystrophy; Hypernatremia; Hyperkalemia

INTRODUCTION

Type 1 myotonic dystrophy (DM1) is a congenital neuromuscular disorder caused by an abnormal expansion of the trinucleotide CTG in the dystrophic myotonia protein kinase (DMPK) gene, which exists on chromosome 19q (1). This disorder affects several organs, such as the heart, eyes, digestive system, and central nervous system, and dystrophic myotonia symptoms are exhibited along with various other clinical conditions in these patients (2). Hypergonadotropic hypogonadism and hyperinsulinemia are well-known endocrine abnormalities found in patients with this disorder, and there are reports of steroid synthesis disruption and a decrease in adrenal response to adrenocorticotrophic hormone (ACTH) (3). However, hypernatremia or hyperkalemia co-occurring in DM1 patients is rare. Smals et al. (4) reported hypernatremia that accompanied myotonic disorder, and Misra et al. (5) reported hyperkalemia. However, to our knowledge, there have been no reports of cases in which the two electrolyte abnormalities occurred simultaneously. Herein we report a case of DM1 that was accompanied by hypernatremia and hyperkalemia.

CASE DESCRIPTION

A 42-yr-old Korean male visited our hospital on August 1, 2011 because of intensified myalgia and muscle weakness. At the initial visit, he was 171.2 cm tall, weighed 65 kg, and had a body mass index (BMI) of 22.5 kg/m², blood pressure of 120/80 mmHg,

pulse rate of 80 beats/min, respiration rate of 20 breaths/min, and a temperature of 36.0°C. He was clearly conscious, but showed signs of overall tiredness and chronic illness. The patient exhibited symptoms of whole-body hair loss, and there were also observations of ptosis bilaterally. There were no indications of edema in the peripheral limbs; sensation in the upper and lower limbs was normal according to the neurologic examination, but his motor ability was slightly decreased. So an electromyogram (EMG) was performed. Myotonic discharge was observed, where small EMG waves (within 10 ms) continued to increase and attenuate in several muscles. This result is a characteristically observed in myotonic dystrophy, so the relevant DNA tests were performed. A PCT-Southern analysis was performed with a biotin-(CTG)_n 10 probe to investigate the abnormal expansion of (CTG)_n. The results showed that the patient had abnormal amplification of 1,200 bp PCR, which indicated that the (CTG)_n of the DMPK gene had been amplified to an approximate 300 recurrence rate. Based on these results, the patient was diagnosed with a classic form of type 1 myotonic dystrophy with more than 100 repeated sequence numbers.

A peripheral blood test revealed a hemoglobin level of 13.5 g/dL, a white blood cell count of 5,220/μL, a platelets count of 177,000/μL. Results of a biochemical serum test except muscle enzymes were in the normal range, but showed evidence of both hypernatremia and hyperkalemia, with 148 mEq/L sodium, 5.8 mEq/L potassium. In the urinalysis, sodium excretion was 107 mM/L, potassium excretion was 10 mM/L, plasma osmolality was 288 mOsm/kg, and urine osmolality was 711 mOsm/kg,

yielding a TTKG of 0.7. The patient's urine quantity was less than 1 L/d, and there was no water loss in the form of insensible loss. And it was only cured by normal saline hydration. So the hypernatremia was considered to be caused by primary hypodipsia.

Hyperkalemia is diagnosed mostly as a result of laboratory error, pseudohyperkalemia, acidosis, an increase in diet, hemolysis, and renal failure. Other than these causes, renin and aldosterone secretion, potassium secretion of the renal tubule and abnormalities in potassium absorption by extra-renal organs, can occasionally induce hyperkalemia (7). The patient's TTKG was less than 5, which indicated a decrease in potassium excretion in the urine. A baseline morning endocrine profile revealed a normal fasting glucose, a renin activity of 5.6 ng/mL/h (normal 0.65-3.2 ng/mL/h), an aldosterone of 56.7 pg/mL (normal 50-194 pg/mL), a cortisol level of 23.6 pg/mL (normal 7-25 µg/dL). Renin activity in the blood was considerably elevated, indicating an endocrine abnormality. The plasma renin activity increased from 5.6 ng/mL/h before the stimulus to 7.9 ng/mL/h two hours after intravenous administration of furosemide (20 mg), while aldosterone showed a weak response from 239 pg/mL to 319 pg/mL. In the rapid ACTH stimulation test, both cortisol and aldosterone showed no response 30 and 60 min after a stimulus was applied. Especially aldosterone was decreased rather. Perturbation of the renin-angiotensin-aldosterone system resulted in appropriately enhanced renin activity but with a subnormal aldosterone response, which appeared to be due to adrenal hyporesponsiveness. And it has been corrected by hydrocortisone. So the cause of hyperkalemia was thought to be the selective hyperreninemic hypoaldosteronism.

After hospitalization, the patient's myalgia improved as the potassium in the patient's blood returned to normal with the administration of diuretics, fluid treatment, and hydrocortisone. Thus, we determined that the myalgia and muscle weakness from DM1 had appeared as a form of secondary hyperkalemia through periodic paralysis due to selective hypoaldosteronism. Hypernatremia was considered to be caused by primary hypodipsia also treated by fluid therapy.

DISCUSSION

Type 1 myotonic dystrophy is an inherited autosomal dominant disorder, which is caused by over-expression of CTG trinucleotide inside the 3'-untranslated region of the gene encoding DMPK (6). The endocrine complications of this disorder include a reduced response of human growth hormone to insulin, arginine, and L-dopa, as well as abnormalities of thyroid function, hypergonadotropic hypogonadism, and hyperinsulinemia with insulin resistance. Such abnormalities present somewhat differently in different people and are closely associated with the period of the disorder and age (2, 3). However, the renin-angioten-

sin-aldosterone system is known to be normal in this disorder.

Elevated potassium has been reported in DM1 and thought to be due to the well-known membrane abnormality with resultant potassium leakage (7). A single patient with hyperkalemia and DM1 has also been reported, although this patient suffered from concurrent Addison's disease and hyperthyroidism (8). The other report documents clinically significant hyperkalemia in three unrelated subjects with DM1 with an apparent mineralocorticoid abnormality suggestive of hyperreninaemic hypoaldosteronism (5). Interestingly, hypoaldosteronism has been reported in the closely related condition of hyperkalaemic periodic paralysis (9). The possibility of hyperkalaemic periodic paralysis was ruled out in our case by EMG, muscle biopsy and genetic testing. Furthermore, the fractional urinary excretion of potassium was low (i.e. 5%) as seen in hypoaldosteronism and is not consistent with muscle leakage of potassium.

Selective hyperreninemic hypoaldosteronism can occur rarely as a result from a conversion disorder of angiotensin I (AI) or II (AII), or from abnormalities in the AII receptor (10). Conditions such as congenital adrenal hyperplasia, isolated mineralocorticoid deficiency and drugs such as heparin can also result in low aldosterone and elevated renin activity. Patients with myotonic dystrophy are reported to have high levels of atrial natriuretic peptide, a hormone known to stimulate renin activity and disrupt aldosterone synthesis, resulting in necrosis or atrophy of the adrenal cortex (11). There are also reports that myotonic dystrophy patients have highly active cytokines, such as tumor necrosis factor (TNF) and interleukin-1 (IL-1), which stimulate the secretion of renin and suppress the production of aldosterone (12). The hypothalamic-pituitary-adrenal (HPA) axis is also abnormally activated in DM1 with elevated baseline ACTH, hyperresponsiveness of ACTH to CRH-mediated stimuli such as naloxone (13). Thus, patients suffering from a chronic illness such as DM1 display several metabolic correlates of chronic stress which may impact adversely on the renin-angiotensin-aldosterone axis. The current case demonstrates significant hyperkalemia in a subject with normal renal function. But the baseline aldosterone level was low with high renin activities. The use of potent stimuli, such as furosemide, provoked a significant rise in the level of renin activity, and to a lesser degree in aldosterone. This subnormal aldosterone response was further uncovered with the additional exposure to AII infusion. The abnormality does not appear to involve the renin-AI-AII system itself, or the ACTH response of aldosterone which appeared to be affected to a lesser magnitude (14, 15).

Hypernatremia is also rarely observed in myotonic dystrophy patients, and is known to be caused by neurogenic disorders of osmoregulation in addition to previously reported endocrine abnormalities. Impaired Arginine vasopressin (AVP) secretion in response to osmotic stimuli and reduced thirst might be responsible for such failure (16). The patient in our case also had

hypernatremia. But he has minimum volume of maximally concentrated urine without water loss in the form of insensible loss. And it was only cured by normal saline hydration. So the hypernatremia seemed to be caused by primary hypodipsia.

It is unclear which is the exact mechanism of electrolyte abnormalities associated with DM1. A multisystem abnormality with a high degree of variability and thus responses may be related to the degree of CTG expansion. Also the electrolyte abnormalities may be related to the defective signal transduction associated with DMPK per se as mentioned above. Therefore potassium homeostasis that is known to be controlled by several converging hormonal systems may not be sufficient to overcome mineralocorticoid replacement (5). Also it is suggested that hypernatremia in patients with DM1 may have neurogenic disorders of osmoregulation in addition to previously reported endocrine abnormalities (16).

In conclusion, DM1 can demonstrate various clinical aspects, since it affects the endocrine and neurogenic system. As reported here, the electrolyte abnormalities are uncommon but attention should be paid to care for DM1 patients.

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