Hypokalemic periodic paralysis due to the SCN4A R672H mutation in a Turkish family

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Hypokalemic periodic paralysis (HypoPP) is an autosomal dominant disorder characterized by episodic attacks of muscle weakness associated with a decrease in blood potassium levels. Recently, mutations in the gene coding for the skeletal muscle voltage-gated sodium channel alpha subunit (SCN4A) have been reported. We detected the R672H mutation in one HypoPP Turkish family.

Key words: hypokalemic periodic paralysis, R672H mutation, Turkish family.

Hypokalemic periodic paralysis (HypoPP) is a rare inherited disorder, with an overall incidence in the general population of about 0.4-1 cases per 100,0001. The mode of inheritance of HypoPP is autosomal dominant, but approximately one-third of the cases may be sporadic. HypoPP is a channelopathy caused by mutations in calcium or sodium channels2. Patients present with episodic attacks of muscle weakness of varying severity with hypokalemia. The onset of the disease is usually in the first or second decade of life. Here, we report HypoPP due to the SCN4A R672H mutation in a Turkish family.

Case Report

A 14-year-old boy was admitted to our hospital because of sudden onset of general weakness of all extremities and inability to walk on awakening. This was his first attack, and his recent meal was rich in carbohydrates. He denied nausea, vomiting, diarrhea, or use of drugs. His family history revealed that his maternal uncle had recurrent attacks of muscle weakness in childhood, but his mother had no history of similar episodes.

On physical and neurological examination, his vital signs were normal. His thyroid gland was not enlarged. Cardiopulmonary examination was unremarkable. He had symmetric flaccid paralysis with areflexia in the upper and lower extremities. No fasciculations, myoclonus, muscular atrophy, or pyramidal or cerebellar signs were observed. The remainder of the physical and neurological examination was normal.

On laboratory examination, routine biochemistry, liver enzymes and complete blood count were normal except for potassium level of 2.1 (3.5–5 mmol/L). His thyroid functions were also normal. Urine pH, glucose, sodium, potassium, chloride, and urine osmolar gap were normal. ECG also showed no abnormality.

Considering the clinical pattern and biochemical abnormalities, he was diagnosed as HypoPP and was treated with potassium intravenously followed by oral administration for a few days. After six hours, he had recovered completely. Genetic examination was carried out and presence of a mutation of the sodium channel R672H was confirmed in our patient and in his mother. The R672H was detected by direct sequencing of the SCN4A gene from genomic DNA (extracted from EDTA whole blood).

Discussion

Periodic paralyses (PP) are a group of rare, heterogeneous disorders, characterized clinically by episodic, sudden onset, flaccid paralysis of a single, more than one or all skeletal muscles,
with usually complete recovery. HypoPP is the most common form of PP. Symptoms typically begin in the first or second decade. Attacks of paralysis usually occur on awakening in the night or in the early morning. Weakness may be focal or generalized, usually sparing facial and respiratory muscles. The symptoms are more severe in males. Frequency of individual attacks can vary from daily to a few episodes in a lifetime. Attacks occur spontaneously or are provoked by prolonged rest after vigorous exercise or a carbohydrate-rich meal on the previous day. Attacks can also be triggered by stress including viral illness, lack of sleep and some drugs (e.g. beta agonists, corticosteroids and insulin). In our case, the carbohydrate-rich meal might have been the precipitating factor since his attack occurred in the early morning of the following day.

Diagnosis of familial or primary HypoPP is established by demonstrating a low serum potassium level during a paralytic attack and by excluding secondary causes of hypokalemia such as gastroenteritis, hyperaldosteronism, and renal tubular acidosis, etc. We did not establish secondary causes of hypokalemia in our patient.

Familial HypoPP is an autosomal dominant muscle disorder caused by point mutations in the calcium channel subunit CACNA1S. About 10% of patients have the specific mutations of the skeletal muscle sodium channel gene (SCN4A). The mutations comprise the intramembrane subunit and thus impair muscle cell excitability. Severity, incidence and duration of weakness differ between individuals depending on the type of affected channels and on the type of genetic defects in the same channel. Those may be different phenotypic manifestations of the same genetic defect and same ion channel in individuals of the same family, as in our family. Ke et al. reported a R672H mutation in the SCN4A gene in five patients and also in five normal relatives of two Chinese families. The R672H mutation may transport as incomplete penetrance, especially in women. In the present family, the mother was not affected in her lifetime.

In conclusion, although HypoPP is a rare disease, it should be considered in the differential diagnosis of acute flaccid paralysis because the treatment is easy and prevention is possible.

REFERENCES