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LETTERS

De Barsy syndrome and ATP6V0A2-CDG

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We read with interest the nice review of Morava *et al*[1] on the autosomal recessive cutis laxa syndromes. The authors mention the De Barsy syndrome and state that the genetic background of the De Barsy syndrome has not yet been identified. However, in the paper by Kornak *et al*[2] on impaired glycosylation and cutis laxa caused by mutations in *ATP6V0A2* (ATP6V0A2-CDG according to the novel nomenclature[3,4]), one of the patients (see patient CoFe in Table 1 of Kornak *et al*[2]) shows the full clinical picture of the De Barsy syndrome, including cutis laxa, facial dysmorphy, dwarfism, psychomotor retardation, dystonia, congenital hip dysplasia, and corneal dystrophy necessitating repeated corneal transplantation. These data suggest that a subgroup of patients with De Barsy syndrome[5] belongs to the spectrum of ATP6V0A2-CDG. Another cause of De Barsy syndrome has very recently been identified as mutations in *PYCR1*, coding for a mitochondrial enzyme involved in proline metabolism.[6] Therefore, we recommend a systematic screen for ATP6V0A2-CDG and for mutations in *PYCR1* in patients with De Barsy syndrome.

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Reply to Leao-Teles *et al*

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We appreciate the comments[1] on our review on autosomal recessive cutis laxa syndromes,[2] especially the novel information on the Portuguese patient CoFe[3] (Table 1, Kornak *et al*), who was diagnosed with a combined N- and O-linked glycosylation disorder and ATP6V0A2-CDG. De Barsy syndrome is a challenging diagnosis, and has overlapping features with ARCL type 2, including cutis laxa, short stature, late closure of the fontanel, congenital hip dysplasia, some aspects of facial dysmorphism and psychomotor retardation.[4] Still, dystonic movements and progressive corneal abnormalities are highly suggestive of De Barsy syndrome. So far no cobble-stone-like brain dysgenesis has been observed in De Barsy syndrome patients. Although the clinical differentiation is not always straightforward, progeroid features, the presence of pergamen-like skin and the absence of subcutaneous fat are distinctive.[2] Interestingly, some of the patients, recently reported to have *PYCR1* mutations, were previously diagnosed with De Barsy syndrome,[5] while other De Barsy patients were found to not harbour *PYCR1* mutations (unreported data), thus supporting genetic heterogeneity. We would appreciate further description and photo documentation of this unique patient, reported by Leao-Teles, as in our own cohort of six patients with De Barsy syndrome and those studied by Kornak *et al* (personal communication) none of the children had either N-linked or O-linked glycosylation abnormalities, nor mutations in the *ATP6V0A2* gene. Eye anomalies are common in N-glycosylation disorders,[6] and strabismus and high myopia have been reported in combined glycosylation disorders.[4] The exceptional observation of corneal abnormalities with a movement disorder in association with ATP6V0A2-CDG indeed widens the range of symptoms evoking glycosylation studies in patients with cutis laxa.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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