Int J Pharm Bio Sci 2016 July ; 7(3): (B) 205-209

Original Research Article Pathology

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

ORIGINAL RESEARCH: IMAGING FEATURES IN A CASE OF WILSON'S DISEASE WITH DELAYED CLINICAL PRESENTATION

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ABSTRACT

The aim of this article is to review and describe the ultrasound (US) and magnetic resonance imaging (MRI) features in Wilson's disease with a note on importance of early detection and treatment. Wilson's disease is an autosomal recessive disease which affects copper transport thereby resulting in copper accumulation in organs like brain, liver, cornea etc. Although prevalence of Wilson's disease is low, it is very important to promptly identify, diagnose and treat it as it is a treatable cause of liver disease. A 10 year old developmentally normal child presented with complaints similar to Wilson's disease. The clinical suspicion of Wilson's disease was confirmed by the presence of the elevated value of 24 hour urinary copper after D-penicillamine challenge test and with the help of imaging features. This patient also had hypersplenism.

KEYWORDS: Wilson's, Hypersplenism, Delayed Presentation, Coarse spleen

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INTRODUCTION

Wilson's disease is an autosomal recessive disease which affects copper transport thereby resulting in copper accumulation in organs like brain, liver, cornea etc [1,2]. Although prevalence of Wilson's disease is low, it is very important to promptly identify, diagnose and treat it, as it is a treatable cause of liver disease[3]. Progressive deterioration of the performance of an otherwise normal child should raise the suspicion of the Wilsons. The neurologic symptoms which occur in Wilson's disease is considered to be the result of accumulation of copper in brain resulting in destruction of nerve cells. The diagnosis is made considering the clinical symptoms, signs .serum ceruloplasmin levels, elevated copper level in urine and liver biopsy.

CASE REPORT

This is a case of 10 years old developmentally normal male child, resident of Andaman, second born of consanguineous marriage who presented with complaints of deterioration in school performance, difficulty in speech and progressive stiffness of upper and lower limbs. The patient also had a history of abdominal pain and bilious vomiting. There were no remarkable family history and no significant past history. On clinical examination, pallor, splenomegaly, dystonia and dysarthria was present. Ophthalmological examination revealed KF ring. With these clinical findings, the possibility of Wilson's disease was considered. Blood investigations also revealed pancytopenia (HB-9.1 g/dl, Total count-2000 cells/cu.mm, platelets-0.45 lakh per cu/mm) and deranged PT, PTT, INR. Liver and renal function tests showed normal values. These laboratory values along with splenomegaly favoured the diagnosis of hypersplenism. Ultrasound of the abdomen done showed coarse echotexture of liver and enlarged spleen with heterogenous echotexture (Figure.1).

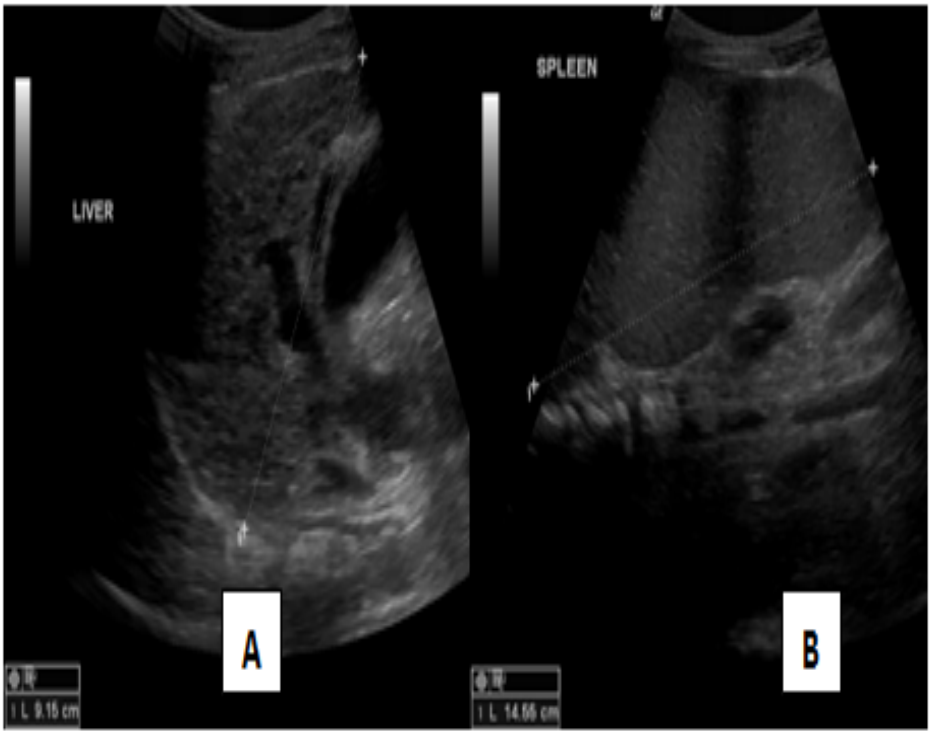

Figure 1
Coarse echotexture of liver (A) and enlarged spleen (B) with heterogenous echotexture

MRI was performed with the following sequences: Axial T1,Axial T2 and T2 FLAIR, TSE T1 sagittal FLAIR ,axial GRE and diffusion-weighted images with b-values of 1000 s/sq mm.MRI brain was done which showed bilateral symmetrical T1 and T2 hyperintensity in basal ganglia (involving putamen, globus pallidus, caudate nucleus**).** Basal ganglia hyperintensity was seen in T2 FLAIR sequence also (Figure 2). Sparing of white matter was seen. On diffusion weighted imaging, there was mild hyperintensity seen in bilateral basal ganglia (Figure 3) ,but the hyperintensities in the ADC map indicated that it is not true restricted diffusion. On gradient echo images, there were some subtle hypointensities which could represent metal deposition (Figure 4).

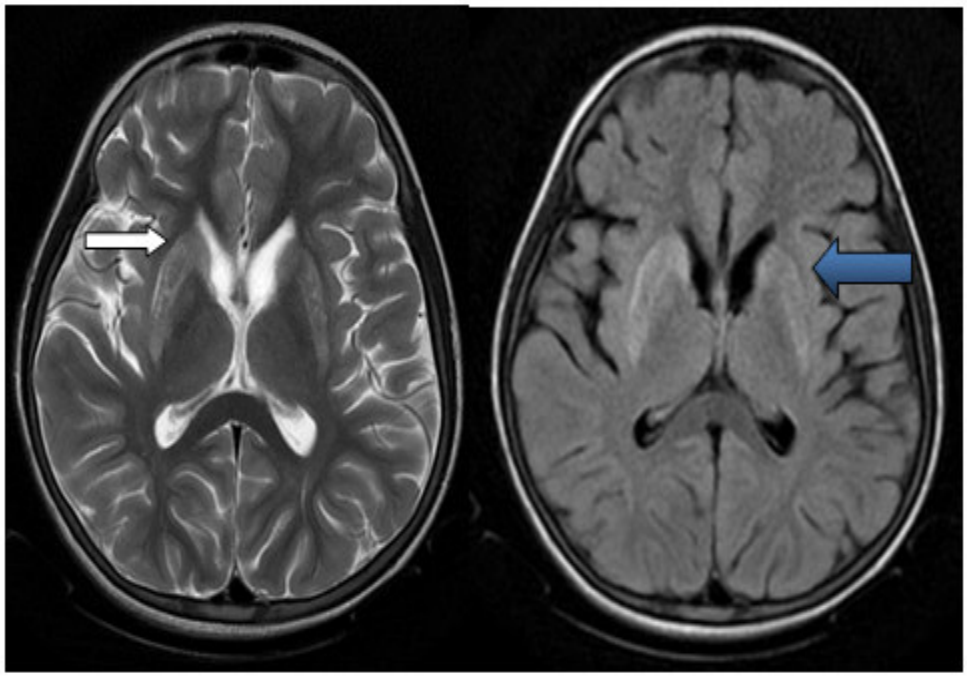

Figure 2
T2 (thin arrow) and T2 FLAIR axial section showing T2 hyperintensity (thick blue arrow) involving basal ganglia

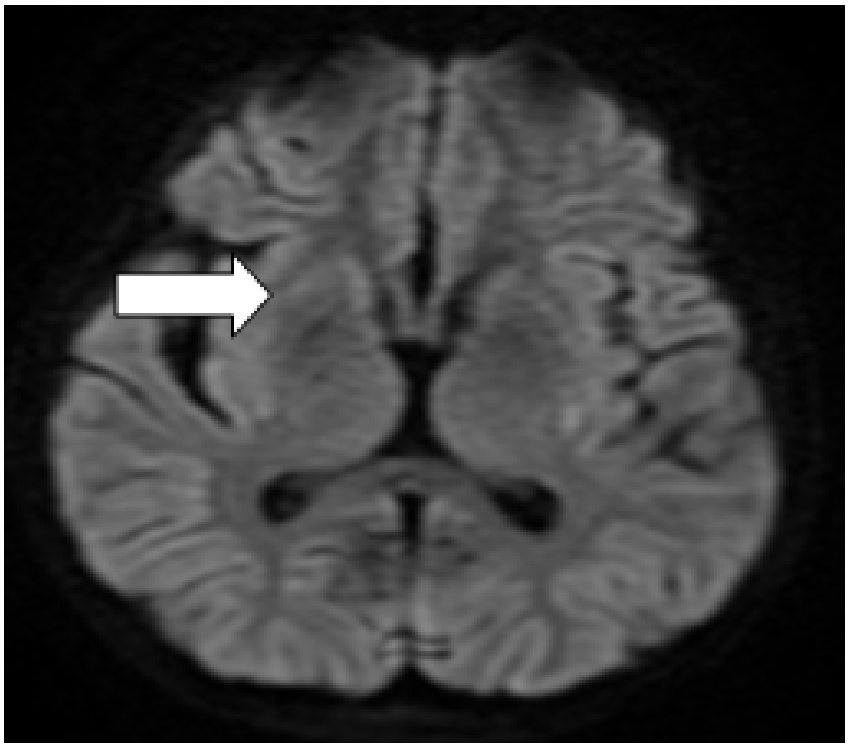

Figure 3
DWI image showing mild hyperintensity in basal ganglia (thick arrow)

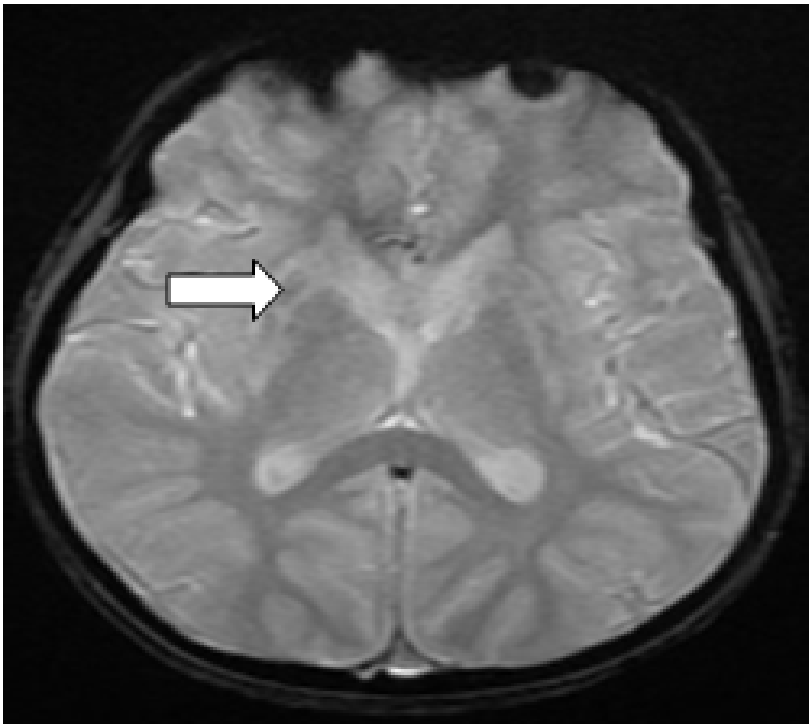

Figure 4
Gradient sequence axial image (GRE sequence).
Mild hypointensity in basal ganglia suggesting metal deposition

With above mentioned imaging features and clinical findings, a diagnosis of Wilson's disease was made. This was further confirmed by the presence of elevated value of 24 hour urinary copper after D- penicillamine challenge test which was found to be elevated (1232.51 mcg/dl). Patient was started on Zinc and trihexiphenidyl as the patient was not able to afford the high cost of Trientine. In view of hypersplenism, hematologist's opinion was taken.Since splenectomy was contraindicated due to complications which can develop later, patient had been planned for partial splenic artery embolization .

DISCUSSION

Wilson's disease is an autosomal recessive disease which affects copper transport thereby resulting in copper accumulation in organs like brain,liver,cornea[1,2].Although prevalence of Wilson's disease is low, it is very important to promptly identify, diagnose and treat it as it is a treatable cause of liver disease[3]. It occurs due to defect in copper metabolism[4] .The mutation in ATPB7 gene which is responsible for encoding membrane bound copper transporting ATP ase[3] which leads to impaired biliary excretion and copper getting accumulated in liver and other tissues[5,6] which further results in hepatic and neurological symptoms. Neurological symptoms described are assumed to be due to the copper accumulation in brain resulting in destruction of nerve cells [7,8]. Wilson's disease is named after Dr Samuel Alexander Kinnier Wilson, who first described the condition in 1912. Age at presentation ranges from 5-50 years, although peak age of presentation is 8-16 years[9] Till date, no single laboratory test is established in order to make a diagnosis of Wilson's disease. A combination of laboratory tests like low serum ceruloplasmin (<20 md/dl), high copper content in liver (>250microgram/gram of dry liver),24 hour urine copper level>100 gram and clinical findings like KF ring with supporting imaging evidence is helpful in making an accurate diagnosis. In our case, Wilson's disease was confirmed by the presence of high 24 hour urine copper level, KF ring and with the imaging features in abdominal ultrasound and MRI of the brain.

Various imaging modalities can be used but most beneficial and easily available imaging in evaluating a patient for Wilson's disease include ultrasound abdomen, Computed tomography and Magnetic resonance imaging of brain. At any stage of Wilson's disease, patient can present with signs of liver damage, jaundice or ascites. In our case, patient presented late with involvement of liver and spleen i.e, with sonographic findings like coarse echotexture of liver and the spleen with splenomegaly and features of hypersplenism. Ultrasound of the liver may show irregular contour with increased echogenicity and presence of variable echogenicity nodules (both hypoechoic and hyperechoic) which may be few or multiple[10]. Hypersplenism has been described both in patients with cirrhosis and in patients with Wilson's disease[11]. MRI brain is useful in diagnosis as well as in assessment of treatment response. Typical imaging findings described in literature are signal changes involving basal ganglia (globus pallidus, putamen,

thalamus, caudate nucleus and sub thalamus),midbrain (substantia nigra, red nuclei, tegmentum, inferior tectum and crura),pons (dorsal as well as ventral),cerebellum (superior, dentate nuclei and middle peduncles), cerebral white matter (mostly frontal lobe) , cerebral cortex[12,13]. The most widely described finding is T2 hyperintensity in basal ganglia although in later stages brain atrophy also can be seen[14,15].In our case, there was no cortical, cerebellar or brainstem involvement was seen. It has been stated in studies that T1 hyperintensity in globus pallidus, putamen and mesencephalon is seen when there is predominant hepatic involvement and T2 hyperintesity in above mentioned areas are seen in cerebral involvement[16].In our case, T1 and T2 hyperintensities were noted in basal ganglia. This can be explained by the late presentation of the patient. Another characteristic sign described in wilson's disease in MRI brain is face of giant panda sign which occurs as a result of high signal intensity in tegmentum normal signal intensity in red nuclei representing eye of panda, normal signal intensity in lateral portion of pars reticulata of substantia nigra mimicking ear of panda and hypointensity in superior colliculus appearing like chin of panda [17].

CONCLUSION

Suspected patients with Wilson's disease need to be evaluated completely clinically, with imaging and laboratory investigations as necessary to prevent morbidity due to neurologic complications and also to prevent late irreversible complications like cirrhosis as in our case by the early initiation of the treatment.

REFERENCES

1. Fatemi N, Sarkar B.Structural and functional insights of wilson disease copper - transporting ATPase.J Bioenerg Biomembr 2002;34:339-49
2. Vasanthan.M.,Kalaiselvi.V.S. A case of neurogenic form of wilson's disease – a rare disorder incopper transport.Int J Pharm Bio Sci 2013 Oct; 4(4): (B) 1377 - 1379
3. Young-Hye Cho, Dong-Wook Jeong, Sang-Yeoup Lee, Son-Ki Park, Ki-Tae Yoon,Yun-Jin Kim et al A Case of Wilson's Disease in Patient with Mildly Elevated Liver Enzymes. Korean J Fam Med. 2011 Mar; 32(3): 205–208.
4. Van Wassenaer-van Hall HN, Van den Heuvel AG, Algra A, Hoogenraad TU, Mali WPTM. Wilson disease: findings at MR imaging and CT of the brain with clinical correlation. Radiology1996; 198:531 –536
5. Mathangi Jayaraman, Sudarshana N, Vidya Natarajan, Umashankar Vetrivel, Sulochana. K.N. Elucidation Of Structure - Function Relationship In Families Of Copper Binding Proteins In Homo Sapiens -A Bioinformatics Approach.Int J Pharm Bio Sci 2012 July; 3(3): (B) 647 - 662
6. Petrukhin K, Fischer SG, Piratsu M, et al. Mapping,cloning and genetic characterization of the region containing the Wilson disease gene. Nat Genet 1993;5:338–343
7. Nazer H, Brismar J, al-Kawi MZ, et al. Magnetic resonance imaging of the brain in Wilson disease. Neuroradiology 1993;35:130–33
8. Thöumas KA, Aquilonius SM, Bergstrom K, et al. Magnetic resonance imaging of the brain in Wilson disease. Neuroradiology 1993;35:134–41
9. Walshe JM. Wilson's disease. In: Vinken PJ, Bruyn GW, Klawans HL, eds. Handbook of Clinical Neurology, vol.49. Amsterdam: Elsevier Science Publishers; 1986. p. 223-238
10. Okan Akhan,, Erhan Akpinar, Aytekin Oto, Mert Kö roglu, Mustafa N. Özmen, Deniz Akata ,Bijan Bijan ;Unusual imaging findings in Wilson's disease Hepatobiliary–Pancreas; European Radiology 2002 December, 12 (3), S66-S69
11. G.Thomas Strickland, N-K. Chang and William M. Beckner; Hypersplenism in Wilson's disease; Gut. 1972 Mar; 13(3): 220–224.
12. A D King, J M Walshe, B E Kendall, R J Chinn, M N Paley, I D Wilkinson, S Halligan and M A Hall-Craggs.Cranial MR imaging in Wilson's disease. American Journal of Roentgenology. 1996; 167: 1579-1584.
13. Saatci I, Topcu M, Baltaoglu FF, et al. Cranial MR findings in Wilson disease. Acta Radiol 1997;38:250–58
14. Das SK, Ray K. Wilson's disease: an update. Nat Clin Pract Neurol 2006;2:482–493
15. Sinha S, Taly AB, Ravishankar S, et al. Wilson's disease:cranial MRI observations and clinical correlation. Neuroradiology 2006;48:613–621
16. Kim TJ, Kim IO, Kim WS, Cheon JE, Moon SG, Kwon JW, et al. MR imaging of the brain in Wilson disease of childhood: Findings before and after treatment with clinical correlation. AJNR Am J Neuroradiol. 2006;27:1373–1378
17. Hitoshi S, Iwata M, Yoshikawa K. Midbrain pathology of Wilson's disease: MRI analysis of three cases. J Neurol Neurosurg Psychiatry. 1991;54:624–6.