Reporte de caso: Enfermedad de Wilson, un reto diagnóstico.

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RESUMEN

Antecedentes: La enfermedad de Wilson es un trastorno genético de transmisión autosómica recesiva, producida por la mutación del gen ATP7B. Es considerada una enfermedad rara o huérfana debido a su baja prevalencia. Sin embargo, es una enfermedad crónica que puede llevar al deterioro de la calidad de vida del paciente poniéndolo en riesgo de muerte, por lo que se considera una enfermedad catastrófica. El gen ATP7B es determinante en el proceso de eliminación del cobre del organismo, por tanto, la mutación génica implica a su acumulación principalmente en el hígado y Sistema Nervioso Central (SNC). El diagnóstico de la enfermedad en etapas tempranas es vital para el control de los síntomas y evitar el deterioro hepático, neurológico y/o psiquiátrico del paciente. Sin embargo, la inespecificidad de los síntomas, así como la tardía edad de inicio de estos, dificulta su diagnóstico oportuno. La detección de los signos clínicos de la enfermedad y las anomalías genéticas asociadas, son necesarias para iniciar un tratamiento efectivo, si bien la enfermedad no es curable, el tratamiento farmacológico oportuno con medicamentos quelantes, minimizan los efectos del cobre en el organismo.
Objetivos: Determinar las características clínicas y el genotipo y de un paciente con diagnóstico clínico de la enfermedad de Wilson y analizar su evolución durante el tratamiento recibido.
Materiales y Métodos: Estudio de caso. Se describieron las características clínicas y genéticas del individuo con diagnóstico presuntivo de enfermedad de Wilson (WD). Se realizó el análisis genético de las variantes presentadas por el paciente mediante secuenciación genómica y otras pruebas de química sanguínea para relacionar los signos y síntomas con la variante presentada por el paciente. La investigación tuvo la aprobación ético-científica del comité de ética investigación de la Universidad Simón Bolívar de Barranquilla, Colombia. Fue acorde con los requisitos de no maleficencia, beneficencia y autonomía y

establecidos en las normas vigentes sobre investigación en seres humanos, contempladas en la Declaración de Helsinki de la Asociación Médica Mundial y la Resolución 8430 de 1993 del Ministerio de Salud de Colombia.
Resultados: La edad de aparición de la enfermedad en el paciente estudiado es de 25 años. El paciente presentó manifestaciones psiquiátricas, neurológicas y hepáticas; acompañado de signos característicos de la enfermedad de Wilson: Ceruloplasmina baja, Cobre sérico disminuido y Cobre en orina aumentado y anillo de Kayser, el cual debido a la buena adherencia al tratamiento ha desaparecido. El paciente presentó dos mutaciones asociadas con la enfermedad de Wilson de acuerdo con la literatura: Transversión de una base T por una G (M [A T G]> R [A G G]) en heterocigosis cercana al sitio dador del splicing del intrón 13 (c.3060+5G>T) y deleción de una base C (c.3402delC) generando una alteración en el marco de lectura dando lugar a un codón de parada prematuro (p.Ala1135Glnfs*13).
Conclusiones: En la actualidad, el paciente se encuentra en aceptables condiciones generales a pesar de los notables efectos de invalidez que provoca la enfermedad de Wilson en las personas afectadas. Se considera que la satisfactoria evolución del sujeto está asociada a una buena adherencia al tratamiento, a la intervención multidisciplinaria y al incondicional apoyo psicosocial recibido por su núcleo familiar

Palabras clave: Enfermedades huérfanas, ATPasas Transportadoras de Cobre, Genotipo, Enfermedad de Wilson, Proteína ATP7A

ABSTRACT

Background: Wilson's disease is an autosomal recessive genetic transmission disorder, caused by the mutation of the ATP7B gene. It is considered a rare or orphan disease due to its low prevalence. However, it is a chronic disease that can lead to the deterioration of the patient's quality of life putting him at risk of death, which is why it is considered a catastrophic disease. The ATP7B gene is decisive in the process of eliminating copper from the body, therefore, gene mutation leads to its accumulation mainly in the liver and Central Nervous System (CNS). The diagnosis of the disease in early stages is vital for the control of the symptoms and to avoid the hepatic, neurological and / or psychiatric deterioration of the patient. However, the non-specificity of the symptoms, as well as the late age of onset of these, hinders their timely diagnosis. The detection of the clinical signs of the disease and the associated genetic abnormalities, are necessary to initiate an effective treatment, although the disease is not curable, the timely pharmacological treatment with chelating drugs minimizes the effects of copper in the organism
Objective: To determine the clinical characteristics and genotype and of a patient with a clinical diagnosis of Wilson's disease and analyze its evolution during the treatment received, for the disclosure of a clinical case, in order to generate timely diagnostic guidelines in these patients
Materials and Methods: The genetic analysis of the variants presented by the patient was performed by genomic sequencing and other blood chemistry tests to relate the signs and symptoms with the variant presented by the patient

Results: The age of onset of the disease in the patient studied is 25 years. The patient presented psychiatric, neurological and hepatic manifestations; accompanied by characteristic signs of Wilson's disease: Low ceruloplasmin, decreased serum copper and Increased urine copper and Kayser's ring, which due to good adherence to treatment has disappeared. The patient presented two mutations associated with Wilson's disease according to the literature: Transversion of a T base by a G (M [ATG]> R [AGG]) in heterozygosis close to the intron splicing donor site 13 (c. 3060 + 5G> T) and deletion of a C base (c.3402delC) generating an alteration in the reading frame resulting in a premature stop codon (e.g. Ala1135Glnfs * 13).

Conclusions:

At present, the patient is in acceptable general conditions despite the notable effects of disability caused by Wilson's disease in affected people. The satisfactory evolution of the subject is associated with good adherence to treatment, multidisciplinary intervention and unconditional psychosocial support received by their family nucleus.

KeyWords: Orphan diseases, copper absorption, genotype, Wilson's disease, ATP7B gene.

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