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Fetal left ventricular non compaction cardiomyopathy and fatal outcome due to deficiency of mitochondrial trifunctional protein

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Introduction: Mitochondrial trifunctional protein (TFP), an enzyme of fatty acid beta-oxidation, is a multienzyme complex composed of four molecules of the alpha-subunit (HADHA) and four molecules of the beta-subunit (HADHB). The most common TFP disorder is LCHAD deficiency caused by the c.1528G>C (p.Glu510Gln) mutation in the HADHA gene. HADHB mutations are relatively rare. We report a fetal case with fatal outcome having a novel HADHB mutation.

Methods: The parents were of Turkish origin, with history of a pregnancy loss due to fetal heart failure and hydrops. In the next pregnancy the fetus developed left ventricular non compaction and increasing pleural effu-sions after 31 gestational weeks. The fetus was small for gestational age and the long bones were short. The baby was born by caesarean section severely asphyxiated at 32 gestational weeks. Medical decision was taken to withdraw intensive care due to failure to thrive and a suspicion of severe mitochondrial disorder. The autopsy was withheld. Consanguinity was present in the parents and paternal grandparents.

Results: Post mortem brain MRI suggested microcephaly with a simplified gyral pattern. The lateral cerebral ventricles were normal. Chromosome analysis was normal (46,XX). Fibroblasts cultured from the skin biopsy of the baby revealed the large homozygous deletion c.1109+243_1438-703del in the HADHB gene, and heterozygous mutations were detected in both parents. The deletion has not been reported earlier.

Conclusion: Trifunctional protein deficiency is a relatively rare disorder. Mutations in the HADHB gene cause a systemic disorder with cardiomyopathy originating in fetal life. It is important to differentiate systemic meta-bolic diseases from disorders that affect only the cardiac muscle. Understanding the molecular genetic defect of the patient allows counseling of the family. In this case, the finding has significance for future pregnancies because of a 25 % risk of recurrence. The specific diagnosis was made even though autopsy was withheld.