Primary hyperoxaluria type I: organic aciduria diagnosed in plasma

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Background: Primary hyperoxaluria type I (PH1) is a rare autosomal recessive inborn error of glyoxylate metabolism, caused by a deficiency of the liver-specific peroxisomal enzyme alanine:glyoxylate aminotransferase. The disorder results in overproduction and excessive urinary excretion of oxalate, causing recurrent urolithiasis and nephrocalcinosis.

Patient and methods: The patient, a 38-year-old woman, was referred to our laboratory with severe arthritis in the hips and knees, calcinosis, and stage V chronic renal failure under hemodialysis.

No urine samples were available to perform organic acids analysis so we studied patient plasma. Samples were extracted with ethyl acetate and analyzed by GC-MS.

Results: Plasmatic organic acids profile in two different samples revealed a markedly increased concentration of oxalate (131 and 125 μmol/L; controls: 0-5) and glycolate (362 and 338 μmol/L; controls: 9-42). Glycine concentration was normal (17 and 15 μmol/L; controls: 0-24).

Conclusions: The usual biochemical indicator of PH1 is a persistently and markedly elevated urine oxalate. In the absence of urine samples, this biochemical diagnosis can also be done in plasma samples. PH1 is a treatable organic aciduria and an early and accurate diagnosis preserves renal function of the patients. So, it is important to screen for PH1 in patients with recurrent urolithiasis or unexplained renal insufficiency.

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Clinical and genetic investigation of 6 Iranian cases of glutaric aciduria type I

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Background: Glutaric Aciduria type I is an autosomal recessive disorder caused by mutations in glutaryl-CoA dehydrogenase gene (GCDH). Although newborn screening can reduce adverse outcomes, it is not done in Iran. We investigated clinical and genetic aspects of 6 Iranian GA-1 patients.

Methods: The diagnosis was made by urinary organic acid and/or acylcarnitine analysis. Genomic DNA was extracted from peripheral blood lymphocytes.

Results: Six patients (4♂, 2♀) mean diagnosis age was 6.5±6.1 yrs. All 4 couples were first cousin. Presentations: Macrocephaly 6/6, Developmental Delay/ Regression & Dystonia 4/6, Normal Development 2/6. MRS: Hydrocephaly 6/6, Frontotemporal Atrophy 4/6, Temporal lobe arachnoid cysts 2/6. Mean urine Glutaric acid: 3-Or Glutaric acid levels: 2051±1026, 29.5±19.4 mmol/mmol, respectively. DNA analysis: 2 siblings homozygote 181G>C, One homozygote 881G>A, One heterozygote 1204C>T & 707T>C, the other 2 siblings results are pending. Except one previously reported mutation (1204C>T by Bierly et al 1996) others were new in Iran. After therapy among 4 symptomatic patients the heterozygote one had repeated metabolic acidosis attacks and others remained unchanged.

Conclusion: Our study indicates necessity of newborn screening to lower diagnosis age of GA-1 in Iran, also suggests that different presentation and treatment response may be due to mutation diversity which should be noted in therapy and genetic consultation.