FAMILIAL HYPOMAGNESEMIA WITH SECONDARY HYPOCALCEMIA CAUSED BY TRPM6 GENE MUTATIONS

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Familial Hypomagnesemia with Secondary Hypocalcemia (HSH) is a rare autosomal recessive disorder that presents in infancy with neurological symptoms of magnesium dependent hypocalcemia. We describe a patient with severe hypomagnesemia in whom genetic analysis revealed two novel mutations that affect function of the Transient Receptor Potential cation channel, subfamily M, member 6 (TRPM6) gene and confirmed the diagnosis of HSH.

A 37-year-old African-American male presented with fatigue of several weeks duration. Physical examination revealed a positive Trousseau's sign. Laboratory data included a serum magnesium level of 0.6 mg/dl, potassium 3.6 mg/dl, corrected calcium 7.5 mg/dl, phosphorus 3.2 mg/dl, creatinine 0.8 mg/dl, PTH 9 pg/ml and a fractional excretion of magnesium of 2.42. Review of his pediatric charts revealed a history of hypocalcemia and hypomagnesemia causing convulsions and weakness when not taking high dose magnesium supplements regularly. A sample of the patient's blood was sent for TRPM6 genetic analysis to Philipps University, Marburg, Germany. This revealed the patient to be compound heterozygous for two novel STOP mutations of the TRPM6 gene, proving the diagnosis of HSH. To our knowledge, this is the first reported case of HSH in an African-American. He was treated with intravenous magnesium sulfate with resolution of symptoms. He has been stable on an oral maintenance dose of 4000 mg of magnesium oxide daily.

Recently, mutations in TRPM6, a gene that is crucial in intestinal magnesium transport, have been identified as the primary underlying defect in HSH. TRPM6 is expressed in both intestinal epithelia and kidney tubules. The inappropriately high fractional excretion rate of magnesium seen in HSH indicates concomitant renal wasting apart from impaired intestinal absorption. Untreated, this disorder may be fatal or result in permanent neurological damage. Symptomatic relief and normal development requires lifelong administration of large doses of magnesium supplements.