P-179 - DEFICIENCY OF ARGINASE: REPORT OF THE FIRST CASE CONFIRMED IN COSTA RICA

Saborío P², Badilla R², Quesada J², Reuben A¹, Camacho N¹, Jiménez M¹, Saborío M²

(1) Laboratorio Nacional de Tamizaje Neonatal y Alto Riesgo. San José-Costa Rica. (2) Servicio de Genética Médica y Metabolismo, Hospital Nacional de Niños. Caja Costarricense de Seguro Social. San José-Costa Rica. psaborior@tamizajecr.com

INTRODUCTION: Argininemia is an Urea Cycle defect, caused by deficient activity or the total absence of the enzyme Arginase, coded by the ARG1 gene. Arginase deficiency causes elevation of serum Arginine levels and secondarily an increase in serum ammonium levels, milder than expected in the other disorders of the Urea cycle. This disease is inherited in an autosomal recessive manner. Clinical manifestations of this disease are: progressive spasticity, seizures and intellectual disability after the second year of life, when not treated early. OBJECTIVE: This report presents the first biochemically and molecularly confirmed case of Arginase deficiency detected by the National Newborn Screening Program in Costa Rica. MATERIALS AND METHODS: We describe the clinical and biochemical findings of a newborn who, despite being asymptomatic, presents increased serum Arginine levels, detected by Newborn Screening. RESULTS: Mass tandem Spectrometry from dried blood spot detected a sustained increase level of Arginine in three consecutive samples. Subsequently plasma amino acid chromatography was requested showing an increase of serum arginine levels more than 6 times the cut-off for age. Serum Ornithine, Citrulline and Ammonia levels where within normal range. Urine organic acids analysis by GC-MS gas chromatography-Mass Spectrometry showed only a moderate peak of succinic acid. Next Generation Sequencing (NGS) for Urea Cycle disorders was performed reporting the variant NM_000045.32AEB_A: 101_128.c.382G> A- (p.Asp128Asn) in the ARG1 gene, in a homozygous state. Discussion and CONCLUSIONS: The homozygous mutation NM_000045.32AEB_A: 101_128.c.382G>A- (p.Asp128Asn), in ARG1, has been reported as a variant of unknown significance. Biochemical findings such as serum elevation of Arginine levels, the absence of Argininosuccinic Acid or Orotic Acid in urine organic acid analysis and normal serum levels of other aminoacid within the Urea Cycle support the clinical effect of the mutation in the Urea Cycle. Prior to the development of a neurological deficit, a diet restricted in Arginine was initiated and close monitoring is maintained. A new disease-causing mutationin in the ARG1 gene is documented in the first patient with a confirmed diagnosis of Arginase Deficiency in Costa Rica through the National Newborn Screening Program.