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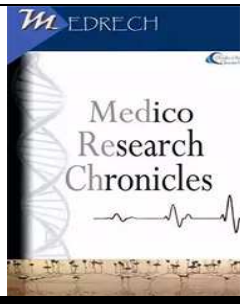

A CASE STUDY OF NEUROLOGICAL INVOLVEMENT IN WILSON'S DISEASE

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ABSTRACT

Background: Wilson's disease is a rare autosomal recessive disorder characterized by the accumulation of copper in the liver, brain, cornea and kidneys. This is a hospital-based study; there are no community-based prevalence and incidence studies of Wilson's disease in India. **Case Summary:** A33 yr. male patient presented to medicine department with complaints of slurring of speech, difficulty in walking since 15 days and abdominal distension. Using the elevated levels of ceruloplasmin, urine copper and the presence of KF rings on both eyes Wilson's disease with decompensated cirrhosis was confirmed. The patient started on zinc and antioxidants. Gradually he showed improvement in clinical signs. The patient was follow up regularly.
Conclusion: Wilson's disease is an inherited metabolic disorder. Early diagnosis and appropriate management help to prevent the systemic complications. Siblings needed to be screened to prevent manifestations. It also points out the need to suspect Wilson's disease in any young patient presented with the unexplained liver disease.

CASE STUDY

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INTRODUCTION

Wilson's disease is a rare autosomal recessive disorder of copper metabolism caused by mutation of ATP7B gene on chromosome 13 resulting in a systemic overload of copper. It is also known as hepatolenticular degeneration (hepatoliver, lenticular- brain), where the copper is deposited in brain, liver, kidney, eyes etc. The ATP7B gene encodes P-type adenosine triphosphate family of copper transporter protein (ceruloplasmin); due to the mutation in this gene in Wilson's disease synthesis of ceruloplasmin is impaired. Copper is an essential content of many metabolic enzymes. Normal estimated total body copper is 50-100mg, and average daily intake is 2-5mg.The amount of copper in the body is normal at birth. Afterwards, it increases steadily. The symptoms usually begin between the age of 5 and 45 years. Hepatic manifestations presented with acute hepatitis which may progress to

fulminant liver failure characterised by ascites, spider nevi, palmar erythema and digital clubbing. Neurological damage causes tremor, choreoathetosis, dystonia and dementia. Neurologic symptoms in Wilson disease (WD) are rare and appear at an older age compared to hepatic symptoms and manifest in patients with misdiagnosed liver disease. Neurologic symptoms in WD are caused by nervous tissue damage that is primarily a consequence of extrahepatic copper toxicity Kayser Fleisher ring is the salient feature. It is characterised by a greenish-brown discolouration of corneal margin which gradually disappears with treatment.

COPPER METABOLISM AND DEPOSITION

After absorption copper is transported to hepatocytes where it is incorporated with enzymes and copper-binding proteins (Ceruloplasmin). Excess copper forms complex with apometallothionine and the coppermetallothionine complex is excreted via bile.

In Wilson's disease incorporation of copper to ceruloplasmin and excretion of excess copper into bile are impaired. Excess copper generates free radicals resulting in oxidation of lipids and proteins. It also accumulates in liver and damages the hepatocytes. Once the liver copper level increases, it started to get a deposit in other organs. The deliverance of free copper into the blood causes hemolysis and renal tubulopathy.

Low serum ceruloplasmin is a pointer to the diagnosis. Other parameters include high free serum copper, high urine copper excretion and D- penicillamine challenge test [1]. Wilson's disease is a genetic disorder that found worldwide.

The prevalence of Wilson's disease is 1 per 30,000 individuals, and the incidence is 10-30 million cases. There is no community-based prevalence in India, but it is more common where consanguinity is prevalent.[2]

This case is a unique presentation of Wilson's disease with clear KF rings and without neurological involvement. Timely diagnosis and appropriate management helped to reduce the morbidity and mortality.

Hence it points out the need to suspect Wilson's disease in any young patient presented with the unexplained liver cirrhosis.

CASE PRESENTATION

33 yr male patient presented to medicine department with complaints of slurring of speech(dysarthria is present in 85 to 97 percent of patient with neurological Wilson disease) and difficulty in walking since 15 days (ataxia or gait abnormality in 30 to 75 percent patient). Patient having spasm of facial muscle called as risus sardonicus). patient had repeated history hospitalisation for black stool and bilateral pedal edema and abdominal distension. Had past h/o of hemetemesis 4-5 episode 1 yr back. Use abd s/o liver cirrhosis with splenomegaly. On CT abd pelvis s/o liver cirrhosis, splenomegaly, portal hypertension with multiple dilated tortuous portosystemic collaterals in splenic hilum with diameter of 23 mm. The fibroscan report is 10.1 . Sr ceruloplasmin level 7.4 mg/dl(which is low, seen in 95 percent pt). On examination KF ring was visible to naked eyes and confirmed over slit lamp examination(seen in 50 percent pt with hepatic involvement and 98 percent with neurological involvement or psychiatric presentation).On MRI s/o changes include T2 hyper-intensities in the basal ganglia, thalami and white matter, T2 hypo-intensities in the basal ganglia, and atrophy. The patient was started on oral zinc. The patient recovery was slow.

Fig. 1. Visible KF ring

Fig 2. KF ring on slit slamp.

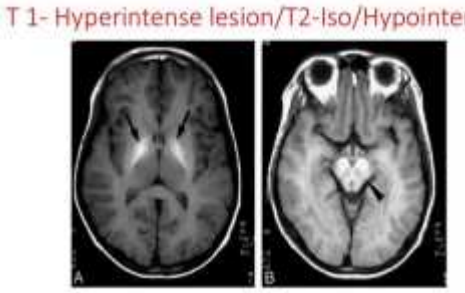

Fig 3. T1 and T2 MRI images.

Fig 4. Face of panda sign.

The initial diagnosis was made as shunt encephalopathy with liver cirrhosis and started with hepatoprotectants, N- Acetylcysteine and antioxidants. Elevated CRP (4.7mg/dl) and Procalcitonin(1.6ng/ml) indicated the presence of infection and started with IV antibiotics paracetamol was ordered for elevated body temperature. Control of oedema was achieved with spironolactone. On the third day of admission, her Sr. Ceruloplasmin level was found to be lower 7.4. On suspected of Wilson's disease a slit lamp examination of eyes was performed and revealed the presence of Kayser Fleisher ring on both eyes.

DISCUSSION

Wilson's disease is a rare autosomal recessive disorder characterised by the accumulation of copper in the liver, brain, cornea and kidneys. It may be present at any age, the majority between 5 and 35 years. It is a progressive disease and could be fatal if left untreated, but the timely diagnosis remains a challenge.[4]

Our patient had slurring of speech, difficulty in walking, abdominal , elevated LFTs which indicates the liver disease, the initial feature of Wilson's disease. It occurs when the excess copper accumulated in the lenticular region of the brain and presented with difficulty in walking, anxiety, mood swings and depression.[4,5]

Neurologic symptoms in Wilson disease (WD) are rare and appear at an older age compared to hepatic symptoms and manifest in patients with misdiagnosed liver disease. Neurologic symptoms in WD are caused by nervous tissue damage that is primarily a consequence of extrahepatic copper toxicity. Copper levels in brain tissues as well as cerebrospinal fluid (CSF) are diffusely increased by a factor of 10 and its toxicity involves various mechanisms such as mitochondrial toxicity, oxidative stress, cell membrane damage, crosslinking of DNA, and inhibition of enzymes. Excess copper is initially taken-up and buffered by astrocytes and oligodendrocytes but ultimately causes dysfunction of blood-brain-barrier and demyelination. Most severe neuropathological abnormalities, including tissue rarefaction, reactive astrogliosis, myelin pallor, and presence of iron-laden macrophages, are typically present in the putamen while other basal ganglia, thalami, and brainstem are usually less affected. The most common neurologic symptoms of WD are movement disorders including tremor, dystonia, Parkinsonism, ataxia and chorea which are associated with dysphagia, dysarthria and drooling. Patients usually manifest with various combinations of these symptoms while purely mono symptomatic presentation is rare. Neurologic symptoms are largely reversible with anti-copper treatment, but a significant number of patients are left with residual impairment. Kf ring, is visible in approximately 50 percent of patient at the time of presentation with hepatic disease. Most importantly, brain damage and neurologic symptoms can be prevented with an early initiation of anti-copper treatment.

Treatment of Wilson's disease includes copper chelators like Penicillamine and Zinc. Hepatoprotectants were used as a supportive measure, where the liver transplantation is the life saving measure of advanced Wilson's disease.[4]

CONCLUSION

Wilson's disease is an inherited metabolic disorder. It should be suspected in young patients presented with unexplained hepatic complications. Early diagnosis and appropriate management help to prevent the systemic complications. Adherence to ther-apy, low copper diet and proper follow-up shows a significant reduction in morbidity and mortality. Liver transplantation is recommended in acute liver failure. Neurological manifestation of Wilson are largely reversible if diagnosed and treated with anti-copper earlier. but most patients have at least minor residual neuropsychiatric

impairment and approximately 20% of patients have unfavourable outcome with severe disability or death. The prognosis of WD is much better when treatment is started before neurologic symptoms develop.

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