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Case Study

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A CASE REPORT: WILSON'S DISEASE ASSOCIATED WITH HYPERSENSITIVITY REACTIONS DUE TO PENICILLAMINE

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ABSTRACT

Wilson's disease is a rare genetic disorder characterized by copper metabolism dysfunction, leading to copper accumulation in various organs, predominantly the liver and brain. We present a case of a 52-year-old male with a history of hypotension and liver cirrhosis who presented with ill-defined erythematous plaques and exfoliation of skin over the face, chest, and back, sparing the skin over the buttocks and bilaterally up to the knees. This presentation followed the administration of intravenous penicillamine, which led to hypersensitivity reactions. Laboratory investigations revealed elevated copper levels, suggestive of Wilson's disease, along with findings of liver parenchymal disease, thickened gallbladder wall, splenomegaly, raised corticoechogenicity of bilateral kidneys, and gross ascites on abdominal ultrasonography. Despite supportive care with intravenous fluids, analgesics, antiemetics, and antibiotics, the patient's skin manifestations persisted, albeit with improvement in other symptoms. The patient was discharged with incomplete resolution of skin rashes and advised to apply soft paraffin cream and avoid sunlight exposure. This case highlights the importance of considering Wilson's disease in patients presenting with skin manifestations, especially following drug administration, and underscores the need for comprehensive management to address both acute symptoms and underlying disease pathology.

KEYWORDS: Wilson's Disease, Hypersensitivity Reaction, Liver Cirrhosis, Skin Manifestations.

INTRODUCTION

Wilson's disease, also known as hepatolenticular degeneration, is an autosomal recessive condition that causes the body to accumulate too much copper. Though it can also impact other organ systems, its primary targets are the brain's basal ganglia and the liver. Wilson disease protein (ATP7B) gene mutations result in Wilson disease, an autosomal recessive disorder. A copy of the gene from each parent must be inherited for an individual to be impacted. In addition to a clinical examination, the diagnosis is challenging and requires liver biopsy, blood test, and urine test results. It may be possible to screen afflicted people's relatives through genetic testing.[1] Six metal-binding domains and eight transmembrane domains make up ATP7B, a P-type ATPase that transports copper across membranes in an ATP-dependent manner.4 In hepatocytes, this protein has two distinct purposes. Initially, it provides copper to the trans-Golgi network (TGN) so that it may be integrated into the primary copper-transport protein released into the circulation, caeruloplasmin. By moving to late endosomal or lysosomal compartments and securing copper in vesicles for export over the apical (canalicular) membrane, it secondly aids in the biliary outflow of excess copper.[2] Brain and liver-related symptoms are the norm. Symptoms associated with the liver include weakness, ascites, itching, leg edema, and yellowing skin. Tremors, muscular stiffness, difficulty speaking, personality changes, anxiety, and auditory or visual hallucinations are examples of brain or neurological symptoms.[1] In the past, clinical history and biochemical analysis have been used to diagnose WD. A person with WD can be diagnosed using a variety of clinical symptoms, including cirrhosis, neurological or mental problems, and Kayser Fleischer (KF) rings. When patients just have one or two of the clinical symptoms, it might be challenging. The diagnosis can also be made by biochemical investigation using blood copper, serum ceruloplasmin, liver enzymes, urine copper excretion, hepatic copper quantification, and (if accessible) genetic testing; however, each has limits. If abnormalities in the basal ganglia are observed, imaging, such as MRI of the brain, may be helpful. Numerous developments in diagnostic imaging and genetic testing have demonstrated that early detection is crucial to preventing long-term consequences.[3] Wilson disease treatment is a

lifetime endeavor. Patients may get sicker and sicker every day, so getting help right away can be vital. Delays in treatment could result in permanent harm. Trientine dihydrocholoride, trientine tetrahydrochoride, and penicillamine are approved chelation therapy medications for the treatment of Wilson disease. These medications work by binding, or chelating, copper, increasing the amount of copper excreted in the urine. Zinc acetate is approved for treating Wilson disease. Zinc inhibits the intestinal tract's ability to absorb copper by inducing metallothionein. By doing this, accumulated copper is both drained and kept from reaccumulating. Zinc is mostly used in asymptomatic patients' maintenance regimens; it can also be used in combination with chelators. Over 40 years of significant experience in the USA and Europe attests to its efficacy. The absence of adverse effects is one of zinc therapy's main benefits.[4]

CASE REPORT

A 52 year old male patient with past history of Hypotension, and liver cirrhosis presented with chief complaints of ill-defined erythematous plaques with exfoliation of skin over face, chest and back with sparring of skin over buttocks and bilaterally up to knees (Fig.1-4). About 7-8 days before patient was administered with Inj Penicillamine and developed hypersensitivity reactions. The patient denied any history of consuming alcohol, or illegal drug abuse and smoking cigarette. Patient was administered with IV treatments including Inj. Albumin, Inj. Noradrenaline, Inj. Pantoprazole, Inj. Ondansetron, Inj. Piperacillin + Tazobactam and Inj. Hydrocortisone. To fulfil haematological requirements Inj. PCV and Inj. Plasma were given to the patient respectively. On physical examination, He was Afebrile, had a heart rate 114 beats/min and blood pressure of 104/70 mm Hg and respiratory rate 18cycle/min. The remainder of his physical exam was normal. Laboratory investigations showed (Reference ranges of laboratory data are included in parentheses): Hb: 8.10 g/dl (12-16),RBC: 2.51 millions/cmm(3.5-5.5), PCV: 23.90 % (37-64), MCV: 74 fL (80-100), MCH: 33.90 pg (27-34), MCHC : 33g/dl (32-36). RDW 13.1% (11-16), WBC: 9900/cmm(4000-11000), Neutrophils: 77%, Lymphocytes: 16 %, Eosinophils: 2%, Monocytes: 2%, Basophils 1%, Platelets 44000/µl(140,000-400,000), Urea: 59 (14-40 mg/dL), Serum creatinine: 1.56mg/dL (0.7-1.4mg/dL), Total Bilirubin: 1.80 (0.1-4.2 mg/dL), Direct Bilirubin: 0.50mg/dL (9-14 mg/dL), Creatinine 1.2mg/dl (0.5-1.6), SGPT: 20g/dL (0-40g/dL), SGOT : 43g/dL(0-37g/dL), Serum Total protein : 5.20g/dL(6-8g/dL), Serum Albumin : 2.68g/dL (3.2-5 g/dL), Serum Globulin : 2.52g/dL (2.3-3.6g/dL), Serum Sodium :125 mEq/L (135-145mEq/L), Serum Potassium: 3.40 mEq/L (3.5-5.1mEq/L). Apart from this, patient's coagulation profile was also evaluated which turned out to be normal. The levels of ESR and CRP rose significantly to 32mm and 9.60mg/L which indicates the presence of infection and inflammation. On the next day, USG abdomen findings suggested of coarsened liver surface with irregularities which may prognose towards Liver parenchymal disease. The wall of Gall bladder was of the thickness of 5mm. The size of the spleen was enlarged to 140mm. Surprisingly, bilateral kidneys denoted raised corticoechogenecity and moreover gross ascites was also found. After a few days of treatment patient was discharged with the incomplete resolution of symptoms. After complete treatment, patient was having rashes and redness on the skin for which he was advised to apply soft paraffin cream.

DISCUSSION

Wilson's disease, which is linked to neurological, psychiatric, ophthalmological, and hepatic symptoms, is an autosomal-recessive disorder of copper metabolism brought on by mutations in ATP7B. Neurological outcomes are still inconsistent despite the use of decoppering treatments to stop the disease from getting worse and to lessen symptoms.[2] Wilson disease is characterized by copper accumulation that begins at birth, although symptoms may not show up for years or even decades. While symptoms can appear at any age, they typically do so between the ages of five and thirty-five. Depending on which organs are impacted, Wilson disease presents with different symptoms. Wilson's disease can affect a person's liver, brain, and spinal cord. They might come under attack simultaneously. This may result in a collection of seemingly unrelated symptoms.[5] Since Wilson's original description, advancements in diagnosis have made it possible to assess for WD and establish the diagnosis in people who are suspected of having the disorder but have not yet developed neurological symptoms. These include the ability to recognize KF rings, the fact that the majority of patients have low serum ceruloplasmin concentrations, the ability to detect liver disease through biochemical testing, imaging, liver biopsy for histology, and the ability to measure the concentration of copper in the tissue. Genotype analysis by direct examination for disease-specific ATP7B mutations, including whole-exome/genome sequencing, is the new development.[6] Wilson's disease medication therapy focuses on decoppering by using zinc, which lowers intestinal copper absorption, or chelators, which increase copper excretion. Since diagnostic tests to detect presymptomatic disease were not available, these treatments were initially limited to symptomatic patients. It is now known that treating asymptomatic patients can significantly reduce morbidity and death due to advancements in diagnostics.65 Up until 1951, Wilson's disease was increasingly lethal. However, the first intramuscular application of dimercaprol, a copper chelator, was limited in its therapeutic use due to a high rate of side effects. The advantages of penicillamine, an oral active copper chelator, were first shown by Walshe in 1956. 68 Trientine was introduced as a substitute chelator in 1969, particularly for people who couldn't handle penicillamine. 69 Another chelator that veterinarians use to treat animal copper poisoning and

has been shown to help with Wilson's disease is ammonium tetrathiomolybdate (TM). 70 Wilson's disease is currently treated primarily with lifetime medication, usually in the form of an oral active copper chelator. When a patient has end-stage liver disease, acute liver failure, and is not responding to medication, liver transplantation may be an option.[7]

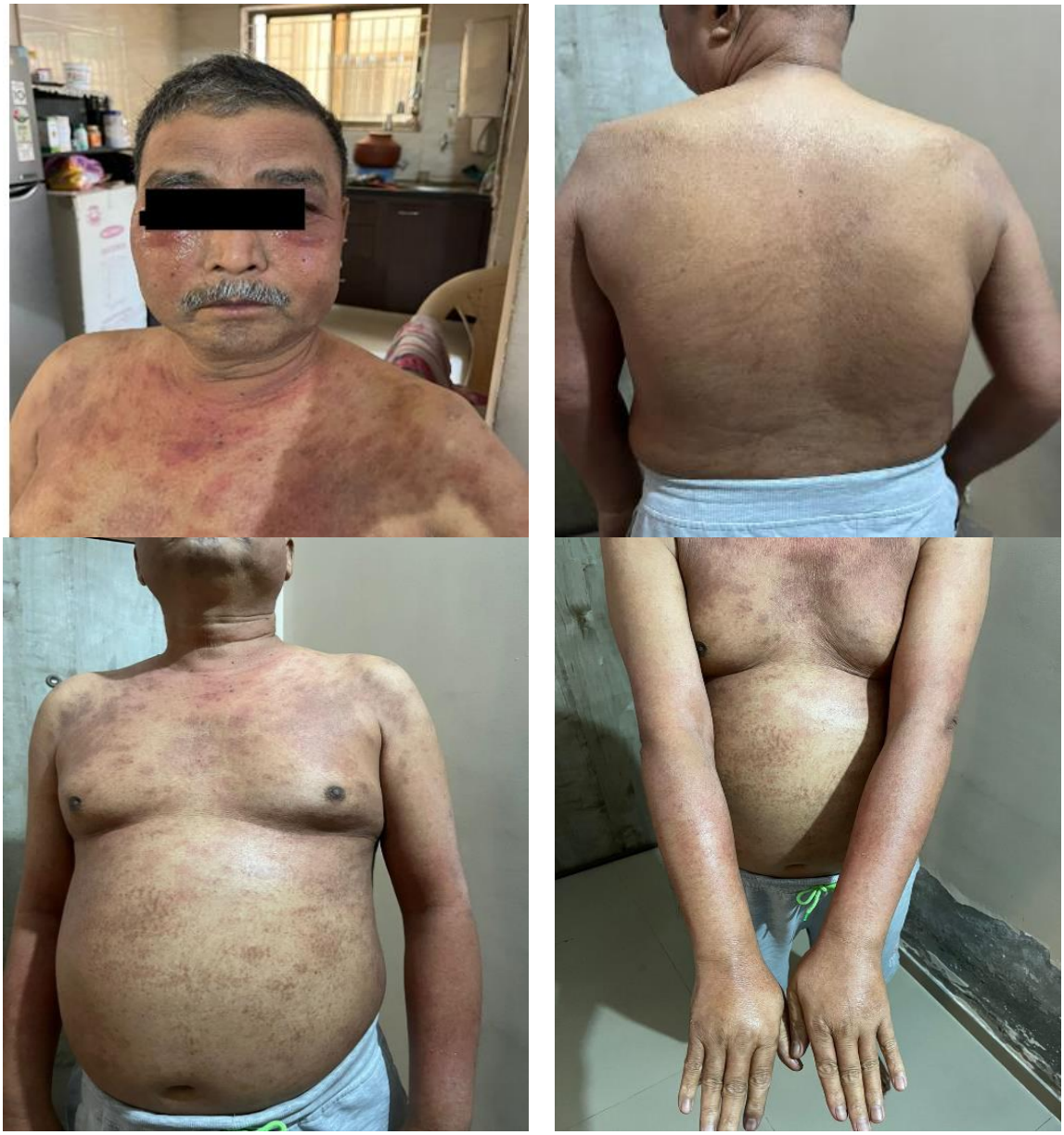

Fig. 1-4: Representation of The Hypersensitivity Reactions Caused Due To Penicillamine.

CONCLUSION

In conclusion, this is a case of an adult male who was diagnosed by WD, a condition which is mainly caused by elevation of copper levels in the body. The symptoms and complications of this condition range from mild to severe. The patient had a history of getting administered with Inj. Penicillamine due to which he developed hypersensitivity reactions on the skin. Before administering penicillin a sensitivity test should have been performed in order to avoid any lethal reactions. Patient should have knowledge about his medication and disease correctly. They should not self-medication or buy a OTC preparation without consultation of physician.

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