P-065 - INCIDENTAL DETECTION OF ARGENTINE FAMILY WITH GLA MUTATION FOR FABRY DISEASE THROUGH PRECONCEPTIONAL TEST BY NEXT GENERATION SEQUENCING MULTIGENE PANEL

Valdez RM¹, Lotersztein V¹,³, Reisin RC², Klurfan M³, Rozenfeld P⁴

(1) Hospital Militar Central, Servicio de Genética. (2) Hospital Británico. (3) Fundación IERUSHA. Ciudad Autónoma de Buenos Aires - Argentina. (4) Servicio de Diagnóstico de Enfermedades Lisosomales (DIEL), UNLP-Argentina.
ritavaldez@hotmail.com

Fabry Disease is a X-linked lysosomal storage disorder caused by decreased or absent activity of the enzyme α-galactosidase A, due to mutations in GLA gene. The majority are point mutations (missense, nonsense and splice sites mutations), although there are also 'short-length' and gross rearrangements. There is no obvious 'hot spot', and the majority are non-recurrent private mutations. In general, patients with Fabry disease are detected by clinical suspicion, the genetic study being part of the diagnostic confirmation. We present a family in which a GLA pathogenic mutation was detected: c.1069C>T (p.Gln357*) as an incidental finding in the index case (female), through a preconceptional multigenetic panel by Next Generation Sequencing (NGS), including GLA gene. No family history of renal disease, neither stroke nor heart disease was detected. Family mutation test was carried out on her relatives; her mother as well as one of her sisters and a niece were found heterozygous for the mutation; his father, the other sister, her maternal grandmother and her aunt do not carry the mutation. Comprehensive evaluations were carried out in the heterozygous patients (ophthalmological, cerebral MRI, echocardiogram, echostress test, cardiac MRI, and renal function studies), detecting only cornea verticilata in the three adult heterozygous, and a mild cardiac hypertrophy with a symptomatic paroxysmal supraventricular tachycardia in the mother. The patients continue in clinical follow-up, maintaining expectant behavior in relation to specific treatments for Fabry Disease. We conclude this is a fresh mutation occurred in the mother of the index case, transmitted to two of her daughters. This variant has not been reported yet in the literature. With the increasing indiscriminate access to molecular studies by multigenetic panels by NGS, it is very likely that more incidental cases of patients with pathogenic mutations of unsuspected diseases will be detected. Genetic counseling by a specialist prior to each molecular study is essential, even in these cases of prenuptial or preconceptional commercial genetic tests.