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CASE REPORT

Hypomagnesemia with Secondary Hypocalcemia (HSH): a Case Report

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SUMMARY

Background: **Hypomagnesemia with secondary hypocalcemia is an inherited condition caused by the body's inability to absorb and retain magnesium that is taken in through the diet. As a result, magnesium levels in the blood are severely low (hypomagnesemia). Shortages of magnesium and calcium can cause neurological problems that begin in infancy, including painful muscle spasms (tetany) and seizures.**

Methods: **We reported a case hypomagnesemia with secondary hypocalcemia. A 10-year-old male patient from a Han Chinese family, was admitted with recurrent convulsions over the past two years. Two years ago, the patient fell to the ground without obvious inducement, with numbness of the limbs accompanied by convulsions, unconscious disorder, and hypocalcemia. CT scans of the head showed multiple symmetrical calcifications in basal ganglia, corona radiata, and dentate nucleus of cerebellum.**

Results: **During hospitalization, the patient was given calcium carbonate D_3 tablets 600 mg each time, 3 times/d, calcitriol capsule 0.25 μg each time, 2 times/d, potassium chloride sustained-release tablets (Bundaxu) 2 tablets each time, 3 times/d, mixture of potassium aspartic acid (150 mg/d) and magnesium aspartic acid (140 mg/d) (Panangin) 2 tablets each time, 3 times/d, and intravenous infusion of magnesium sulfate 5 g each time, 2 times/d. The patient was continuously treated with oral medication after discharge. One month later, the level of Mg^{2+}, Ca^{2+}, K^+, and phosphorus in blood were 0.92 mmol/L, 2.41 mmol/L, 3.94 mmol/L, and 1.54 mmol/L, respectively.**

Conclusions: **Primary hypomagnesemia followed by hypocalcemia is a rare type of para-thyroid hypoplasia, clinically characterized by hypomagnesium, blood calcium and blood potassium, and our conclusions are helpful for the accumulation and summary of follow-up cases.**

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KEYWORDS

hypomagnesemia with secondary hypocalcemia, parathyroid hormone, painful muscle spasms, seizure, serum magnesium

INTRODUCTION

Hypomagnesemia with secondary hypocalcemia (HSH) is an autosomal recessive genetic disorder of magnesium malabsorption in the intestinal tract. The reason is

that the intestinal tract cannot normally absorb or retain magnesium ions in the diet which leads to reduced intestinal magnesium absorption and decreased serum magnesium levels. So hypomagnesemia is characterized by very low levels of magnesium in the blood, which is believed to be the cause of reduced parathyroid hormone (PTH) secretion by the parathyroid gland. Hypomagnesemia impairs the function of the parathyroid glands, which are small hormone-producing glands located in the neck. Normally, the parathyroid glands secrete PTH that increases blood calcium levels when they are low. Magnesium is required for the production and secretion of PTH, so when magnesium is too low, PTH is insufficiently produced and the levels of blood calcium are also reduced (hypocalcemia). The hypocalcemia is described as "secondary" because it occurs as a consequence of hypomagnesemia. Shortages of magnesium and calcium can cause neurological problems that begin in infancy, including painful muscle spasms (tetany) and seizures. If left untreated, HSH can lead to developmental delay, intellectual disability, a failure to gain weight and grow at the expected rate (failure to thrive), and heart failure. We report a case of hypomagnesemia with secondary hypocalcemia, and the details are shown below.

CASE PRESENTATION

A 10-year-old male patient from a Han Chinese family, was admitted with recurrent convulsions over the past two year. Two years ago, the patient fell to the ground without obvious inducement, with numbness of the limbs accompanied by convulsions, unconscious disorder, and hypocalcemia. After calcium supplement was given, the patient improved. After stopping taking calcium tablets, the patient had minor convulsions from time to time. On May 5, 2021, the patient fell to the ground again with limb twitching, tetany, nausea and vomiting. The results of serum electrolyte were as follows: serum sodium and blood chlorine were normal, blood Mg^{2+} was 0.61 mmol/L (normal reference value 0.70 - 1.00 mmol/L), blood Ca^{2+} was 1.08 mmol/L (normal reference value 2.10 - 2.55 mmol/L), blood K^{+} was 2.54 mmol/L (normal reference value 3.60 - 5.50 mmol/L), and blood phosphorus was 1.29 mmol/L (normal reference value 0.81 - 1.45 mmol/L).

CT scans of the head showed multiple symmetrical calcifications in basal ganglia, corona radiata, and dentate nucleus of cerebellum. The patient was given oral administration of calcium carbonate D3 tablets (Calcierge), calcitriol capsules (Luogaequan), and potassium chloride, and intravenous drip of calcium gluconate and magnesium sulfate. The patient's convulsions were relieved and he was diagnosed as hypomagnesium, hypocalcium, and hypokalemia with undetermined etiology. The patient had no previous history of other diseases. The patient had a natural birth at term with no abnormal growth and development, and he was not engaged in chemical work. In the family, the parents are not close relatives, and the cousin has a similar history (calcium and potassium supplements to control symptoms), no other family genetic history.

The patient was conscious and had a negative Chvostek sign and a positive Trousseau sign. The muscle strength of the patient's limbs was V level, the muscle tension was normal, and the pathological reflex was not elicited. The levels of Mg^{2+}, Ca^{2+}, K^{+}, phosphorus and parathormone (PTH) in blood were 0.94 mmol/L (0.62 - 1.12 mmol/L), 1.78 mmol/L (2.15 - 2.65 mmol/L), 3.33 mmol/L (3.50 - 5.50 mmol/L), 1.74 mmol/L (0.86 - 1.86 mmol/L), and 107.8 ng/L (10 - 88 ng/L), respectively. The levels of Mg^{2+} and Ca^{2+} in urine were 14.27 mmol/24 hours (2.1 - 8.2 mmol/24 hours) and 5.98 mmol/24 hours (2.5 - 7.5 mmol/24 hours), respectively, and the ratio of calcium to creatinine in urine was 0.512 (0.08 - 0.38). The level of K^{+} in urine was 100.31 mmol/24 hours (51 - 102 mmol/24 hours) under hypokalemia, and phosphorus in urine was 14.57 mmol/24 hours (22 - 48 mmol/24 hours). The level of 25-hydroxyvitamin D_3 was normal low limit, and blood pH and other electrolytes were normal. Parathyroid radionuclide imaging (ECT) showed indistinct development of parathyroid tissue, renal puncture biopsy showed no hypertrophy of paraglomerular apparatus, and X-ray examination showed no obvious abnormalities such as osteomalacia or delayed bone age.

Treatment

During hospitalization, the patient was given calcium carbonate D_3 tablets 600 mg each time, 3 times/d, calcitriol capsule 0.25 μg each time, 2 times/d, potassium chloride sustained-release tablets (Bundaxu) 2 tablets 3 times/d, mixture of potassium aspartic acid (150 mg/d) and magnesium aspartic acid (140 mg/d) (Panangin) 2 tablets each time, 3 times/d, and intravenous infusion of magnesium sulfate 5 g 2 times/d. The patient was continuously treated with oral medication after discharge. One month later, the level of Mg^{2+}, Ca^{2+}, K^{+} and phosphorus in blood were 0.92 mmol/L, 2.41 mmol/L, 3.94 mmol/L, and 1.54 mmol/L, respectively.

Follow-up visit

After discharge, the patient was followed up, and calcitriol capsules, calcium carbonate D_3 tablets, and potassium chloride sustained-release tablets were gradually stopped. Panangin tablets were given alone, from 3 to 4 tablets per day, 3 times per day. The level of Mg^{2+}, Ca^{2+}, K^{+}, and PTH in blood were basically maintained at normal levels. CT scan of skull showed no aggravation of abnormal calcification.

DISCUSSION

The patient has the following characteristics: (1) adolescent onset and long course of disease; (2) having a family history; (3) low calcium convulsions as the main

symptoms, rapid relief after calcium supplements, but the symptoms of repeated attacks; (4) normal development without special body type; (5) electrolyte disorder, severe low level of Mg^{2+}, Ca^{2+} and K^{+} in blood, and high level of the three electrolytes in urine; (6) in the case of hypocalcemia, the elevation of PTH was not significant or slightly higher; (7) after adequate supplementation of Mg^{2+}, Ca^{2+} and K^{+}, the convulsions disappeared and the level of Mg^{2+}, Ca^{2+} and K^{+} in blood returned to normal levels. During the follow-up, only Mg^{2+} and K^{+} were supplemented, and the blood biochemistry remained normal without previous clinical manifestations. Accordingly, the patient was clinically diagnosed as primary hypomagnesemia with secondary hypocalcemia.

Primary hypomagnesemia with secondary hypocalcemia is a rare type of hypoparathyroidism with no accurate prevalence statistics. In 1968, Paunier et al. first reported that a male infant presented at 6 weeks of age with generalized convulsions and coma associated with hypomagnesemia and hypocalcemia [1]. The patient was successfully treated by oral magnesium supplementation, and the defect in magnesium homeostasis was still present at 3 years of age [1]. Hypomagnesemia was considered to be due to either a specific defect in intestinal transport of magnesium or an unknown derangement of magnesium homeostasis [1]. The defect in magnesium metabolism caused severe hypocalcemia which was promptly and completely corrected by oral or parenteral administration of magnesium salts [1]. Oral magnesium supplementation was necessary to maintain satisfactory levels of magnesium and calcium, curing the severe neurological disturbance and, over the 3-year period of study, the boy developed normally [1].

Most of the patients developed the disease at an early age without racial specificity, and both male and female developed the disease. The disease was autosomal recessive or sporadic, and was believed to be caused by mutations in TRPM6 and/or TRPM7 genes. The two genes are expressed in kidney and intestine, and regulate transient receptor potential ion channel, changing intracellular divalent cation concentration such as Mg^{2+} by outward flow of sodium ions. At present, more than 30 TRPM6 mutations, such as point mutation, frame shift mutation, splice mutation, and termination mutation, have been found to reduce Mg^{2+} reabsorption from the intestine and kidney. Hypomagnesium inhibits the secretion of PTH in the parathyroid gland, resulting in hypocalcemia, but the level of phosphorus is normal. Hypomagnesium may cause hypokalemia. The treatment is mainly to consider a lifetime supplement magnesium.

The patient may be heterozygous, with relatively late onset and mild disease and without serious electrolyte disturbance. The maintenance effect was achieved by oral magnesium supplementation only, and the dosage used was small with 4.4 - 5.9 mmol/d. The diagnosis of primary hypomagnesemia secondary to hypocalcemia depends on clinical manifestations and biochemical examination. Gene analysis may contribute to the discovery of mutations, but at present, *in vitro* functional analysis of TRPM6 mutations, i.e., the relationship between mutation and function, is not conclusive. We have not done genetic testing yet.

We believe that clinical differential diagnosis is critical. Diagnosis of hypomagnesemia should be ruled out: (1) insufficient intake; (2) loss of body fluids; (3) Mg^{2+} redistribution after starvation; (4) loss of large amounts of Mg^{2+} through the kidney, that is, diuretic, renal failure, renal tubular acidosis and other factors affect the renal tubule resorption of Mg^{2+}. The patient did not have the above-mentioned medical history and disease characteristics, and the characteristics of hematuria and electrolytes did not meet the above-mentioned conditions.

This patient needs to be identified for other types of hypoparathyroidism (parathyroidism). Based on the patient's history, we excluded parathyroid hypothyroidism secondary to parathyroid surgery, neck radiation therapy or isolated parathyroid hypothyroidism in families. The patient had no other autoimmune or functional disorders and there was no evidence for diagnosis of idiopathic parathyropathy or other types.

In addition, pseudonychia is caused by PTH receptor or post-receptor defect, and can be divided into type i (ia, ib, and ic) and type ii. The patient had no specific body size and no significant elevation of serum PTH, accompanied by multiple electrolyte disturbances, but pseudoparathyroid hypothyroidism and pseudohypoparathyroidism (PPHP) were not well documented.

Electrolyte abnormality but no hypertension should rule out Bartter and Giteman syndrome. The patient had metastatic calcification of the brain, no increase in plasma renin activity and aldosterone, and no significant proliferation of glomerular paravertebral cells. Follow-up treatment ruled out the disease. In addition, the characteristics of electrolyte disturbance in this patient combined with relevant examinations ruled out other renal tubule disease.

CONCLUSION

In conclusion, primary hypomagnesemia followed by hypocalcemia is a rare type of para-thyroid hypoplasia, clinically characterized by hypomagnesemia, blood calcium and blood potassium, which has not been reported in China. Our conclusions are helpful for the accumulation and summary of follow-up cases.

Declaration of Interest:
All authors declared that there were no any potential conflicts of interest.

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