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International Journal of Clinical Case Reports and Reviews
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Case Report

A Case Report: Co-Occurrence of Wilson Disease and Lysosomal Storage Disorder Probably Sialidosis in an Iraqi Patient

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Received Date: May 05, 2025 | **Accepted Date:** May 19, 2025 | **Published Date:** June 02, 2025

Citation: Fadwa G. Hameed, (2025), A Case Report: Co-Occurrence of Wilson Disease and Lysosomal Storage Disorder Probably Sialidosis in an Iraqi Patient, *International Journal of Clinical Case Reports and Reviews*, 26(4); **DOI:10.31579/2690-4861/760**

Abstract:

Rationale:

Both Wilson disease (WD) and Sialidosis are rare autosomal recessive disorders that are caused by mutations on chromosome 13 and chromosome 6, respectively. Here, we report on a patient with coexisting WD and LSD possibly Sialidosis.

Patient concerns:

WD is a disorder of copper metabolism. The main sites of copper accumulation are the liver and the brain, resulting in hepatic symptoms. Sialidosis belongs to a group of diseases known as the lysosomal storage disorders (LSDs). Lysosomes are particles bound in membranes within cells that function as the primary digestive units within cells. Sialidosis is a rare inherited metabolic disorder characterized by a deficiency of the enzyme neuraminidase (sometimes referred to as sialidase). Deficiency of neuraminidase results in the abnormal accumulation of toxic materials in the body. Sialidosis is divided into two types, type I usually becomes apparent during the second decade of life with the development of sudden involuntary muscle contractions (myoclonus), distinctive red spots (cherry-red macules) in the eyes, and sometimes additional neurological findings. Sialidosis type II is usually more severe than type I. Type II often begins during infancy or later during childhood and is characterized by cherry-red macules, mildly coarse facial features, skeletal malformations and mild cognitive impairment.

Diagnosis:

The diagnosis of WD was confirmed by neurological symptoms, metabolism tests, and MRI scans. Genetic analysis was subsequently conducted, and the results revealed pathogenic mutation (c.302c>A (g.52518281) P.H 1069Q (His.1069 Glu) of the ATP7B gene, confirming the diagnosis of WD. The family history was positive for WD with a 9-year-old younger sister also being diagnosed with it. His parents are negative for both Sialidosis and WD.

Interventions:

D-penicillamine and Zinc acetate treatment was initiated for long-term control.

Outcomes:

Normalize liver and spleen, control the copper level to avoid further hepatological,neurological complications.

Lessons:

In this study, we reported on the first case of a child who simultaneously presented WD and Sialidosis, bringing up the possibility of a presumable link between these 2 rare diseases.

Key words: coronary bypass; hemolysis; degree

Introduction

Wilson's disease is a rare autosomal recessive inherited disorder of copper metabolism causing excessive copper accumulation in the liver, brain, cornea and several other organs in the body, requiring specific treatment to remove or detoxify tissue copper and to prevent re-accumulation [1]

Wilson disease (WD) is a rare (1:30,000) autosomal recessive inherited disorder of copper metabolism at the level of the ATP7B copper transporter, resulting in copper accumulation in different organs. Copper accumulation affects the liver, and later the central nervous system [2]

Hepatic symptoms may include elevated liver enzymes, chronic hepatitis, and cirrhosis with end stage liver disease or acute liver failure. Neurologic manifestations include dysarthria, Parkinsonism, tremor, dystonia, chorea, and ataxia as well as cognitive, behavioral and psychiatric changes [3] Kayser-Fleischer (KF) rings may be seen in the eyes. Due to its autosomal recessive inheritance and lack of symptom presentation in the early phase, family screening/history of first-degree relatives in pre-symptomatic patients is of the most importance and should be performed in all cases. A delay in diagnosis, inadequate treatment or non-adherence may lead to progressive copper accumulation and worsening of symptoms [2,4,5]

The inherited human disorders sialidosis and galactosialidosis are the result of deficiencies of glycol protein specific a-neuraminidase (acylneuraminyl hydrolase, EC 3.2.1.18; sialidase) activity [6] These disorders are typically classified as the sialidoses(Sialidosis is caused by mutations of the NEU1 gene. This gene mutation is inherited as an autosomal recessive trait) which have only a neuraminidase deficiency, and the galactosialidoses, which have a coexistent deficiency of P-galactosidase [6,7] The sialidosis disorder, originally termed lipo-mucopolysaccharidosis [8], includes several variants with different degrees of clinical severity, including an adult-onset form known as sialidosis type I and the infantile onset variant known as mucolipidosis I or sialidosis type II [9,10]

The galactosialidosis disorder, which has also been termed the Goldberg Syndrome [11] GM1 gangliosidosis type 4 [12], the cherry-red-spot-myoclonus syndrome with dementia, and the juvenile-onset form of sialidosis type II [13], is also clinically heterogeneous [14,15] The primary defect in the sialidoses is thought to be a mutation in the neuraminidase structural gene. Obligate heterozygotes show a gene-dosage effect and have approximately half the normal neuraminidase levels [16,17]Obligate galactosialidosis heterozygotes have not consistently shown a reduction in either ,B-galactosidase or a-neuraminidase [6,9,13-17] Children with sialidosis type II may develop an abnormally enlarged liver (hepatomegaly) and/or spleen (splenomegaly), a specific assortment of bone deformities known as dysostosis multiplex, coarse facial features, delays in reaching developmental milestones, and cognitive impairment. Bone deformities associated with dysostosis multiplex include premature closure (fusion) of the fibrous joints (sutures) between certain bones of the skull, a thickened skullcap (calvaria), an enlarged skull, widely spaced teeth, thickened collarbones (clavicles), and abnormalities of the ribs, pelvic bones, certain long bones and other bones of the body. A diagnosis of sialidosis is made based upon identification of characteristic symptoms, a detailed patient history, a thorough clinical evaluation and a variety of specialized tests. An examination of urine may reveal increased levels of oligosaccharides. A urine test is usually followed up by blood tests and a skin biopsy (surgical removal and microscopic study of skin tissue). These tests can reveal low levels of the enzyme alpha-neuraminidase in blood and skin tissue [18]

Case report:

10 years old male child (36 kg.) presented to Rare Diseases Clinic in AL-Emamain Al-kadhmyain medical city hospital/Iraq-Baghdad, presented with un explained huge splenomegaly without evidence of portal hypertension. Diagnosed with Wilson disease since feb.2019, genetic analysis detects pathogenic mutation (c.302>A (g.52518281) P.H1069Q (His.1069Glu) of the ATP7B gene. O/E. Liver = 4cm Bcm, Spleen = 6 cm Bcm. His family mentioned there is a mood changes and behavioral problem.

Patient was on D-penicillamine initially then switched to Zinc acetate for maintenance.

Laboratory

Negative serology for hepatitis B and C, chemistry panel showed:

-Total Bilirubin levels were 1.2 (up to 1mg/dL), Direct bilirubin 0.9 (up to 0.25 mg/dl), Albumin 64(28-54 g/l), Alkaline phosphatase 321 IU/L,Aspartate transaminase 103 IU/L,Alanine transaminase 80 IU/L.

-Hb 11, WBc 2.4, PLT 104,000.

-Urinary copper/24hr. 100 (<40microgram/24hr), Urinary copper with penicillamine challenge test 683 (<40microgram/24hr), s.ceruloplasmine 20mg,

s.copper 113 microgram.

-s. IgG.17,456(up to17,000).

After one year (Feb.2020) of treatment and follow up:

-Total Bilirubin levels were 1 (up to 1mg/dL), Direct bilirubin 0.6 (up to 0.25 mg/dl), Albumin 34.6 (28-54 g/l), Alkaline phosphatase 221 IU/L,Aspartate transaminase28 IU/L,Alanine transaminase 47 IU/L.

-Hb 10.4 g/dl ,WBc 2.5(10e3/Ul.),PLT 79.2 (10e3/Ul.).

-Urinary copper/24hr. 39(<40microgram/24hr).

-Acid lipase 0.35(0.2-2nmol/spot*3h),beta galactosidase 0.31(0.5-3.2 nmol/spot*21h), .), ANA 0.78(<1 negative), IgG 1433.18(540-1822 mg/dl.), S.Ca 8.2(8.7-10.4mg/dl.). Blood count shows HBG 10.4 g/dl., MCV 72. fl, PL 79.2(10/UL).

Imaging:

MRI of abdomen demonstrated liver atrophy or congested inferior segment of right lobe with elongation of lateral segment. Spleen increased in size 16.5*7.6 cm; Abdominal ultrasound detected liver atrophy with splenomegaly.

Discussion:

Therapies for WD include chelating agents, PCA, and trientine, which increase urinary copper excretion and zinc salts that inhibit intestinal copper absorption. The goal of initial treatment of WD is to reestablish copper balance, whereas the maintenance phase serves to maintain these levels without inducing copper deficiency[19] Maintenance represents lifelong therapy, unless a patient undergoes liver transplant [20] However, despite its side effects and limitations, current medical treatment for WD is effective in avoiding disease progression and liver transplant for the majority of patients provided treatment is tailored and optimized to the patient's needs and comorbidities. Sialidoses are autosomal recessive disorders caused by NEU1 gene mutations and are classified on the basis of their phenotype and onset age. Genetically diagnosed patients with an especially mild phenotype, no retinal abnormalities and normal urinary sialic acid. This observation suggests that genetic analysis or the demonstration of the neuraminidase enzyme deficiency in cultured fibroblasts are needed to detect and diagnose mildest phenotypes [21]

Based on the age at onset of the symptoms, type II sialidosis is further divided into three subtypes: (i) congenital or hydropic (in utero); (ii) infantile (0–12 months); and (iii) juvenile (2–20 years) [22,23] In the infantile/juvenile sub type, characteristic features include hepatosplenomegaly, dysostosis multiplex, coarse facies, cherry-red spot, myoclonus, and severe mental retardation. Some clinical manifestations such as ataxia and hearing loss may become progressively severe with age [22]

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DOI:10.31579/2690-4861/760