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Case Report

A Case Report on Familial Hypokalemic Periodic Paralysis

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Abstract

Introduction: Periodic Paralysis (PP) is a rare neuromuscular disease related to a defect in muscle ion channels, characterized by sporadic episodes of painless muscle weakness that can be precipitated by vigorous exercise, prolonged fasting, or carbohydrate-rich meals. PP is classified as hypokalemic when episodes occur associated with low levels of potassium in the blood. The crises start in late childhood or early adolescence and vary in frequency and duration. Treatment during the acute phase is administration of potassium chloride [1-4].

Case Report: A 12-year-old female adolescent appealed to the emergency department due to sudden onset of tetraparesis. She had no difficulty breathing or signs of respiratory distress. Neurological examination showed grade II muscle strength in the lower limbs and grade III in the upper limbs. Osteotendinous reflexes were absent. Facial mimic was present.

The mother promptly reported a family history of periodic hypokalemic paralysis affecting several members.

Blood analysis showed an isolated severe hypokalemia of 1.7 - 2.0 mEq/L. Electrocardiogram (EKG) showed prolonged PQ interval, mild ST depression, prominent U waves.

Slow correction of potassium was promptly started with gradual recovery of muscle strength and EKG stabilization. She was discharged 20 hours after therapy onset and medicated at home with daily acetazolamide and potassium chloride if onset of symptoms. Genetic study was started for index familial mutations.

Conclusion: Periodic familial paralysis are rare conditions, the most frequent being the hypokalemic form. The diagnosis of PP can be confirmed by genetic tests, which are recommended as first line when there is an intermediate to high degree of clinical suspicion. This case report is intended to emphasize the importance of the clinical history and a complete physical examination on diagnosis. Treatment should not be delayed. Genetic family counselling should be offered [2,3].

Keywords: *Periodic Paralysis (PP); Potassium Chloride; Electrocardiogram (EKG)*

Introduction

Periodic Paralysis is a rare neuromuscular disease related to a defect in muscle ion channels, characterized by sporadic episodes of painless muscle weakness that can occur spontaneously or can be precipitated by rest after vigorous exercise, prolonged fasting, carbohydrate-rich meals, stress, intercurrent viral illness, lack of sleep, menstruation, alcohol, some specific medications (beta agonists, corticosteroids and insulin) [2-4].

PP is classified as hypokalaemic when episodes occur in association with low blood potassium levels or hyperkalaemic when episodes are induced by high potassium levels [2-4].

Hypokalaemic PP is the most common paralysis, however it remains a rare entity with an estimated prevalence of 1 in 100,000. PP may be familiar with an autosomal dominant transmission or may be acquired in patients with thyrotoxicosis. Clinical penetrance is often incomplete, especially in women [1,2].

Mutation in the gene encoding the dihydropyridine-sensitive calcium channel subunit alpha-1 in skeletal muscle is the most common genetic abnormality in hypokalaemic PP and is found in approximately 70% of patients [3,4]. A mutation in the skeletal muscle sodium channel, SCN4A, may also be the cause of this disease [5,6]. Families with the latter mutation show more complete clinical penetrance, affecting both men and women equally [5].

As with all periodic paralysis, attacks occur suddenly with general weakness while consciousness is preserved [2,3].

In hypokalaemic PP, events begin in late childhood or early adolescence. These vary in frequency and duration. They usually last for several hours, but the duration can vary from minutes to days. The episodes can be triggered by rest after vigorous exercise, stress or a high carbohydrate meal. They are often associated with increased release of adrenaline or insulin, which causes potassium movement in cells and low blood potassium levels [1].

Neurological examination during a crisis demonstrates weakness, usually affecting the lower limbs more than the upper limbs. Hyporeflexia or areflexia is typical. Between episodes, neurological examination is usually normal [2-4,6].

The average plasma potassium concentration during an episode is 2.4 mEq/L [7].

Cardiac arrhythmias such as tachycardia, atrial fibrillation, paroxysmal supraventricular tachycardia, or ventricular fibrillation are rare [8]. During episodes, electrocardiogram (ECG) may show findings compatible with hypokalaemia, including ST-segment depression, decreased T-wave amplitude, and increased U-wave amplitude [2,3].

When there is a family history of hypokalemic PP, PP tests are often not used for further diagnostic evaluation. Otherwise, the diagnosis is suggested by hypokalemia during a typical muscle weakness crisis. Even when this is demonstrated, further testing is required to rule out alternative diagnoses. When symptoms are deprecated or after crisis, diagnosis can be difficult because, having a high rate of clinical suspicion, other diagnostic options can be tested and used for genetic testing, provocative tests and electromyography (EMG).

During an acute phase the treatment for outpatients involves the administration of oral potassium. The dose of oral potassium is 0.2 - 0.4 mEq/day. When we have electrocardiographic alterations we need hospitalization and IV infusion of 40 mEq/L in 5% mannitol solution infused at a maximum of 20 mEq/h, not outstrip 200 mEq/day. We have to monitor of potassium levels after treatment [2-4]. Cardiac monitoring is recommended during and after treatment. Recovery may take a few minutes [6-8].

The potassium should not be administered in glucose-containing solutions because patient may suffer from an over-insulin response to carbohydrate loads [2-4].

As prevention patient should be advised to avoid triggers such as stress, fasting exercise, high-carbohydrate and high-salt meals [2].

Dichlorophenamide is accepted for HypoPP and has been associated with reductions in attacks frequency, severity and duration of chronic treatment [2].

Potassium-sparing diuretics are a potential option for chronic treatment of HypoPP.

Case Report

A 12 years old female adolescent appealed to emergency department due to sudden onset of tetraparesis. No respiratory distress or other associated signs or symptoms were present.

A family history of recurrent hypokalaemic paralysis was previously known to the mother, two maternal cousins and maternal grandfather. The mother is followed in neurology consultation and medicated with oral potassium and acetazolamide.

On general examination she was alert and oriented, without signs of respiratory distress. Blood pressure (BP) was 109/56 mmHg and heart rate of 86 bpm. Cardiac and pulmonary auscultation and abdomen examination were normal. During neurological evaluation she presented grade II and grade III muscle strength in lower limbs and upper limbs, respectively. Osteotendinous reflexes were absent.

Venous blood gas analysis showed pH 7.39; HCO_3^- 22.4 mEq/L; potassium 1.7 mEq/L; sodium 142 mEq/L; calcium 1.21 mEq/L; chloride 110 mEq/L; Glucose 123 mg/dL; Lactates 1.7 mmol/L. Analytical evaluation confirmed a hypokalaemia of 2.0 mEq/L. Thyroid function was normal.

Electrocardiogram showed 76 bpm in sinus rhythm with slightly increased PQ interval, mild ST depression and prominent U waves. QTc of 613 msec.

Treatment of PP episodes includes administration of potassium chloride, preventing cardiac arrhythmias and respiratory failure. If hypokalaemia is less than 2.5 mEq/L, or there is oral intolerance, the intravenous route should be chosen, not exceeding 10 mEq/ hour, because of the risk of rebound hyperkalaemia. This was the initial option in the case presented. The administration of glucose serum was avoided, due to the risk of aggravation of hypokalaemia secondary to hyperinsulinism.

Potassium reached the value of 2.3 mEq/L in the first three hours, rising until normal range at 12 hours of treatment. First we observed a normalization of the EKG and then recovery of muscle strength.

With potassium normalization (5 mEq/L) and muscle strength recovery, fluid therapy was suspended.

She was discharged 20 hours after the beginning of therapy and was conducted to perform acetazolamide (250 mg twice a day) as prevention and Potassium Chloride in case of crisis, at home.

After this inaugural episode, she is followed at the neuropediatric consultation. Since then, she has presented two new episodes requiring therapy but not having to resort to the emergency department.

She maintains physical activity and dietary care, carbohydrate and salt restriction.

From the genetic study carried out, the pathogenic variant c3716G> Ap (Arg1239His) was detected in heterozygote in the CACNA1S gene, confirming the genetic etiology of hypokalaemic periodic paralysis.

Discussion and Conclusion

Familial periodic paralysis is a rare condition, the most frequent being the hypokalemic form [2-4]. Hypokalemic PP usually begins in childhood or adolescence, with spontaneous episodes of focal or generalized paralysis that may last minutes to hours associated with hypokalemia (< 2.5 mEq/L), with preservation of consciousness [2,4-6]. Severe cases present in early childhood, the majority before age 16 years. Weakness may range from slight transient weakness of an isolated group to severe generalized weakness [2,8,9]. The crisis are

more frequent at night and early in the morning and are often precipitated or aggravated by low potassium consumption or excessive urinary or gastrointestinal losses; high carbohydrate or sodium diet; use of diuretics, corticosteroids, insulin or β-agonists; infections; emotional stress; vigorous physical exercise and cold exposure [2,3,7,8].

Myopathy may develop in affected individuals, which results in progressive muscle weakness in the proximal muscles of the lower limbs. Myopathy can occur without paralytic symptoms [3].

The diagnosis of PP can be confirmed by genetic testing, recommended as first line when intermediate to high clinical suspicion is suspected. All PP have an autosomal dominant transmission. In the absence of an identified genetic mutation in approximately 30% of patients, paralysis subtypes can be distinguished based on clinical presentation and serum potassium levels during crisis or episodes [3,4].

In the hypokalemic form, treatment is based on the acute phase, restoring potassium levels by replacing approximately 40 mEq potassium chloride. The post-crisis phase should focus on the importance of lifestyle changes, avoiding possible triggers and inhibitors of carbonic anhydrase, with acetazolamide being the most used [1,2,4].

PP as rare conditions requires studies related to therapeutic approaches during and after attacks, as well as long-term follow-up [8,9]. Approximately 70% of cases result from mutation in the calcium channel gene CACNA1S - type 1 hypokalaemic paralysis. This gene encodes the voltage-dependent calcium channel α1 subunit of the skeletal muscle, which is located primarily in the membrane of the transverse tubular system [3].

This case report aims to emphasize the need for a good clinical history and a complete objective examination for proper diagnosis and treatment options.

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