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Case Report

A Case Report on Wilson's Disease

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ABSTRACT

Wilson's disease is a chronic, progressive disease with a genetically determined autosomal recessive mode of inheritance and multi-systemic condition, in which the copper is accumulated in the Kidneys, Eyes, Liver and especially in the basal ganglia in the central nervous system. In Wilson's disease, the cirrhotic state of the liver is combined with degenerative changes in the lenticular nuclei of the brain, also known as hepato-lenticular degeneration. A 14-year-old male was admitted to the department of Paediatric with chief complaints of tremors of both upper limbs in the last 6 months, increased in intensity for 2 months. He was unable to button and unbutton the dress, handwriting was altered. He had splenomegaly, cirrhosis of the liver, bilateral Kayser-Fleischer rings, and gynecomastia. On investigation, his alkaline Phosphatase and albumin levels were increased and globulin, ceruloplasmin and serum copper levels were decreased. The patient was kept under copper chelators such as D-Penicillamine and zinc acetate. Gradually he showed improvement in clinical signs and Liver function tests. Prior recognition and awareness of Hepatic manifestations, KF rings, and involuntary movements of limbs will be useful for quick diagnosis and for preventing manifestations in siblings as this is an inherited metabolic disorder.

Keywords: Kayser-Fleischer ring, Hepato-lenticular degeneration, Autosomal recessive disorder, Tremors, Copper accumulation.

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INTRODUCTION

Friedrich Theodor Von Frerichs reported the first Wilson's disease case in 1861. But it wasn't until Alexander Kinnier Wilson recorded several cases in 1912 that it became well known.[11]

Wilson's disease is a rare autosomal recessive disorder caused due to defect in the copper metabolism.[1] The long arm of chromosome 13 contain locus for WD this chromosome is accounting for encoding ATP7B expressed mainly in the liver. Copper transportation within the cells and it's excretion after being incorporated into ceruloplasmin through bile is done by ATP7B, this is how copper is primarily excreted.[11]

A mutation in the ATP7B gene can cause copper to build up inside the cytoplasm of hepatocytes, which can then necrotize and release copper into the blood plasma, causing copper overload in the eyes, kidneys, central nervous system, particularly the basal ganglia, and other organs.[1,11] The development of the central nervous system, the production of energy, the formation of connective tissue, the synthesis of melanin, the metabolism of iron, angiogenesis, all these depend on copper.[6] Acute renal failure, gastroenteritis, and chronic liver disease are a few signs and symptoms of copper toxicity.[6]

If WD symptoms first arise in childhood, hepatic abnormalities are more likely to develop. If Wilson's disease symptoms appear between the second and third decades of life, 50% of individuals will experience neurological symptoms. The most prevalent neurological symptoms are dysarthria, dystonia and since the first cases were documented in 1912, cognitive abnormalities have also been noted. One of the most prevalent deficits is memory change, but dementia in untreated instances has also been observed among other cognitive changes.[11]

In Wilson's disease, the cirrhotic state of the liver is combined with degenerative changes in the lenticular nuclei of the brain, also known as hepato-lenticular degeneration. Copper-containing alpha-2 globulin (serum ceruloplasmin) deficiency is the most consistent biochemical abnormality in Wilson's disease, which consists of 95% serum copper.[9] It helps to maintain hepatic copper homeostasis. The factors that influence serum ceruloplasmin concentration are diet, hormone concentration, and other

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genetic disorders, in Wilson's disease the ceruloplasmin levels are reduced[4,5] Wilson's disease affects 1 out of every 30,000 people, with an incidence of 10 to 30 million cases. It is more observed where consanguinity marriages are more (South India).[1]

Kayser-Fleischer ring is the salient feature of Wilson's disease seen in children.[3] Wilson's Disease can now be directly diagnosed genetically using ATP7B mutations to support the clinical diagnosis.[8]

Since the use of chelating drugs can increase copper blood concentration and raise copper renal excretion, some physicians prefer the use of zinc sulphate or acetate, which has a less aggressive profile in terms of collateral symptoms and may prevent symptoms from initially deteriorating.[11]

CASE SUMMARY

A 14-year male patient was admitted to the paediatric department with complaints of Tremors in both upper limbs for 6 months, which increased in intensity over 2 months. He was unable to button and unbutton the dress, his handwriting was altered and the patient has a history of jaundice and joint pains 1 year back. On admission, the patient presented with pallor, icterus, and gynecomastia. He also presented with signs of cerebellar incoordination (Finger nose test).

The patient weighed 60.4 kgs with a normal body temperature. His USG of the abdomen showed splenomegaly, cirrhosis of the liver with regenerative nodules, and mild distension with portal HTN and dilated Common Bile Duct (CBD). His brain MRI

Table 1: Lab Investigations.

Table 1.1: Haematological Parameters.

Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Haemoglobin (gm/decilitre)	13.4	13.3	14.6	13.9	13.1	14.0
PCV (%)	38	33	42	39	37	40
TLC (cells/cu.mm)	7,600	6,800	7,900	7,100	6,900	6,500
PC (L/cu.mm)	98,000	90,000	82,000	93,000	88,000	82,000
Neutrophils (%)	68	-	-	65	-	-
Lymphocytes (%)	-	-	-	32	-	-
Eosinophil's (%)	4.0	-	-	-	-	-
Sr. Copper (µg/dL)	< 25	-	-	-	-	-
Sr. ceruloplasmin(g/L)	0.03 g/L	-	-	-	-	-

Table 1.2: Renal Function Tests.

Parameters	Day 1	Day 2	Day 3	Day 4	Day 5
Sr. Creatinine (mg/dL)	1.2	1.0	1.1	1.1	1.1
Sr. Sodium (mmol/lit)	136	132	137	134	134
Sr. Potassium (mmol/lit)	3.7	5.9	4.1	3.6	3.8

Table 1.3: Liver Function Tests.

Parameters	Day 1	Day 6
Total Bilirubin (mg/dL)	1.0	0.8
Direct bilirubin (mg/dL)	0.4	0.3
Indirect bilirubin (mg/dL)	0.6	0.5
SGPT (U/L)	33	23
SGOT (U/L)	40	27
ALP (U/L)	298	420
Total protein (gm/dL)	6.8	6.8
Albumin (gm/dL)	5.1	4.8
Globulin (gm/dL)	1.7	2.0

showed an altered signal in the bilateral, Corpus striatum with faint T2, flair hyper-intensity in the pons, and midbrain findings C/W Wilson's disease. His ophthalmic report showed KF ring++ bilateral in the anterior segment.

Urinary copper–15.30 µg/L

On performing the Leipzig scoring system, the score of the patient was found to be 7, where the diagnosis is established.

DISCUSSION

Copper accumulation in the liver, brain, cornea, and kidneys is a defining feature of Wilson's disease, a rare autosomal recessive disorder of copper metabolism. It can appear at any age, however the majority do so between the ages of 5 and 35. A prompt diagnosis is still difficult even though it is a progressive condition that could be fatal if neglected.

Our patient presented with Tremors in both upper limbs for the last six months, an increase in intensity over two months. His lab investigations revealed that increased levels of alkaline phosphatase, albumin and decreased levels of globulin, serum copper and ceruloplasmin Table 1. KF rings were identified in the patient. His family has a history of Wilson's disease. His parents were married consanguineously. His sibling died of Wilson's disease at the age of 16.

This patient was treated with copper chelators like D-Penicillamine with a dose of 250mg once a day, the frequency was gradually increased to twice daily from the second day, and 50 mg of Zinc acetate was given orally three times a day. Hepato-protectants like Ursodeoxy cholic acid were given with a dose of 300mg orally twice daily from day 3. Along with it, one tablet of heptagon was given twice per day-3. Tremors were reduced by giving 2mg of Trihexyphenidyl once a day and 40mg of pyridoxine once a day orally from day 3. Prophylactically 2mg of Vitamin K was given once a day for three days intravenously, 1gm of Cefepime was given three times a day for 11 days intravenously, 300mg of Amikacin was given twice a day for 11 days intravenously, 3mL of ranitidine IV was given twice a day for 11 days.

The condition of the patient at the time of discharge was stable. The medications suggested at the time of discharge are Tab. D-Penicillamine 250mg TID one hour before food, Tab. Zinc acetate 50mg TID two hours after food. Tab. Ursodeoxycholic acid 300mg BD. Tab. Trihexyphenidyl 2mg OD. Tab. Heptagon 1 tab BD. Tab. Pyridoxine 40mg OD until further advice. The patient was advised to avoid copper-containing food like chocolates, nuts, and shellfish. The patient was advised to join the hospital immediately if they have any symptoms like blood vomiting and altered mental status.

CONCLUSION

Wilson's Disease is a autosomal recessive disorder. Wilson's disease affects 1 out of every 30,000 people. Hepatic manifestations, KF rings, and involuntary movements of limbs are mainly observed in Wilson's disease. So, if any patient is presented with these symptoms, they should be screened for Wilson's disease. Adherence to therapy, avoiding copper-containing food like chocolates, nuts, shellfish, etc. A good follow-up reveals a considerable decrease in morbidity and mortality. In acute liver failure, liver transplantation is advised. It is necessary to check siblings in order to prevent manifestations.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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