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Article Commentary

Implications of non-compaction in association with respiratory chain complex-I deficiency

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With interest we read the article by Dhar et al about a newborn female child with a mitochondrial disorder due to complex-I deficiency who manifested cardiologically with left ventricular hypertrabeculation/non-compaction.[1] We have the following comments and concerns.

Non-compaction is frequently familial;[2] however, the parents were described as being completely normal. Were they investigated for a mitochondrial disorder or non-compaction? Were grandparents or siblings echocardiographically screened for non-compaction or neurologically for mitochondrial disorders? Was the family history positive for sudden cardiac death, heart failure, or stroke/embolism?

It would be interesting to know whether the diagnosis of complex-I deficiency was based on immunohistological findings or whether biochemical investigations were carried out from the muscle biopsy. In case biochemical investigations had been carried out, we would like to know the degree to which the function of complex-I was actually reduced. In addition, were ragged-red fibres, succinate-dehydrogenase hyper-reactive fibres, or cytochrome-c-oxidase-negative fibres present on muscle biopsy? Were crystalloid inclusions or abnormally structured mitochondria found on electron microscopy?

Non-compaction is frequently complicated by ventricular arrhythmias, heart failure, or stroke/embolism.[3] Did the patient or any of her relatives ever develop any of these complications during the 8 years of follow-up? Did morphology of non-compaction change over time; in particular, did hypertrophy increase and had non-compaction disappeared at her last follow-up?

Complex-I deficiency usually manifests as multisystem disease.[4] Was the heart truly the only affected organ in the described patient or were other organs additionally involved? In case the patient had multisystem disease, it would be helpful to know which other organs were affected and whether the affection of other organs was clinical or subclinical. In particular, it is of interest to know whether the brain or the skeletal muscles were additionally involved. Was the psychomotor development of the patient normal or delayed? Did she gain full normal motor functions and were her intellectual abilities unimpaired?

We do not agree with the statement that the described case is the first complex-I defect with non-compaction in the paediatric population. Complex-I deficiency in association with non-compaction has been previously described in the paediatric population by Scalgia et al in 2004 and by Zarrouk-Mahjoub et al in 2011.[5,6]

As complex-I of the respiratory chain is built up of 46 subunits, of which the majority are nuclearly encoded, it could be helpful to screen other nuclearly encoded subunits of complex-I for mutations in this patient.

Overall, we suggest further extensive investigation of the family of this interesting patient to eventually clarify the trait of inheritance, the possible multisystem nature of complex-I deficiency, and whether non-compaction showed dynamic changes over time. It is also essential to know whether any of the frequent complications of non-compaction had occurred during follow-up and whether treatment had to be modified during follow-up. As the pathogenetic background of non-compaction is still unsolved, it is warranted to thoroughly investigate each non-compaction case to eventually contribute to the clarification of the causes and pathogenesis of non-compaction.

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