LETTER

Normal glycosylation screening does not rule out SRD5A3-CDG

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By applying next-generation sequencing in three affected siblings showing mental retardation, cataract, coloboma, dysmorphic features and kyphosis, Kahrizi *et al.*¹ reported a novel mutation in the recently discovered 5 α -reductase type 3 (*SRD5A3*) gene.² The authors suggest that Kahrizi syndrome (MIM 612713) is allelic to the novel type of congenital disorder of glycosylation (SRD5A3-CDG), presenting with variable degree of cerebellar abnormalities, ataxia and eye malformations and caused by different *SRD5A3* mutations.^{2,3} They emphasize the need for direct genetic testing for *SRD5A3* in patients with coloboma or cataract in combination with mental retardation. However, the potential for biochemical screening of glycosylation abnormalities was underestimated on the basis of insufficient information.

Screening for CDG in the index family (CVH385) clearly showed abnormal N-glycosylation of transferrin, as described by Cantagrel *et al.*² In addition, the CDG screening of the original patient described by Al-Gazali *et al.*⁴ was only reported to be normal initially, but was clearly abnormal in three different samples at different ages (6 months, 1 year and 10 years) using radioimmunoassay, transferrin isoelectric focusing (TIEF) or mass spectrometry.² Furthermore, all patients, as described by Cantagrel *et al.*² and by Morava *et al.*,³ show abnormal CDG type I glycosylation profiles on multiple occasions.

We also would like to emphasize that the biochemical mechanism, underlying the somewhat clinically similar Peters' Plus syndrome (MIM 261540), is completely different. The abnormal Glc β 1-3Fuc O-linked disaccharides on thrombospondin type 1 repeats of Peters' Plus syndrome⁵ are not present in serum transferrin and, thus, TIEF screening is not indicated in the diagnostics of this disease.

It is important to note that so far all other patients reported with *SRD5A3* mutations were children, and Kahrizi's paper¹ is the first report on adults. Abnormal glycosylation evaluated in plasma might be less evident with aging, and TIEF might become normal, especially

in adults.⁶ These variable and age-dependent changes in serum glycosylation pattern (eg, normal results at old or very young age) are known for other types of CDG as well.⁷ Owing to the indicative cerebello-ocular presentation in SRD5A3-CDG, we agree with the authors' remark to continue with direct testing for *SRD5A3* mutations in highly suspected cases, even when CDG screening is normal.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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