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WILSON'S DISEASE A RARE AND FATAL DISEASE: CASE REPORT AND REVIEW OF LITERATURE

General Medicine

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ABSTRACT

Wilson's disease is a rare inherited autosomal recessive disorder of copper metabolism leading to various clinical, biochemical and radiological features. In this disorder there is accumulation of copper in various tissues like liver, brain, cornea, etc., due to impairment in excretion of copper from body. In today's world Wilson's disease has been evolved from fatal disease to a treatable condition were life expectancy and quality of life has been increased to a great extent. With advancement in diagnostic modalities there has been a drastic change in understanding the disease pathology and to find treatment for better outcome for the patients. Earlier when there were delay in diagnosis and treatment of these patients, it led to early fatalities but is uncommon now. We present you a case of a 20 year male patient who was diagnosed with Wilson disease after he developed liver cirrhosis which proved fatal for him.

KEYWORDS

Wilsons Disease, Copper, Ceruloplasmin, Kayser Fleisher Ring, Penicillamine

INTRODUCTION

Wilson's disease is an autosomal recessive disorder of copper metabolism. ATP 7B gene is affected in Wilson's disease. Due to nonfunctional gene, there is defective excretion of copper from body leading to excessive accumulation of copper in organ system leading to various systemic manifestation [1, 2]. With increase in awareness and recent advancement in diagnosis and management of patients of Wilson's disease there is early diagnosis and better treatment outcome in patients of Wilson's disease [3].

Various diagnostic modalities like ophthalmological examination for Kayser Fleischer ring, serum ceruloplasmin levels, serum copper levels, urinary copper levels, radiological studies like USG abdomen and CT abdomen, with liver biopsy and gene analysis for ATP 7B has made it possible to diagnose Wilson's disease early [4, 5]. However these modalities still remains unavailable in rural areas which lead to delayed diagnosis and treatment of these patients leading to poor outcome [6, 7].

Earlier it was difficult to diagnose and treat these cases leading to increased morbidity and mortality in these patients, but in today's world we have a range of treatment modalities available depending on stage of patient's disease starting from chelation therapy to liver transplant which is almost curable. With early diagnosis of patients of Wilson's disease even before liver cell failure, patient can be started on chelation therapy by zinc, penicillamine or tetrathiomolybdate to decrease copper overload in organ system by decreasing absorption of dietary copper [7].

If due to some reason patients diagnosis is delayed and patient lands up in liver cirrhosis, Liver transplant remains last resort for treatment in patients of Wilson's disease [7]. Today even after recent advancement and availability of liver transplant as a treatment approach in patients of liver cirrhosis in patients of Wilson's disease, there are various challenges involved in this procedure making it one of the biggest hurdle involved in treatment of patients of Wilson's disease. Hence early diagnosis and proper treatment can delay the progression of patients to decompensated liver cirrhosis and can delay morbidity and mortality [7].

Case Presentation

A 20 years nonalcoholic male was referred from a primary health care facility to a tertiary care hospital with complaints of abdominal distention, weight loss and fatigability since 3 months. Patient had similar complaints in past for which ascitic tapping was done multiple times in last 2 years. Patient was never investigated for similar complaints in past and was neither started on any therapy. Patient used to access primary health care whenever he had distention in abdomen and was tapped every time he visited with similar complaints. Finally when frequency of abdominal distention increased with other symptoms of generalized weakness and weight loss patient was referred to tertiary care hospital for further management.

On presentation to casualty of our hospital, patient was found to have tense ascites and was severely cachexic. Patient gave history of weight loss of approximately 7 to 10 kg's in last 2 years. Patient consumed mixed diet. Patient had no problem in achieving his milestones which were equivalent with his age. Patient had normal cognition, intelligence and completed secondary education. Later he indulged in occupation of farming with his father.

On clinical examination patient was conscious, alert, afebrile, cooperative, averagely built and poorly nourished. Vitally patient had pulse of 124/min regularly regular, normal in character with no radio radial or radio femoral delay with all peripheral pulses palpable. Patient had blood pressure of 100/70 mm hg and spo2 of 98% on room air with respiratory rate of 24/min. There was grade 1 pallor present. No cyanosis, icterus, clubbing, lymphadenopathy or edema was seen. There was circular corneal deposits, shrunken eyes and cheeks, distention of abdomen with dilated veins over it.

On inspection of his abdomen, there was diffuse distention of abdomen, everted umbilicus with stretched shiny skin overlying [Figure *1*]. Dilated veins over abdomen were also seen. Multiple marks of previous ascitic tapping seen over the skin of right iliac fossa. On palpation there was no tenderness noted. There were no palpable organs noted on palpation. Fluid thrill was present.

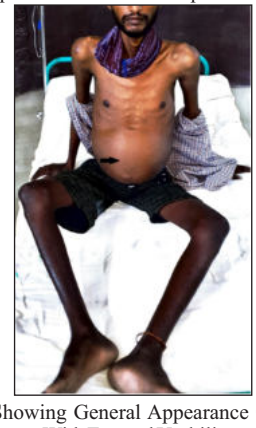

Figure 1: Image Showing General Appearance Of The Patient And Distention Of Abdomen With Everted Umbilicus

Rest of systemic examination were normal. In Cardiovascular examination, both heart sounds were heard with no murmur. In respiratory system examination, there were normal vesicular breath sounds heard over both sides. In Neurological examination there was presence of wing beating tremor seen involving both the upper limbs with no other neurological deficits.

Patient's chest x-ray and electrocardiogram was normal. His hemoglobin and mean corpuscular volume was low with normal platelet and white blood cell count.

His serum sodium and potassium levels were normal with normal renal function test. His total bilirubin was raised. He had normal total protein levels with lower levels of albumin and higher levels of globulin with reversal of A: G ratio. His SGOT and SGPT were borderline raised. He had raised PT-INR and test for HIV, HBsAg, HCV, rapid malarial antigen, dengue and leptospira were negative. Urine microscopy was normal. Ascitic fluid cytology showed no nucleated cells, with normal protein and sugar with sterile ascitic fluid culture. Serum ascitic albumin gradient was raised. Patient's serum ceruloplasmin levels and serum copper levels were low with higher 24 hours urinary copper levels. Table 1 shows laboratory investigations of the patient.

Table 1: Laboratory investigation

Investigations	Patients values	Reference range
Hemoglobin	7.1 gm/dl	14-17.5 gm/dl
MCV	78.6 femtoliter	80-100 femtoliter
Platelet	176000 / microliter	150000 to 450000 / microliter
WBC	4700 / microliter	4500 to 11000 / microliter
Sodium	138.6 mEq/L	135-145 mEq/L
Potassium	3.92 mEq/L	3.5-5.5 mEq/L
Creatinine	0.68 mg/dl	0.7-1.3 mg/dl
Urea	27 mg/dl	6-30 mg/dl
Total bilirubin	1.4 mg/dl	0.3-1.2 mg/dl
Direct bilirubin	0.7 mg/dl	0.1-0.3 mg/dl
Indirect bilirubin	0.7 mg/dl	0.2-0.8 mg/dl
Total protein	6.4 g/dl	6-8.3 g/dl
Albumin	1.9 g/dl	3.4-5.4 g/dl
globulin	4.5 g/dl	2-3.9 gm/dl
A: G ratio	0.42	1.1-2.5
SGOT	134 unit/liter	8-45 units/liter
SGPT	62 unit/liter	7-56 units/liter
PT-INR	1.73	< 1.1
Ascitic fluid cytology	No cells	Less than 300 WBC / microliter
Ascitic fluid protein	0.6 gm/dl	0.3-4.0 gm/dl
Ascitic fluid glucose	7 mg/dl	7-10 mg/dl
Ascitic fluid culture	No growth	No growth
Serum ascites albumin gradient	1.3 gm/dl	>1.1 gm/dl is high and <1.1 gm/dl is low
Serum ceruloplasmin	9.18 mg/dl	20-35 mg/dl
Serum copper	10.68 microgram/dl	85-180 microgram/dl
24 hours urinary copper level	64.0 microgram/24 hours	10-30 microgram/24 hours

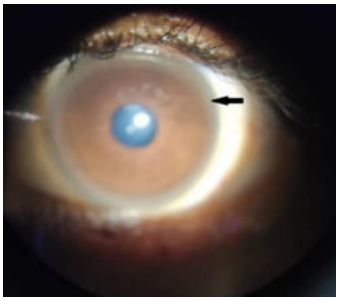

Figure 2: Kayser Fleischer Ring Seen On Slit Lamp Examination

Ophthalmological examination revealed normal extraocular movements with normal head posture. There was normal eyebrow, eyelid, conjunctiva with normal pupils and lens. Kayser fleischer ring was noted in both the corneas on slit lamp examination [Figure *2*].

Ultrasonography of abdomen and pelvis was suggestive of shrunken contracted liver with liver span of 8 cm, irregular surface and raised echogenicity which was suggestive of liver cirrhosis with gross ascites. CT scan of Abdomen and pelvis revealed shrunken liver measuring 9 cm in size with multiple macro-nodules scattered throughout liver parenchyma with loss of normal architecture suggestive of macro-nodular liver cirrhosis [Figure 3].

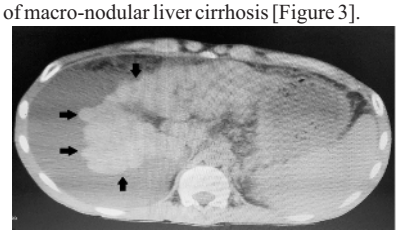

Figure 3: Image showing CT scan of abdomen showing macro nodular liver cirrhosis

MRI Brain plain of the patient was suggestive of mild cerebral and cerebellar atrophy with prominence of ventricular system. Mild T2 flair hyper-intensities were seen in bilateral basal ganglia without T1 hyper-intensities on susceptibility weighted imaging, above mentioned findings were suggestive of Wilson's disease [Figure *4*].

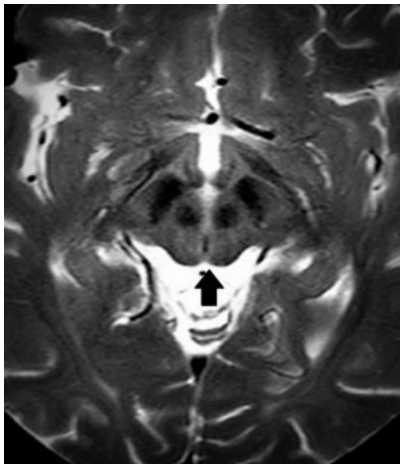

Figure 4: Image showing MRI brain - Face of giant panda sign

Patient was started with zinc, penicillamine and diuretics. Patient was followed up for next 3 months were he progressed rapidly from compensated liver cirrhosis to decompensated liver cirrhosis with complication of hepatic encephalopathy which proved fatal for him even after medical treatment.

DISCUSSION

Wilson's disease is a rarest autosomal recessive disorder which occurs due to mutation of ATP7B gene [1, 2]. ATP7B gene is responsible in formation of copper transporting ATPase 2 protein. ATPase 2 is found primarily in liver, kidneys and central nervous system. It helps to mobilize stored copper from liver to other organ system. It is also responsible for excretion of extra amount of copper from body. ATPase 2 mobilizes stored copper to a protein called ceruloplasmin. Ceruloplasmin helps to mobilize copper from liver to other organ system [4, 6].

In patients of Wilson's disease there is mutation of ATP7B which impair removal of copper from liver and body leading to increase in copper load in body which in-turn lead to accumulation of copper in various organ system and impairment of organ function. Most common organ to involve in Wilson's disease is liver followed by central nervous system leading to range of symptoms in these patients[1, 2].

Diagnosis of Wilson disease is often difficult as it presents with plethora of mild and nonspecific symptoms and it also mimics non-alcoholic steatohepatitis [8]. Patients usually present in childhood, adolescence or early adulthood with liver disease (e.g., hepatitis, acute

liver failure, cirrhosis), neurologic disease (e.g., dysarthria, dystonia, tremor, Parkinsonism), psychiatric disease, Kayser-Fleischer rings which is seen in 1/3 of patients (deposits in descemet membrane of cornea), hemolytic anemia, renal disease (e.g., Fanconi Syndrome). Hepatic presentations are common in early life, while neurologic presentations are usually diagnosed later [5]. Usually in many patients hepatic involvement precedes neurological manifestations [6]. Both basal ganglia and brain stem are equally affected in patients of Wilson's disease. Copper toxicity in these areas leads to various movement disorders and neuropsychiatric manifestations. There are 4 clinical syndromes seen in patients of Wilson's disease which includes, parkinson like syndrome, multiple sclerosis like syndrome, chorea's and ataxias. Patient may have psychiatric manifestations in form of behavioral disorders, affective disorders, and cognitive dysfunctions [6].

There are various laboratory investigations including liver function tests, serum ceruloplasmin, 24- hour urinary copper, and slit lamp examination. Additional laboratory investigation include, increased urinary copper excretion, increased hepatic copper content [3, 5]. Genetic testing has also emerged as a new diagnostic tool, but its application in the clinical routine is limited by its high costs and large number of genetic mutations [3, 6]. Determination of blood ceruloplasmin levels, urinary copper levels and molecular genetics is sufficient to confirm diagnosis of Wilson's disease.

Leipzig score helps in assessing the severity. Score includes KF Ring, neurological symptoms, serum ceruloplasmin levels, Presence of coombs negative hemolytic anemia, liver copper, urinary copper and mutation analysis [5]. Radiological imaging with MRI is useful and is included in Leipzig scoring. MRI can help us to find deposition of copper in brain parenchyma. Face of giant panda sign is specific for Wilson's disease [6].

In treatment of Wilson's disease primarily goal is to decrease copper from body. Diet containing copper rich foods should be avoided e.g., chocolate, nuts, seafood, meat, liver. There are various chelating agents available e.g., Penicillamine, trientine, zinc salts, tetrathiomolybdate. All of these helps to decrease copper levels by either excretion or decrease dietary absorption of copper. There are various ongoing trials for newer treatment modalities for patients of Wilson's disease which include gene therapy, having potential for cure of Wilson's disease and restrict need on liver transplant in near future [5, 6]. Liver transplant remains last resort in patients of de-compensated liver failure. But even with transplantation there are many case reports which suggests that there is no much improvement in neurological symptoms even after liver transplantation [6, 9, 10].

CONCLUSIONS

Through this case presentation we want to encourage early detection of Wilson disease by thorough clinical examination, laboratory and radiological investigation and prompt treatment for the same as Wilson disease remains a treatable disorder in pre-cirrhotic stage and delayed diagnosis can prove fatal. Toxic stores of copper can be removed with copper-chelators like d-penicillamine, tetrathiomolybdate that promote renal excretion of copper, and oral zinc therapy interferes with intestinal absorption of copper. Liver transplantation is the only option for patients with acute fulminant hepatic failure, severely decompensated cirrhosis, or hepatocellular carcinoma. It is usually not indicated for neurologic symptoms.

REFERENCES

1. Liu J, Luan J: Epidemiology, diagnosis, and treatment of Wilson's disease. Intractable Rare Dis Res. 2017;6(4):249-255. doi:10.5582/irdr.2017.01057. 2017, 6:249-255. 10.5582/irdr.2017.01057
2. Aggarwal A, Bhatt M: Advances in Treatment of Wilson Disease. PubMed. 2018, 8:525-2018. 10.7916/D841881D
3. Yuan XZ, Yang RM: Management Perspective of Wilson's Disease: Early Diagnosis and Individualized Therapy. NIH. 2021, 19(4):465-485.
4. ATP7B ATPase copper transporting beta. (2022). Accessed: 25 January: http://https://www.ncbi.nlm.nih.gov/gtr/genes/540/.
5. Ferenci P: Diagnosis of Wilson disease. NIH. 2017, 142:171-180.
6. Kasztelan-Szczerbinska B, Cichoz-Lach H: Wilson's Disease: An Update on the Diagnostic Workup and Management. J Clin Med. 2021, 19(21):5097-2021. 10.3390/jcm10215097
7. Altaf A, Ann P: Wilson's disease. Lancet. 2003, 369:397.
8. Stättermayer AF, Traussnigg S, Dienes HP: Hepatic steatosis in Wilson disease - role of copper and PNPLA3 mutations. J Hepatol. 2015, 63:156-163.
9. Medici V, Mirante VG: Liver transplantation for Wilson's disease: The burden of neurological and psychiatric disorders. NIH. 2005, 11(9):1056.
10. Lankarani KB, Malek-Hosseini SA: Fourteen Years of Experience of Liver Transplantation for Wilson's Disease; a Report on 107 Cases from Shiraz, Iran. NIH. 2016, 11(12):10.1371/journal.pone.0167890