Cystinuria in a 13-Month-Old Girl with Absence of Mutations in the SLC3A1 and SLC7A9 Genes

Sir,

I have two comments on the interesting case report by Krishnamurthy *et al*. on the cystinuria in a 13-month-old girl with absence of mutations in the SLC3A1 and SLC7A9 genes.[1]

First, it is obvious that two major genes responsible for cystinuria have been identified: SLC3A1 (chromosome 2p21) encodes the heavy subunit rBAT of a renal b (0, +) transporter while SLC7A9 (chromosome 19q12) encodes its interacting light subunit b (0, +) AT. Mutations in SLC3A1 are generally associated with an autosomal recessive mode of inheritance whereas SLC7A9 variants result in a broad clinical variability even within the same family. The detection rate for mutations in these genes is larger than 85%, however, it is influenced by the ethnic origin of a patient and the pathophysiological significance of the mutations.[2] The recently published literature review on a set of 94 SLC3A1 and 58 SLC7A9 point mutations known to be associated with cystinuria has shown that there were differences in sequence location, evolutionary conservation, allele frequency, and predicted effect on protein function between these mutations and other genetic variants of the same genes that occur in a large population.[3] Interestingly, the case in question supports the few published anecdotal studies on the absence of mutations in many patients with cystinuria. Obaid *et al*. found in their studied case series on Saudi patients with cystinuria that two out of eight patients had negative molecular testing.[4] Botzenhart *et al*. addressed in their study on a cohort of German patients with cystinuria that the detection rate for mutations in SLC3A1 and SLC7A9 in children was 54% in the SLC3A1 gene for type I chromosomes and 25% in the SLC7A9 gene for nontype I chromosomes.[5] I presume that the lack of detectable mutations in the case in question could point to the role of other yet unrecognized genes involved in the pathogenesis of cystinuria.

Second, I presume that the case in question sent an important clinical message to the practicing pediatricians through augmenting the recommendation that negative molecular investigations should not rule out cystinuria if clinical and biochemical investigations support the diagnosis, and hence, proper treatment must be initiated on that basis.[4]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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