A case of polimalformed fetus with a microdeletion of CTNNA3 gene

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Abstract

We report a case of a male fetus of 20 weeks of gestation with plurimalformed observed by transonic scan and confirmed by MR. The karyotype was 46, XY. Molecular analysis showed a microdeletion of about 100 kb in the CTNNA3 gene.

Key words: chomosomic microdeletion, plurimalformed syndrome, microarray DNA analysis, prenatal diagnosis, new syndrome.

Introduction

Human CTNNA3 (ALPHA-T-CATENIN or VR22) is a cell adhesion molecule.
The gene is on chromosome 10q 21 and contains 18 exons and spans about 1,776 kb. (1, 2). The only till now reported of mutations has been observed in a disease called *Familial arrhythmogenic right ventricular dysplasia, familial, 13* (*ARVD13)* (3, 4). The mutations had been found in 2 of the probands affected by this disease and consisted in different heterozygous mutations, respectively a missense mutation (3, 5) and an in-frame 3-bp deletion (3, 6). The mutation was also present in heterozygosity in the proband's asymptomatic father and paternal aunt, who had mild right ventricular dilation on echocardiography and increased trabeculations in the right ventricular apex on MRI, respectively, as well as in the aunt's asymptomatic son.

Case report

The fetus was the result of the second conception of a healthy non-consanguineous spouse. The 1st born is a 2-year-old normal female.
The familial genetic data were unremarkable.
The karyoype of the couple was normal as much as of the fetus (46, XY).

Echographic data at 20 weeks of gestational age showed: transient cystic hygroma; single umbilical artery; multicystic left kidney and ectopic hypoplastic right kidney in the pelvic region; defect of the thoracic spine severely curved with vertebral cleft. No ecographic dysmorphic face (Figure 1). MR confirmed these defects.

Molecular data

Array-based Comparative Genomic Hybridization by planet of 180 k AGILENT kit 4X180, resolution of about 60kb. Result: heterozygotic deletion of 180 kb on the long arm of chromosome 10q21.3 in the CTNNA3 gene from bp 68394411 to bp 68496866.
An abortion was induced and the couple refused the autopsy.

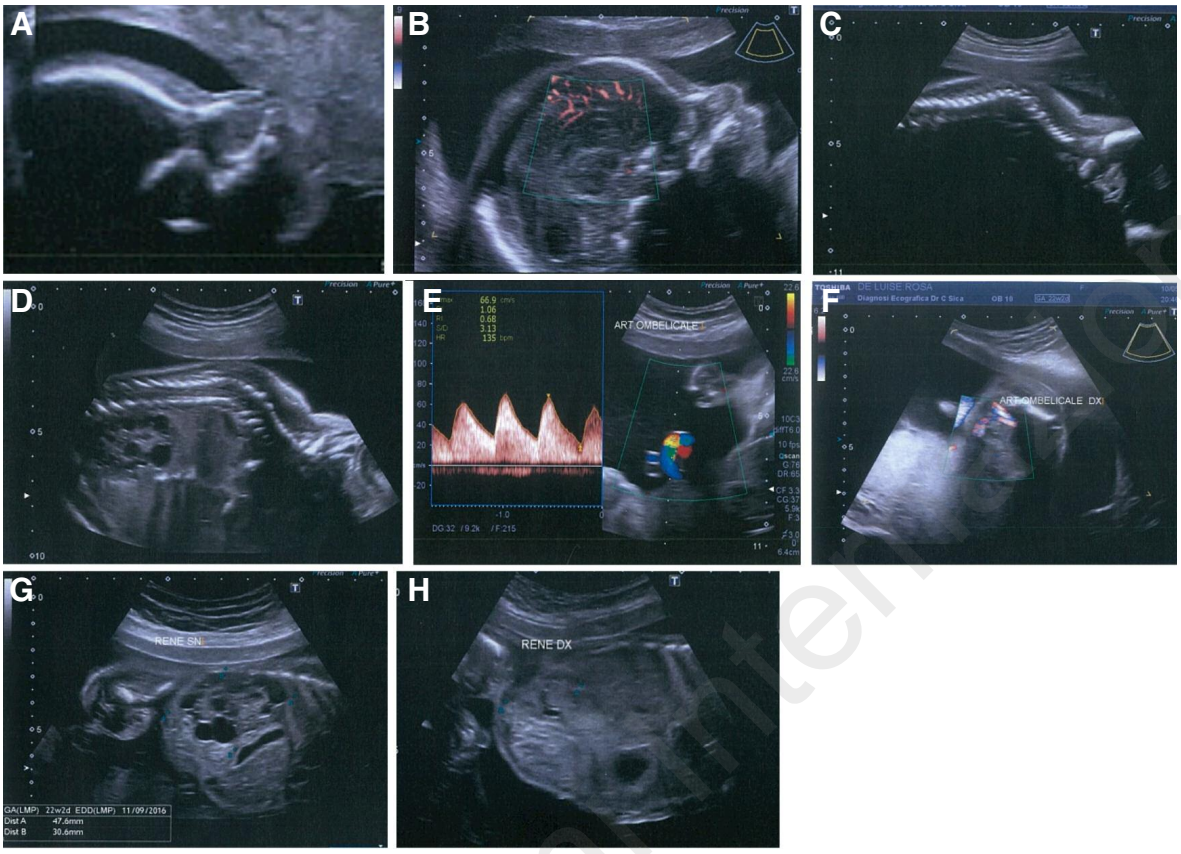

Figure 1. Ecographic data. A, B) Aspects of the face; the vascular picture in 2 is the pericallosal artery; C, D) Toracic spinal column; E, F) Single umbilical artery; G) Left cistic kidney; H) Right ectopic kidney.

Discussion

Before we had known the result of molecular analysis, we have supposed that none of the known genetic plurimalformed syndromes had the sum of signs observed in our case. Cystic kidney, single umbelical artery and vertebral column defects are evident in *VACTERL association* (OMIM 142989) and *Meckel syndrome* (OMIM 249000), but both these diseases differ from ours for other peculiar characteristics.

As previously reported, the molecular defect in our case consists in a microdeletion of 180 kb in the CTNNA3 gene. The human CTNNA3 gene contains 18 exons and spans about 1,776 kb.

The only other mutation of this gene has been observed in a genetic autosomal dominant inherited disease called *Familial arrhythmogenic right ventricular dysplasia, familial, 13 (ARVD13)* (OMIM 615616) also known as *dilated cadiomyopathy 13*. Its main clinical features are quite different from our observation, consisting in structural and functional abnormalities of the right ventricle with progressive fibrofatty myocardial replacement, electrocardiographic depolarization/repolarization changes, re-entrant arrhythmias, sudden death.

Conclusions

The relevance of this case is because our observation was characterized by sum of anomalies which did not fit in none of the known genetic plurimalformed syndromes and because the only known genetic disease with mutations of CTNNA3 gene has been reported in a disease called Arrhythmogenic right ventricular dysplasia, familial, 13 (ARVD13). That is why we retain that our observation is a quite singular case either for clinical or for molecular characteristics.

Note

We have the informed consent for the publication.

Acknowledgment

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