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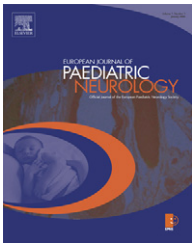

Letters to the Editor

A benign congenital myopathy in an inbred Samaritan family

I read with great interest the article by Lev et al.[1] on a novel form of congenital myopathy in an inbred Samaritan family. The authors presented a mother and two daughters affected by a slow progressive, neonatal onset myopathy with dysmorphic facies and subtle skin abnormalities. With the high intralineage marriages in Samaritan community, it is likely that the present cases are autosomal recessive (AR) inheritance with pseudodominant pedigree as the authors described, although a possibility of autosomal dominant (AD) inheritance cannot be excluded. Muscle biopsy from the mother revealed a numbers of mature-looking muscle fibers with central nuclei and intermyofibrillar disorganization. Molecular analyses of spinal muscular atrophy, X-linked myotubular myopathy and myotonic dystrophy identified no mutation.

Based on the clinicopathological scenario given in the present cases, the differential diagnosis should include AD/recessive centronuclear myopathy (CNM) and COL6-related myopathy/muscular dystrophy. Dermatologic abnormalities raise the possibility of mutant gene expression not only in skeletal muscle but also in skin, which includes collagen VI. It is important to address whether these three patients have any distal joint hyperlaxity, a typical feature of Ullrich congenital muscular dystrophy. Regarding autosomal CNM, both AD and AR forms could fit with the clinical presentations of this family.[2] It is important to address whether the present cases have ophthalmoparesis, a common presentation in ARCNM. Moreover, the biopsy report in the present cases should mention whether there is any type 1 predominance or radial distribution of sarcoplasmic strands from the central nuclei on oxidative stains because both are the common findings of CNM. Recently, Bitoun et al.[3] identified dynamin 2 (*DNM2*) mutations in ADCNM and Pele et al.[4] also found the mutations of protein tyrosine phosphatase-like, member A (*PTPLA*) gene in the animals affected by ARCNM. It is worth sequencing both *DNM2* and *PTPLA* genes in the family presented by Lev et al. before drawing a conclusion of a novel form of congenital myopathy.

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We appreciate Dr. Liewluck's suggestions regarding our article on a novel form of congenital myopathy in an inbred Samaritan family.[1]

The clinical course of our family was unique and unusual compared to other congenital centronuclear myopathies: a very severe neonatal presentation, improvement in childhood and nearly no neurological findings in adulthood. We presume that the inheritance in this highly inbred family is autosomal recessive but cannot rule out dominant inheritance.

We included the different centronuclear myopathies, dominant and recessive, in our differential diagnosis but ruled them out because of the different clinical course. Dynamin 2-related centronuclear myopathy was ruled out because it is

characterized by slowly progressive muscular weakness usually beginning in adolescence or early adulthood.[2] Bilateral ptosis is a constant feature and distal muscle weakness often exceeds proximal involvement. Our patients presented at birth with severe proximal weakness which gradually improved and ptosis was not observed. Therefore we did not think it was necessary to sequence the *DNM2* gene.

Dr. Liewluck suggests sequencing another possible gene only identified in an animal model of centronuclear myopathy: PTPLA.[3] We agree that it would be interesting to analyze this gene in our family and in the case a mutation is found they will represent the first human patients with mutations in this gene.

Our patients have minimal myopathic symptoms with hyperlaxity and no ophthalmoparesis. The dermatologic abnormalities are subtle and expressed as thick skin over the dorsum of the hands. For this reason we, like Dr. Liewluck, assume that the gene involved in this myopathy may also function in connective tissue like the COL6 gene, but the very mild clinical picture described in the mother negates Ullrich congenital muscular dystrophy.[4]

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