CASE REPORT

Gitelman syndrome

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SUMMARY

Hypokalaemia is a common clinical disorder, the cause of which can usually be determined by the patient's clinical history. Gitelman syndrome is an inherited tubulopathy that must be considered in some settings of hypokalaemia. We present the case of a 60-year-old male patient referred to our nephrology department for persistent hypokalaemia. Clinical history was positive for symptoms of orthostatic hypotension and polyuria. There was no history of drugs consumption other than potassium supplements. Complementary evaluation revealed hypokalaemia (2.15 mmol/l), hypomagnesaemia (0.29 mmol/l), metabolic alkalosis (pH 7.535, bicarbonate 34.1 mmol/l), hypereninaemia (281.7 U/ml), increased chloride (160 mmol/l) and sodium (126 mmol/l) urinary excretion and reduced urinary calcium excretion (0.73 mmol/l). Renal function, remainder serum and urinary ionogram, and renal ultrasound were normal. A diagnosis of Gitelman syndrome was established. We reinforced oral supplementation with potassium chloride and magnesium sulfate. Serum potassium stabilised around 3 mmol/l. The aim of our article is to remind Gitelman syndrome in the differential diagnosis of persistent hypokalaemia.

BACKGROUND

Hypokalaemia is a frequent electrolyte disturbance, particularly in hospitalised patients. In most cases of chronic hypokalaemia, the cause is straightforward, usually resulting from unreplenished gastrointestinal or urinary losses. Gitelman syndrome (GS) is an autosomal recessive salt-losing renal tubulopathy that causes hypokalaemia and metabolic alkalosis.[1]

CASE PRESENTATION

We present the case of a 60-year-old Portuguese Caucasian male with persistent hypokalaemia, referred to our nephrology department. This condition had first been found at the age of 55 during hospitalisation for community-acquired pneumonia, and he had been irregularly taking oral magnesium and potassium supplements ever since.

Anamnesis was positive, with a long time history of symptoms of orthostatic hypotension and records of systolic blood pressure always below 120 mm Hg. He referred polyuria and nycturia with no other urinary tract symptoms. His medical history was not significant. Other than the above-mentioned supplements, he denied any drug intake. His family history was negative.

On physical examination he had a blood pressure of 110/70 mm Hg and regular pulse frequency of 80/min, normal hydration and colouration of skin and mucosa. Cardiopulmonary examination was normal with no signs of peripheral oedema. The remaining physical examination was normal.

On gas analysis, he presented a metabolic alkalosis (pH 7.535; pCO_2 40 mm Hg; HCO_3 34.1 mmol/l). Biochemical analysis revealed hypokalaemia (2.46 mmol/l), hypomagnesaemia (0.38 mmol/l) and hypochloraemia (95 mmol/l). Serum creatinine (62 µmol/l), urea (6.3 mmol/l) and remainder ionogram were normal. Further investigation revealed elevated plasma-active renin (281.7 µU/ml; NR 4.4–46.1), normal aldosteronaemia (16.7 ng/ml in orthostatism; NR 4–31), hypocalciuria (0.73 mmol/l; NR 2.5–7.5) and increased urinary excretion of sodium (126.5 mmol/l; NR 20–110) and chloride (160 mmol/l; NR 55–125). Estimated glomerular filtrate rate (MDRD) was 115 ml/min/1.73 m^2 and potassium transtubular gradient was 11.6. Electrocardiogram showed normal sinus rhythm with a rate of 74/min. Renal ultrasound, and renal and adrenal CT revealed normal kidneys.

Based on the association of hypomagnesaemia, hypokalaemia, metabolic alkalosis, hypocalciuria and low-normal blood pressure, the diagnosis of GS was established.

TREATMENT

The patient began oral supplementation with magnesium aspartate/potassium aspartate 250/250 mg four times a day (qid), magnesium aspartate 1229.6 mg once a day (qd) and potassium chloride 600 mg twice daily (bid) and he was encouraged to maintain a high-sodium and high-potassium diet. A therapeutic trial with spironolactone was interrupted due to mammal pain.

OUTCOME AND FOLLOW-UP

Two months later he was asymptomatic with serum potassium 2.9 mmol/l and magnesium 0.52 mmol/l. We reinforced ion supplementation. For professional reasons, the patient went abroad on a permanent basis and the follow-up was lost.

DISCUSSION

Chronic hypokalaemia is a common clinical problem with potentially life-threatening manifestations.

Our patient had a long time history of symptomatic hypotension and persistent hypokalaemia with metabolic alkalosis and hypomagnesaemia. Vomiting and diuretic abuse, the two major diagnoses in this setting, were excluded by measuring a high urinary chloride excretion and by a negative history of diuretic use, respectively. The remaining differential diagnoses were the genetic disorders of Gitelman and Bartter syndromes. Bartter syndrome was improbable because it usually has an earlier onset and a more severe phenotype, urinary calcium excretion is often increased and the magnesaemia is normal or mildly reduced.

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Thus, our final diagnosis was GS (MIM #263 800), an autosomal recessive salt-losing renal tubulopathy. In the vast majority of cases, disease is due to inactivating mutations in the gene that encodes the renal thiazide-sensitive sodium-chloride cotransporter (NCC) present in the epithelial cells of the renal distal convoluted tubule (DCT).[2] It is characterised by hypomagnesaemia, hypocalciuria and secondary hyperaldosteronism that induce hypokalaemia and metabolic alkalosis. Clinical manifestations are similar to the prolonged administration of thiazide diuretics.[3]

GS is often not diagnosed until late childhood or even adulthood. Cramps, paresthesias and fatigue frequently occur. Most patients report recurrent periods of carpopedal spasms during vomiting, diarrhoea or fever. Chondrocalcinosis occurs later in life, and maybe the consequence of hypomagnesaemia.[4] Blood pressure is lower in the general population.

The diagnosis of GS is based on the clinical symptoms and biochemical abnormalities, which include hypomagnesaemia, hypokalaemia, metabolic alkalosis and hypocalciuria. GS patients have a blunted natriuretic response to thiazide, but a prompt natriuresis after furosemide, indicating that the defect is located at the level of the distal tubule. DNA mutation analysis of the gene responsible for GS may confirm the diagnosis.[1 4]

Most asymptomatic patients remain untreated and undergo ambulatory monitoring with low frequency. Progression to renal insufficiency is extremely rare.[5]

Concerning treatment, supplementation with magnesium is indicated, along with a high sodium and high potassium diet. If symptomatic hypokalaemia is not corrected, it can be the associated drugs that antagonise aldosterone activity or block the sodium channel ENaC in the collecting duct. An option is the combination of amiloride, spironolactone or eplerenone with potassium chloride.[1]

Learning points

- Remember Gitelman syndrome in situations of unexplained hypokalaemia, hypomagnesaemia and metabolic alkalosis.
- Gitelman syndrome is an autosomal recessive salt-losing renal tubulopathy.
- Clinical manifestations of Gitelman syndrome mimetise prolonged administration of thiazide diuretics

Competing interests None.

Patient consent Obtained.

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