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Case Report

A Rare Case Report: Wilson's Disease

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ABSTRACT

Wilson's disease is Hepatolenticular degeneration and it is an autosomal recessive disorder. It is an uncommon genetic condition of the metabolism of copper that is predominantly brought on by alterations to the ATP7B gene. A fourteen-year-old male patient arrived with the chief complaints of one episode of convulsions lasting up to 15 to 30 min, abnormal movements of the upper and lower eyelids, postictal drowsiness, up rolling of the eyes, deviation of the mouth angle, low-grade fever, frothing at the mouth, 4 to 5 episodes of vomiting, and cluster pigmented knuckles. The ceruloplasmin test result was 6.82 mg/dL. The brain's CE MRI exhibits generalized cerebral and cerebellar atrophy. Administration of potassium sulfide further enhances copper absorption in the GI tract. Doctors need to identify the symptoms and related symptoms as soon as possible because early disease identification may lessen the severity of Wilson's disease and stop further complications.

Keywords: Hepatolenticular degeneration, ATP7B gene, Ceruloplasmin, Cerebellar atrophy, Postictal drowsiness, Potassium sulfide.

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INTRODUCTION

Wilson's disease, also known as Hepatolenticular degeneration, is a rare genetic condition of copper metabolism characterized by decreased copper being eliminated into the bile, which causes copper to accumulate in numerous organs, predominantly the hepat and encephalon. Wilson's disease is estimated to impact one in every 30,000 to 40,000 people globally; nevertheless, estimates vary. Wilson's disease is primarily because of genetic alterations in the ATP7B gene. This gene is involved in the transportation of copper, a trace element necessary for various physiological processes, including the formation of enzymes essential for metabolism. In Wilson's disease, the defective ATP7B gene further hinders the copper transport mechanism, accelerating the copper build-up in the liver and subsequent release of excess copper into the bloodstream. From there, the copper can deposit in other organs, such as the subthalamus and, the cortex of the brain, eyes, kidneys, and joints, liver, causing various symptoms. While Wilson's disease is an inherited condition, having a family member with the condition is the most significant risk factor. Children have a 25% chance of inheriting the disorder if both parents have a mutant ATP7B gene. Wilson's disease affect people of many ethnicities; however, it is more common in people of European heritage. Wilson's disease comes in two types: the first, where the metabolic blocks occur at a level where low ceruloplasmin also coexists with the disease, and the second, which is the rarest, where the disease can exist with a normal amount of ceruloplasmin. nevertheless, signs of disease are still visible. Stages of this hepatolenticular degeneration autosomal disorder are as follows- Stage 1: the liver's first copper buildup. Stage 2: acute hepatic copper translocation followed by rapid discharge of copper into the bloodstream. Stage 3: Sustained copper accumulation in extrahepatic tissues, such as the brain Chelation therapy is administered in stage 4 to balance the copper levels. A hazardous hydroxyl group builds up when copper levels increase too much, which causes redox imbalance. The cells are damaged by this redox imbalance prompting in clinical symptoms like hepat dysfunction, changes in behavior, difficulties in mobility leading to disablement, and corneal Kayser-Fleischer rings.[1]

Genetic outlook of Wilson's disease: Ctr1 (SLC31A1) is a copper membrane transporter. This membrane transporter facilitates the transfer of metal copper into the cells, in which some of it is related to metallothionein and some are delivered by antioxidant protein 1 to an organelle called the trans-Golgi pathway. When copper concentrations rise, Copper is released into the portal vein via ATP7A. which leads to the liver. CMT1 and metallothionein are transported by hepatocytes, and antioxidant protien1 within the cell, bonds to them. Once here, the ATP7B gene attach to the ferroxidase enzyme and discharges it into the flow of blood, where it is removed via secretion into bile. In Wilson's illness, both functions of ATP7B are defective. Copper gathers in the liver, and ferroxidase enzymes are released in the copper-free form which is swiftly destroyed. The body

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requires copper for various enzymes, including tyrosinase, ferroxidase enzymes, the oxidase cytochrome c, dopamine beta-hydroxylase, and superoxide dismutase. Via the gut, copper enters the body. Copper gets deposited into the various parts of the brain i.e., basal ganglia, putamen, and globus pallidus, these parts are involved in movement. These dination and cognition activities such as promoting mood modulation. Symptoms of this hepatolenticular degeneration are of a neuropsychiatric nature resulting from damage to these tissues.[2] Complications include liver dysfunction, death, neuropsychiatric symptoms, brain damage, spleens welling, ascites, variceal bleeding, and hepatorenal syndrome.[3] Diagnostic tests include Blood tests: The initial step in diagnosing this autosomal recessive disorder is normally to measure copper-related indicators in the blood, such as copper strength in serum, serum ceruloplasmin, and quantitation of urinary copper saturation in urine. Liver enzymes might increase in Wilson's disease due to liver damage. Slit-lamp examination: An eye exam may reveal Kayser-Fleischer rings, which are golden-brown rings in the cornea produced by copper deposition. A small sample of liver tissue may be collected for analysis to determine the degree of copper build-up. Genetic testing: The diagnosis can be validated by finding alterations in the ATP7B gene, which can be extremely helpful for family screening.[4] Pharmacological Therapy: Chelating agents: These drugs aid in the detoxification of excess copper from the body. Chelators like penicillamine and trientine are often utilized. They combine with copper to form complexes, allowing the metal to be eliminated in the urine. Zinc acetate or zinc gluconate: These drugs reduce the quantity of copper in the plasma by limiting copper absorption in the intestines. Non-pharmacological Therapy: Individuals with Wilson's disease are typically recommended to abstain from copper-rich foods such as liver, shellfish, and some nuts. Regular check-ups and blood/urine tests are required to monitor copper levels and liver function. In severe cases with significant liver damage, a liver transplant might be required to replace the damage.[1-4]

CASE REPORT

On June 30, 2023, a fourteen-year-old male patient weighing 29 kg with his guardian arrived at a tertiary care facility with the chief complaints of one episode of convulsions lasting up to 15 to 30 min, abnormal movements of the upper and lower eyelids, postictal drowsiness, up rolling of the eyes, deviation of the mouth angle, low-grade fever, frothing at the mouth, 4 to 5 episodes of vomiting, and cluster pigmented knuckles. Wilson's illness was first noticed in the patient. When he was last seen in January 2018, he was advised to take d penicillamine for two months. No ATP7B gene mutation was discovered in the parent's family history. When examined, the vital signs were normal. His hemoglobin was 10.9 gm/dL, neutrophils were 87%, lymphocytes were 9%, and chloride levels were 108 milliequivalent per litter. The physician advised performing a CE MRI of the brain, which demonstrates symmetrical patches of T2/FLAIR hyperintense signal intensity without diffusion restrictions are seen in bilateral lentiform nuclei, posterior limb of the bilateral internal capsule, bilateral thalami, midbrain, and pons with relative sparing of red nuclei- features are s/o metabolic disorder-likely Wilson's disease. Focal areas of gliosis in the right frontal lobe and bilateral parietal lobes. Focal areas of diffusion restriction in bilateral frontal lobe involving grey matter -s/o acute infarct. The impression is generalized cerebral and cerebellar atrophy. The ceruloplasmin test was 6.82 mg/dL (normal range 20-60 mg/dL). Ultra sonogram shows massive splenomegaly. In the above report, the patient had Wilson's disease type 1. For a suspected manifestation, the patient was hospitalized for 13 days. He was given with following symptomatic treatment: Inj. PHENYTOIN (500 mg/dL)+NS (100 mL), Inj. LEVETIRACITAM (1.4 mL+20 mL NS for 20 min) twice a day, Inj. PANTOP (40 mg/dL) once a day, Inj. EMESET (4 mg/dL) taken as required, Tab. ZINC (25 mg) twice a day, Tab. RISDONE (0.5 mg) at bedtime, Tab. D PENICILLAMINE (250 mg) once a day, Tab. FA (Folic Acid) once a day, Tab. BENADONE (40 mg) in afternoon, Tab. CIPLAR (20 mg) once a day. The doctor began prescribing tablets of d-penicillamine and zinc on the third day of hospitalization. Levetiracetam tablets and injection phenytoin were given for convulsive episodes. For acid reflux, injection pantop. Vomiting was treated with inj. emeset. For controlling copper levels, tab zinc was prescribed. Tab risdone was given for treating psychiatric symptoms, tab d penicillamine was given to treat Wilson's disease, tab FA was given to treat folate levels, tab benadone was given to treat low levels of hemoglobin, and tab ciplar 20 was prescribed to treat anxiety.

DISCUSSION

The significance of Wilson's disease as a potential source of neuropsychiatric symptoms in young people is highlighted in this case study. An inherited metabolic disease called Wilson's disease can be fatal if it is not promptly diagnosed and addressed. The patient in this case is already having a known complaint of Wilson's disease as he was diagnosed with the same in January 2018. The patient exhibits neuropsychiatric symptoms such as postictal drowsiness, up rolling of the eyes, and abnormal motions of the upper and lower eyelids as present complaints. This patient is having type 1 of Wilson's disease category as laboratory data shows low level of ferroxidase enzyme. This autosomal recessive disorder of hepatolenticular degeneration can have a range of neuropsychiatric indicators as warning signs that were present in our patient as chief complaints and that are making diagnosis and treatment difficult. Neuropsychiatric symptoms can significantly improve with early identification and prompt initiation of proper treatment, including copper-chelating medications and zinc therapy, which can also avoid irreparable neurological damage. Other non-pharmacological methods are also useful for the patient and they may reduce the risk of having such diseases in the future. Administration of potassium sulfide further enhances

the absorption of copper in the GI tract. In this case, potassium sulfide was not prescribed. The awareness of pregnancy diet and some lifestyle changes may be beneficial in the case of hepatolenticular disorder. No clinical pharmacist intervention was found in the given treatment. No drug-drug, drug-food, and drug-disease interactions were found in the case.[5]

CONCLUSION

This case study demonstrates and highlights a fourteen-year-old male patient having Wilson's disease with neuropsychiatric manifestation, a highly rare disorder affecting one in 30,000 to 40,000 people globally. Wilson's disease, an inherited condition, is primarily because of genetic alterations in the ATP7B gene. Since early disease identification might reduce the severity of Wilson's disease and prevent subsequent complications, doctors must identify the symptoms and associated consequences as soon as possible.[5]

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ATP7A: ATPase copper transporting alpha (human); **ATP7B:** ATPase copper transporting beta (human); **Ctr1 (SLC31A1):** High-affinity copper uptake protein 1; **CMT:** Damage of the myelin sheath; **CE MRI:** Contrast-enhanced magnetic resonance imaging; **s/o:** Suggestive of; **GI:** Gastrointestinal.

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