Hepatolenticular Degeneration – Is the Term too Narrow to Explain Wilson’s Disease?

Jalees Fatima*, Ritu Karoli**, Zeba Siddiqui***, Ashok Chandra*, Vineet Jain#

Abstract

Wilson’s disease is known for its protean manifestations due to abnormal copper metabolism. Although liver, brain and eyes are the well established sites for the latter but it can be speculated for other organs too. We report a case of Wilson’s disease with tricuspid regurgitation possibly due to abnormal deposition of copper in heart.

Introduction

Wilson’s disease is a rare inherited autosomal recessive disorder of copper metabolism.¹ The prevalence is 1 in 30,000 to 40,000 of the general population. Caused by mutations in ATP7B gene, a membrane bound copper transporting ATPase. Inadequate functioning of the ATPase enzyme in some way reduces excretion of copper in bile. The clinical manifestations are caused by copper toxicity and primarily involve the liver and brain. We are reporting a case of Wilsons disease who had tricuspid regurgitation alongwith classical features of the disease.

Case Report

16 year old boy with past history of self limiting jaundice 1 year back presented with abnormal dystonic movements and rigid posturing of limbs for 2 months and recent onset exertional dyspnoea. A history of impulsive behaviour and temper tantrums was present. He had sialorrhoea, dysarthria, dysphagia and perioral dystonias. His face gave a grinning appearance or a ‘vacuous smile’ (Figure 1). Upper limbs were outstretched and had a coarse wing beating’ movement. Icterus was absent and Kayser- Fleischer rings were present around the cornea which was confirmed by slit lamp examination (Figure 2). Bilateral mild pedal oedema was evident. Neurological

Fig. 1 : Showing typical orofacial dystonia and carpopedal spasm

*Professor, †Assistant professor, ‡Junior Resident, Department of Medicine, Era’s Lucknow Medical College, Sarfarazganj, Hardoi Road, Lucknow – 226003, Uttar Pradesh
Received: 29.05.2012; Revised: 30.07.2013; Accepted: 01.08.2013

© JAPI • JUNE 2014 • VOL. 62

© JAPI • JUNE 2014 • VOL. 62
examination revealed decreased nutrition, normal power and extrapyramidal features like lead pipe rigidity, bradykinesia and tremors. Cardiovascular examination revealed cardiomegaly and a pansystolic murmur in lower left parasternal area. A clinical diagnosis of Wilson’s disease was made and was later substantiated by the following investigations: serum ceruloplasmin – 10 mg/dl (Normal 18-35), serum copper – 7 mM/l (Normal 11-24 mM/l), urinary copper was 180 µg/24 hrs (Normal 20-50). Liver biopsy showed venous congestion and hepatocytes with PAS positive intranuclear clear vacuoles and fragments of portal tracts showing lymphocytic infiltrate and fibrosis. Copper staining of biopsy specimen or quantitative assay of hepatic copper could not be done. There was no evidence of cirrhosis and liver function tests were normal with minimal elevation of transaminases. MRI brain showed bilateral signal alterations, T2/FLAIR hyperintensities (Figure 3) in lentiform nucleus, thalamus and brainstem (midbrain and pons) with cerebellar atrophy. His 2D echocardiogram showed presence of significant Tricuspid regurgitation (Figure 4).

Patient was managed with D-Penicillamine in escalating doses and zinc orally.

Discussion

Wilson’s disease in itself is a rare disease of copper metabolism. The mutation in copper binding ATPase leads to two fundamental defects in copper metabolism – A reduced rate of incorporation of copper into ceruloplasmin and reduction in biliary excretion of copper. Defective copper transporting mechanisms lead to its abnormal deposition in various organs and virtually all manifestations of the disease – cirrhosis, haemolytic anaemia, renal tubular changes, Kayser Fleischer rings and the cerebral damage.

The disease presents itself usually in second decade of life. In childhood the liver disorder often takes the form of attacks of jaundice, unexplained hepatosplenomegaly, thrombocytopenia and bleeding. Rarely there is clear evidence of cirrhosis alone. Hepatic abnormalities may be asymptomatic. The first neurological manifestations are most often extrapyramidal with proclivity to affect oropharyngeal musculature.

Our patient presented with the classic syndrome of dysphagia and drooling, rigidity and slowness of movements, grinning appearance and the mouth constantly agape. In addition he also had features of right heart failure and during screening he was found to have tricuspid regurgitation which has not been reported earlier.

It has been established that copper deposition in the liver is the initial disturbance and the hepatic stage...
of the disease precedes neurological involvement. In our case however, the hepatic involvement was in the pre-cirrhotic stage.

Ideally treatment in Wilson’s disease should start before the appearance of neurological signs. D-penicillamine was previously the primary anticopper agent but now plays a minor role due to its toxicity and because it often worsens existing neurological disease. It should always be accompanied by pyridoxine 25 mg/day. Triethylene tetramine (trientine) is a less toxic chelator. Zinc which blocks the intestinal absorption of copper is also a suitable option.

An important aspect of treatment is the screening of relatives for abnormalities of copper and ceruloplasmin. All presymptomatic patients should be treated prophylactically and penicillamine treatment should be given lifelong as the disease is nearly 100% penetrant. All symptomatic patients should also be treated lifelong. With treatment, liver function usually recovers after about a year with some residual dysfunction. Neurological improvement usually improves after 6 to 24 months. It is therefore highly essential to maintain compliance despite this latency in clinical response.

Cardiovascular abnormalities are very rare in Wilson’s disease and Kuan first reported four modes of cardiac involvement: arrhythmia, cardiomyopathy, cardiac death and autonomic dysfunction. Meenakshi S et al have analysed ECG findings in 50 patients of Wilson’s disease and concluded that ECG abnormalities are not uncommon in these patients and presumably depict an underlying cardiomyopathy. Hlubocka Z et al in a series of 42 patients with Wilson’s disease had concluded after detailed cardiac evaluation that cardiac involvement in these patients was mild, with presence of left ventricle remodelling and arrhythmia. Isolated tricuspid regurgitation has yet not been reported to best of our knowledge. In our case it may be due to abnormal copper deposition.

Tricuspid regurgitation may also have been an unrelated finding in this case - this possibility cannot be completely ruled out.

**Conclusion**

Wilson’s disease is known for its protean manifestations due to abnormal copper metabolism. It is possible that this metabolic disorder affects other organs less well recognised. The presence of cardiac involvement in patients with Wilson’s disease states a need for search of specific organ-oriented therapy as add on in the management of these patients because it can cause serious consequences and even sudden death.

**References**