Familial Hypomagnesemia: A novel mutation of TRPM6 gene associated with severe migraine

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Background: Familial hypomagnesemia with secondary hypocalcemia (OMIM 602014) is an autosomal recessive disorder resulting in electrolyte abnormalities, typically presenting shortly after birth. It is clinically characterized by seizures and tetany. On the other hand, there is evidence that magnesium deficiency plays a crucial role in the pathogenesis of migraine headaches. **Case Report:** We investigate the case of an 18-year-old Moroccan woman born to first-degree cousins, who presented to the emergency department with headaches and cramps. Blood tests revealed low levels of magnesium (<0.50 mg/dL; normal range: 1.6–2.6 mg/dL) and calcium (6.97 mg/dL; normal range: 8.7–10.4 mg/dL). Genomic DNA was isolated from the proband's peripheral blood. Sequencing was performed for the following genes: ATP1A1, BSND, CASR, CLCNKA, CLCNKB, CLDN16, CLDN19, CNNM2, EGF, EGFR, FAM111A, FXYD2, HNF1B, KCNA1, KCNJ10, PCBD1, SARS2, SLC12A3, and TRPM6. The proband was promptly treated with intravenous magnesium sulfate ($MgSO_4$) until normalization of serum values, alongside anti-inflammatory drugs. After thorough genetic counseling, Gitelman and Bartter syndromes were ruled out.

Genetic testing : Interestingly, genetic testing identified a novel homozygous mutation in the TRPM6 gene (NM_017662.5:c.902dup; p.(Ser302Valfs*16)) leading to the formation of a truncated the protein, resulting in loss of function of both alleles.

Discussion and conclusions: Here we describe, for the first time, a case of a young woman carrying a novel pathogenic homozygous variant c.902dup in TRPM6 gene, known cause of familial hypomagnesemia (#MIM 602014). Our preliminary results underscore the important role of magnesium in migraine pathophysiology, thus opening a new potential therapeutical window for this disabling disease.
Whole Familial genetic testing in progress.

24-28 Ottobre 2025
Padova Congress
55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA