Postnatal Prognosis of Fetal Noncompaction Is Uncertain In Sibs Carrying a PKP2 Deletion

Josef Finsterer, MD, PhD1 and Sinda Zarrouk-Mahjoub, PhD2

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Letter to the Editor

In a recent article, Ramond et al. reported about two neonate sibs with left-ventricular hypertrabeculation / noncompaction (LVHT) carrying a homozygous PKP2 deletion1. The female neonate died 12 weeks after gestation from intractable heart failure1. The male fetus underwent termination of pregnancy1. Their parents were consanguineous and heterozygous each for the mutation1. We have the following comments and concerns.

Obviously, the diagnosis of LVHT in the male fetus prompted treating physicians to propose termination of pregnancy. We regard such an approach as highly unethical for several reasons. First, the diagnosis of LVHT was established upon fetal ultrasound and it is well known that fetal echocardiography has its false positives and false negatives. Secondly, there is absence of a golden standard and uniform criteria for diagnosing LVHT2. The interobserver variability for diagnosing LVHT is particularly high for echocardiography. Following these arguments it is possible that the diagnosis of LVHT was false positive in the male fetus. Third, the prognosis of fetal LVHT is not necessarily poor. In a study of 18 patients in whom LVHT was diagnosed already intrauterine only 3 died from heart failure postnatally3. Three patients received a pacemaker and two underwent heart transplantation3. The remaining patients are alive without treatment3. It was concluded that the prognosis of fetal LVHT is favourable if affected patients receive appropriate treatment3. Fourth, there are no studies available, which allow concluding that fetal LVHT with fatal outcome in one sib has also a poor prognosis in the other.

Concerning the assumption that the PKP2 deletion was responsible for the development of LVHT, it has to be stressed that a causal relation between any of the mutations in >40 genes and several chromosomal defects so far described and LVHT has never been proven4. Thus far, LVHT is associated with genetic disease but several arguments can be raised against a causal relation.

Overall, the postnatal prognosis of fetal LVHT remains uncertain prohibiting recommendations for termination of pregnancy and causality of the PKP2 deletion for LVHT remains unproven.

References

1 Krankenanstalt Rudolfstiftung, Vienna, Austria
2 Genomics Platform, Pasteur Institute of Tunis, Tunisia