Prenatal diagnosis in severe cases: a new gain in Portuguese neonatal screening laboratory

Carmen Sousa[1], Célia Nogueira[1], Helena Fonseca[1], Ana Marcão[1], Hugo Rocha[1], Lurdes Lopes[1], Elisa Leão[2], Juliette Garcia[3], Ana Bela Couceiro[4] and Laura Vilarinho[1]

[1] Newborn Screening Unit Genetics Department – National Institute of Health Dr. Ricardo Jorge, Porto – Portugal
[2]Hospital S.João, Porto, Portugal
[3]Hospital Santa Maria, Lisboa, Portugal
[4]Maternidade Bissaya Barreto,Coimbra, Portugal

Introduction

The Portuguese neonatal screening, based on MS/MS technology, allows since 2004 the tracing of 25 diseases, in a single laboratory in all Portuguese newborns. Following this expansion, the molecular study was also implemented for most diseases, thus allowing confirmation and prenatal diagnosis in severe cases.

Methods

Five prenatal diagnoses were made in pregnant women (first-trimester) who had children affected with severe forms of CPT2 deficiency, ARG1 deficiency, MAD deficiency and LCHAD deficiency. Disease-causing mutations were previously identified in the index patients of families 1 and 2. Molecular genetic characterization of the probands of families 3-5 was given by the geneticists who requested prenatal.

Genomic DNA was isolated from whole blood, cultured amniotic fluid cells or chorionic villous samples (CVS) by standard methods. Mutations were detected through direct sequencing of PCR products, performed on an automatic sequencer.

In all samples maternal was excluded contamination (Molecular Unit-INSA).

Results

Three prenatal diagnoses were performed on mothers with affected children, found through neonatal screening: CPT2D, MADD and LCHADD. Two other prenatal diagnoses for ARG1D were requested from Italy (Family 4) and France Centers (Family 5). Results revealed two affected *fetus* (Family 1 and 2) and three heterozygous carriers (Family 3-5) (Table 1). The probands cases from families 1 and 3 deceased with 2 years and 2 days of life respectively.

Table 1- DNA-based prenatal diagnosis in 5 families

		***ETFDH* Genotype**			
Family 1	Exon	Proband	Mother	Father	**CVS**
	1	c.34+5G>C	c.34+5G>C	WT	c.34+5G>C
	12	c.1601C>T[1]	WT	c.1601C>T[1]	c.1601C>T[1]
		***CPT2* Genotype**			
Family 2	Exon	Proband	Mother	Father	**CVS**
	1	c.110_111dupGC[2]	WT	c.110_111dupGC[2]	c.110_111dupGC[2]
	1	c.110_111dupGC[2]	c.110_111dupGC	WT	c.110_111dupGC[2]
		***HADHA* Genotype**			
Family 3	Exon	Proband	Mother	Father	**CVS**
	15	c.1528G>C[3]	WT	c.1528G>C[3]	c.1528G>C[3]
	15	c.1528G>C[3]	c.1528G>C[3]	WT	WT
		***ARG1* Genotype**			
Family 4	Exon	Proband	Mother	Father	**CVS**
	1	c.23T>G	WT	c.23T>G	c.23T>G
	1	c.23T>G	c.23T>G	WT	WT
5	Intron				**Amniocytes**
	4	c.466-2A>G[4]	WT	c.466-2A>G[4]	c.466-2A>G[4]
	4	c.466-2A>G[4]	c.466-2A>G[4]	WT	WT

Discussion

Molecular prenatal diagnosis for severe forms can establish the diagnosis in the first trimester of pregnancy. Nevertheless, this procedure is conditioned by prior knowledge of responsible mutations in the index cases.

References

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