**P-178 - MOLECULAR CHARACTERIZATION OF ORNITHINE TRANSCARBAMILASE (OTC) GENE IN ARGENTINEAN PATIENTS**

Crespo C¹, Bernal AC², Eiroa HD², Gravina LP¹

(1) Laboratorio de Biología Molecular-Genética, Hospital de Pediatría Garrahan. (2) Servicio de Errores Congénitos del Metabolismo, Hospital de Pediatría Garrahan. Ciudad de Buenos Aires-Argentina. carocrespo1986@gmail.com

**INTRODUCTION:** Ornithine Transcarbamylase Deficiency (OTCD) is an X-linked inborn error of the urea cycle that causes hyperammonemia, due to mutations in the OTC gene. More than 500 variants have been described, including disease-causing mutations and polymorphisms, most of them being missense substitutions. The onset of OTCD symptoms is variable: hemizygous males with the neonatal-onset form resulting from null alleles present with a hyperammonemic coma in the first week of life, whereas heterozygous females and hemizygous males with partial defects in the OTC gene show various degrees of clinical symptoms later in life or even in adulthood. Besides, heterozygous women for an OTC mutation present a wide spectrum of clinical manifestations depending on the pattern of X inactivation in the liver, ranging from asymptomatic to almost as severe as in affected males. **OBJECTIVE:** Describe molecular characterization of OTC gene in OTCD patients from Argentina. **METHODS:** DNA was extracted from peripheral blood from 33 individuals, corresponding to 12 unrelated families. Samples were sequenced by analysis of the 10 exons and the exon-intron boundaries of the OTC gene. Computational algorithms were applied to assess the severity of de novo missense mutations. **RESULTS:** A total of 12 patients (5 males and 7 females) were diagnosed with OTCD based on biochemical findings and confirmed by molecular analysis. Maternal carrier status was confirmed for 2 males and 3 females patients, while in 3 female patients, mutations had occurred de novo. Carrier status was detected in 7 females who remain asymptomatic, and ruled out in 6. Ten different sequence variations were identified, including 5 novel substitutions. All of them, except for p.(Arg129His), found in two unrelated families, were private mutations. All the novel substitutions (p.(Ile85Ser), p.(His168Tyr), p.(Ser203Pro), p.(Pro305Leu) and p.(Asp297Thrfs26)), were predicted to be deleterious by in silico tools. **CONCLUSION:** This study supports that OTCD is a heterogeneous disorder at the molecular level, such as described in other populations. Molecular analysis remains specially useful for detecting female relatives at risk of not only having another affected child but also presenting potentially fatal hyperammonemic crisis.