HOMOZYGOUS SLC2A9 MUTATION CAUSING SEVERE HYPOURICEMIA AND REVERSIBLE EXERTIONAL ACUTE RENAL FAILURE

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Objectives:

We present a case with homozygous mutation of glucose transporter SLC2A9 (GLUT9) causing severe hereditary renal hypouricemia (HRH) complicated by exercise induced acute renal failure (EIARF). Our findings provide further evidence for the key role played by GLUT9 in renal uric acid (UA) handling.

Methods:

Identification of point mutations in coding exons in SLC2A9 gene. PCR and direct sequencing.

Results:

A 30 year old man presented in the emergency department with severe back pain and nausea. The clinical examination revealed only mild dehydration with postural hypotension. His past medical history was remarkable only for repeated episodes of EIARF in the age of 15, 17, 28 and 30, which completely resolved after re-hydration. Family history was unremarkable. He was admitted in the renal ward for investigation and treatment of a new episode of EIARF. Blood tests were remarkable only for urea (52mg/dl), creatinine (2mg/dl) and uric acid (0.2mg/dl). Urine tests showed impaired concentrating ability with a specific gravity of 1.009 despite dehydration. The fractional excretion of UA (FeUA) was remarkably high at 150%. Renal ultrasound revealed a mildly increased echogenicity. He was treated with normal saline which resulted in a rapid restoration of kidney function. A genetic analysis was performed to explore the possibility of renal hypouricemia as the triggering factor for EIARF. He was found to carry a homozygous deletion of exons 8-12 in the solute carrier family 2 member 9 (SLC2A9, OMIM 606142) gene, coding for GLUT9 (Figure), along with 4 already known polymorphisms: c.49G>A (+/+), c.235T>C (+/+), c.288G>A (+/+), c.480T>C (+/+). This homozygous mutation was highly compatible with the phenotype of HRH. Patients usually present with symptoms such as nausea, abdominal pain, mild fever and acute renal failure after exercise. Two types of HRH have been described. Type-1, caused by SLC22A12 gene mutations coding for the urate transporter URAT1, is manifested by serum UA levels of 1-2mg/dl and FeUA of 40-90%. Type-2 is caused by SLC2A9 mutations and is characterized by very high FeUA (90-150%) and very low serum UA levels (<1mg/dl). Both types cause nephrolithiasis and EIARF, which has been attributed to ischemic kidney injury and aggregation of organic anions in the renal tubules.

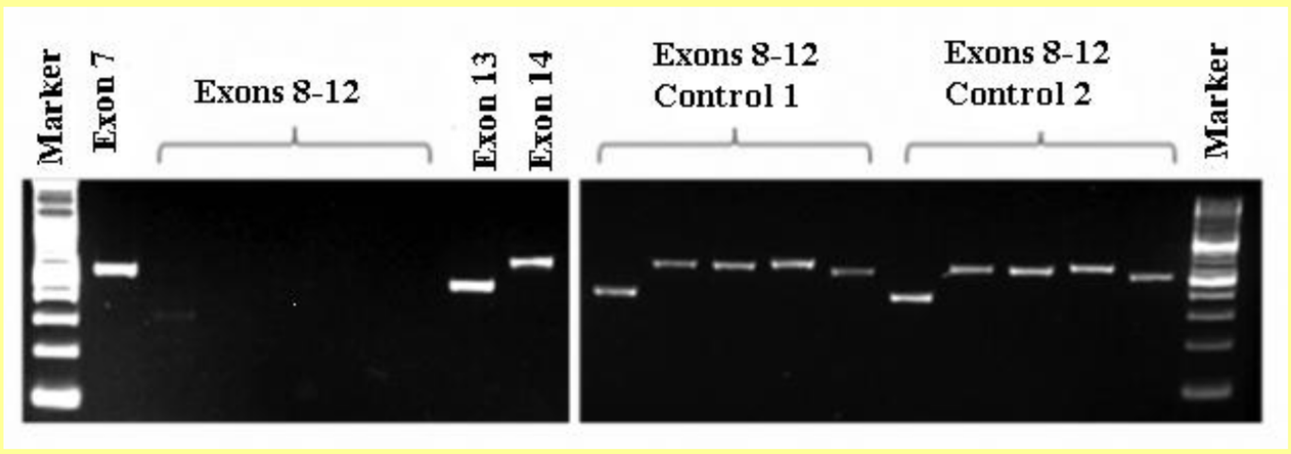

Figure. PCR, Restriction enzyme analysis. Indications of homozygous deletion of exons 8-12 in the SLC2A9 gene in the patient in comparison with controls

Conclusions:

The reported mutation in SLC2A9 gene, causing severe loss of function of GLUT9, results in HRH associated with repeated episodes of EIARF.

References:

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DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014
PosterSessionOnline.com