Annals of Hepatology 30 (2025) 101791

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Abstracts Asociación Mexicana de Hepatología (AMH) 2024

Hyperonitinemia-Hyperammonemia-Homocitrullinuria syndrome. Neonatal presentation with acute liver failure.

César U. Amaro-Reynoso, Jose L. Flores-Castillo, Catherine N. Pineda-Cely, Rodrigo Vázquez-Frías

Pediatric Gastroenterology & Nutrition, Children's Hospital of Mexico "Federico Gomez", National Institute of Health, Mexico City, Mexico

Introduction and Objectives: Urea cycle defects occur in 1/35,000 live births and Hyperonitinemia-Hyperammonemia-Homocitrullinuria (HHH) syndrome represents 1-4% of this group of diseases, which represents an autosomal recessive defect due to variants of the SLC25A15 gene. The present work describes the first case of HHH syndrome reported in Mexico.

Materials and Patients: We present a 5-month-old female infant, daughter of the second pregnancy of non-consanguineous parents, originally from Quintana Roo, born at term with intrauterine growth restriction, presented early neonatal sepsis and required ventilatory and hemodynamic treatment, in the second week she presented Cholestasis with normal GGT, coagulopathy, which did not correct after treatment with vitamin K, and irritability with hyperammonemia up to 640umol/L, which led to the diagnosis of neonatal acute liver failure.

At the initial approach, infectious etiology was ruled out, with high suspicion of gestational alloimmune liver disease, due to the presence of elevations of alpha-fetoprotein 12,410ng/mL and ferritin 1,590ng/mL. Gaucher disease, Niemann Pick, and lysosomal acid lipase deficiency were ruled out. Metabolic screen with hyperornithinemia (435.79 mmol/L). The genetic study found a pathogenic variant in a homozygous state of the acceptor site of the splicing of intron 2 of the SLC25A15 gene.

Two doses of human immunoglobulin and supportive treatment for liver failure with menadione and ammonium binders were administered with a favorable therapeutic response; the liver failure was remitted 4 weeks after the established management.

Results: The present work describes the first case of HHH syndrome reported in Mexico, which presented with neonatal acute liver failure associated with two of the three biochemical characteristics described due to hyperammonemia and hyperornithinemia. Likewise, a homozygous variant was identified in SLC25A15 and classified as pathogenic.

Conclusions: This report highlights the first documented case of HHH syndrome in Mexico, emphasizing its association with neonatal acute liver failure, hyperammonemia, and hyperornithinemia. The identification of a pathogenic homozygous variant in the SLC25A15 gene reinforces the importance of genetic studies for early diagnosis and targeted management of urea cycle disorders.

Ethical statement: This work complies with current regulations on bioethical research, obtained authorization from the institution's ethics committee, and does not contain personal information that would allow the patient to be identified.

Declaration of interests: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

https://doi.org/10.1016/j.aohep.2025.101792

The GDF11 represses the Stat3 signaling pathway, conferring metabolic, inflammatory, and oncogenic restrictions in cells derived from human hepatocellular carcinoma.

Melissa Sánchez-Rodríguez[1,2], Monserrat Gerardo-Ramírez[3], Arturo Simoni-Nieves[4], María Concepción Gutiérrez-Ruiz[2], Roxana U Miranda-Labra[2], Verónica Souza[2], Leticia Bucio-Ortiz[2], Alejandro Escobedo-Calvario[1,2], Luis E. Gomez-Quiroz[2,3]

[1] *Experimental Biology Postgraduate, DCBS, Universidad Autónoma Metropolitana Iztapalapa, Mexico City, Mexico*
[2] *Experimental and Translational Medicine Area, Health Science Department, Universidad Autónoma Metropolitana-Iztapalapa, Mexico City, Mexico*
[3] *Department of Biochemistry and Molecular Genetics, University of Virginia, Charlottesville, VA, USA*
[4] *The foundation for liver research, London, UK*

Introduction and Objectives: GDF11 has shown potential in displaying anti-tumor effects in cells derived from human HCC, but the molecular mechanisms that lead to this, as well as the early transcriptomic response of GDF11 in HCC, remain a mystery. To identify potential targets for therapeutic intervention revealed by GDF11 treatment in HCC.

Materials and Patients: Huh7 cells were treated for 12 h with 50 ng/ml of GDF11, and sequencing was performed using the Illumina HiSeq4000 platform. The results were filtered with a $p \leq 0.01$, $\pm$ 1.5-fold change, and an FDR= 0.05. Functional and enrichment analysis was done using the Ingenuity Pathway Analysis (IPA) program.

Results: Our data show 1450 differentially expressed genes. It is observed that GDF11 has a profound impact on highly oncogenic pathways, highlighting the Stat3 pathway, beta-catenin, and HIF-1 alpha, among others. Functional analysis revealed that GDF11 could