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Ciliopathy due to genetic alterations of TULP3 as an uncommon cause of hepatorenocardiac fibrosis

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Palabras clave: TULP3. Cholestasis. Hepatorenocardiac fibrosis.

Dear Editor,

Hepatorenocardiac fibrosis is a group of rare, clinically and genetically heterogeneous inherited disorders affecting the development and degenerative function of the liver and kidneys. It is associated with ciliopathies, a group of diseases characterized by dysfunction of the primary cilium, a key organelle in cell signaling. We present a clinical case of ciliopathy linked to a genetic alteration in the protein TULP3 (TUB Like Protein 3) as a cause of hepatorenocardiac fibrosis.

CLINICAL CASE

A 40-year-old patient with no relevant medical history was being followed up for long-standing chronic cholestasis of unknown etiology, with a negative autoimmune study. She was being treated with ursodeoxycholic acid and bezafibrate without adequate response, pending initiation of odexibat. Her family history was reviewed with findings of chronic cholestasis in four of her siblings and another liver transplant recipient for advanced chronic liver disease. A fibroscan with 16 kPa was performed, an abdominal ultrasound showed hepatic steatosis and splenomegaly, and a gastroscopy showed gastropathy due to portal

hypertension. A liver biopsy was performed with histological changes consistent with active cholangiopathic chronic liver disease (Figure 1). To complete the study, a genetic panel was performed with findings of homozygosity for a clinically pathogenic variant in the TULP3 gene related to hepatorenocardial degenerative fibrosis. After the results were obtained, she was referred to nephrology and cardiology clinics for evaluation, ruling out renal or cardiac involvement.

DISCUSSION

Genetic alterations in TULP3 have recently been identified as a monogenic cause of hepatorenocardiac fibrosis. This pathology, of autosomal recessive inheritance, is characterized by progressive and degenerative liver fibrosis that can manifest during childhood or early adulthood, in some cases requiring liver transplantation. In addition, it can be associated with the variable and late onset of fibrocystic kidney disease and hypertrophic cardiomyopathy.

The clinical onset of the disease manifests mainly at the liver level, in the form of cholestasis in most cases and, less frequently, through complications secondary to portal hypertension.

The study of monogenic diseases associated with progressive organic fibrosis represents a key opportunity for the early detection of individuals at high risk of progression to end-stage liver and kidney disease, allowing for timely and effective clinical management. Given its hereditary nature and the associated family implications, the importance of adequate genetic counseling as an integral part of the diagnostic and therapeutic approach is emphasized.

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BIBLIOGRAPHY

1. Jafari Khamirani H, Palicharla VR, Dastgheib SA, Dianatpour M, Imanieh MH et al. A pathogenic variant of TULP3 causes renal and hepatic fibrocystic disease. Front Genet. 2022 Oct 7;13:1021037. doi: 10.3389/fgene.2022.1021037.

2. Devane J, Ott E, Olinger EG, Epting D, Decker E, Friedrich A, Bachmann N et al. Progressive liver, kidney, and heart degeneration in children and adults affected by TULP3 mutations. Am J Hum Genet. 2022 May 5;109(5):928-943. doi: 10.1016/j.ajhg.2022.03.015.

3. Zheng M, Hakim A, Konkwo C, Deaton AM, Ward LD, Silveira MG et al. Advancing diagnosis and management of liver disease in adults through exome sequencing. EBioMedicine. 2023 Sep;95:104747. doi: 10.1016/j.ebiom.2023.104747.

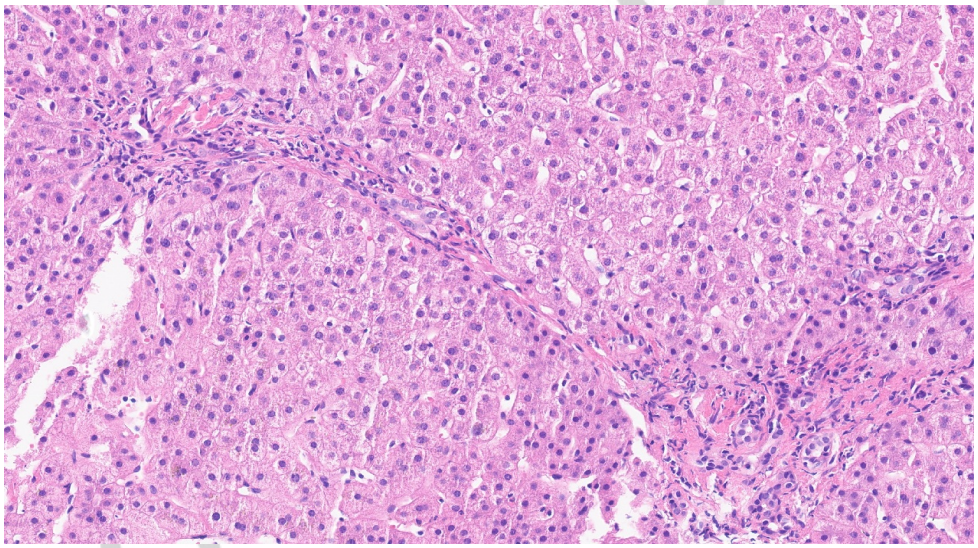

Figure 1: Fibrous portal reinforcement forming porto-portal septa along with focal cholangitis phenomena. Hematoxylin-eosin 15x.