

Brain MRI Abnormalities in Children with Wilson's Disease: Is it Indicator for Liver Transplantation?

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Abstract

Background: Wilson's Disease (WD) is an autosomal recessive disorder of copper metabolism with a prevalence of about 1 in 30000 people. It's more common with parental consanguinity. The adenosine triphosphate 7B (ATP7B) gene, coding the copper transporting P-type ATPase has been reported to have 380 variants. Copper leads to tissue damage by accumulating in many organs including mainly the liver and brain. Neurological manifestations of WD are ascribed to abnormal deposition of copper in brain tissues, especially deep gray matter (basal ganglia and thalamus) and subcortical white matter. Wilson's disease can present clinically by liver disease, neurological disorder or psychiatric illness. In childhood, hepatic manifestations predominate with a highly variable spectrum ranging from self-limiting hepatitis to fulminant hepatic failure.

Aim of Study: The aim of this study was to detect brain changes by magnetic resonance imaging in children with Wilson's disease and their correlation with clinical and biochemical findings.

Patients and Methods: This study included 70 patients. 35 patients with WD and 35 patients with other Chronic Liver Disease (CLD) as control. WD group involved 20 males and 15 females. Their mean age was (12.73 ± 2.86) year. Control group included 35 patients with CLD (20 with Autoimmune Hepatitis (AIH), two with sclerosing cholangitis and 13 with chronic HCV).

Results: Among WD group, we reported 15 patients (42.8%) had abnormal MRI. T1 weighted images showed bilateral symmetrical hyperintensity signal of globus pallidus in two patients (5.7%), hypointensity signal of left globus pallidus in one patient (2.8%) and bilateral symmetrical hyperintensity in thalami in one patient (2.8%). T2 and FLAIR hyperintensity signals mainly involving basal ganglia were present in 11 patients (31.4%). Ventricular system was affected in two patients (5.7%), it was prominent in one patient and the other patient had hydrocephalus. Patients were followed-up over a period of 6-18 months and we reported that three WD patients (20%) from those who had abnormal MRI dete-

riorated rapidly and were candidates for LT, while none of other patients needed LT.

Conclusions: Bilateral symmetrical hyperintense signals in T2 weighted and FLAIR images mainly involving basal ganglia are specific for WD and represent CNS involvement of WD. Abnormal MRI may be a bad prognostic factor as 20% from abnormal MRI WD subgroup deteriorated rapidly and were candidates for LT.

Key Words: Wilson's disease – Chronic liver disease – Autoimmune hepatitis – Alanine transaminase – Aspartate transaminase – MRI – LT – HCV.

Introduction

WILSON'S Disease (WD) is an autosomal recessive disorder of copper transport characterized by reduced copper incorporation into ceruloplasmin and by impaired biliary excretion of copper. This results in progressive copper accumulation in the liver and subsequently in the brain, cornea and other tissues with resultant damage [1]. The pivotal point to achieve the best outcome relies on a timely and accurate diagnosis. This is associated with healthy life-span in patients who are adherent to an effective medical regimen [2]. Scoring system entails a diagnostic approach, in which a variety of clinical and biochemical tests are included. Commonly used biochemical tests are serum ceruloplasmin concentration, 24-hour urinary copper

Abbreviations:

WD : Wilson's Disease.
CLD : Chronic Liver Disease.
AIH : Autoimmune Hepatitis.
ALT : Alanine Transaminase.
AST : Aspartate Transaminase.
MRI : Magnetic Resonant Imaging.
PT : Prothrombin Time.
LT : Liver Transplantation.
KF : Kayser Fleischer ring.

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excretion and hepatic copper quantitation [3]. Neurologic symptoms of WD typically occur between the ages 20-40 years, however the range is very large. The youngest WD patient with neurologic symptoms was aged 6 and the oldest 72 years. The most common neurologic symptoms of WD are movement disorders including tremor, dystonia, parkinsonism and ataxia, which are frequently associated with dysphagia, dysarthria and drooling [4]. Current treatment options for WD, based on drugs leading to negative copper body balance like chelators or Zinc salts, were introduced more than 40 years ago and are generally effective in the majority of WD cases if used lifelong. However, especially in neurological patients, treatment may lead to neurological deterioration, which is often irreversible. Further, almost 50% of neurologically affected WD patients present with persistent neurological deficits despite the use of anti-copper treatment [5].

Magnetic resonance imaging is a sensitive method to evaluate the brains of patients with WD. Copper, unlike iron, manganese, or calcium is not directly visualized by any of the current imaging technologies but MRI of the brain shows tissue injury, edema, gliosis, or cavitation caused by excessive copper deposition [6]. Neurologic involvement of WD can progress rapidly to a severe debilitating condition [7]. However, there is still paucity of data about brain changes in WD in pediatric age.

Patients and Methods

This study included 70 patients recruited from Pediatric Hepatology, Gastroenterology and Nutrition Department, National Liver Institute, Menoufia University from Jan. 2017 – Dec. 2020, 35 patients with WD and 35 patients with other CLD as control. Then WD group was subdivided in two groups: Normal MRI group and abnormal MRI group. WD group involved 20 males and 15 females. Their mean age was (12.73 ± 2.86) years. Control group included 35 patients with other CLD (20 with Autoimmune Hepatitis (AIH), two with sclerosing cholangitis and 13 with chronic HCV. They were 16 males and 19 females. Their mean age was (12.74 ± 3.12) years.

Inclusion criteria for WD patients:

Initial diagnosis of WD was made if the patient had hepatic and/or neurologic disease in addition to at least two of the following six criteria:

- 1- Positive family history of WD.
- 2- Low ceruloplasmin level ($<20\text{mg}\%$).

3- Presence of Kayser Filusher (KF) ring.

4- Liver biopsy suggestive of WD (positive staining of copper associated protein (rhodanine or orcein stain), presence of glycogenated nuclei, micro- or macrovesicular steatosis, or ultra-structural changes defined by electron microscopy) as measurement of hepatic copper content is not available in Egypt.

5- Elevated baseline 24-hours urinary copper excretion (more than $100 \mu\text{g}/24$ hours or more than $1600 \mu\text{g}/24$ hours after D-Penicillamine challenge test).

6- Coomb's negative hemolytic anemia [8].

All patients were subjected to the following: Full history taking, thorough clinical examination and the following investigations: Liver function tests, PT & INR, kidney function tests, complete blood count, serum ceruloplasmin, 24 hours urinary copper, abdominal US, liver biopsy (when possible) and brain MRI. Data at time of diagnosis of previously diagnosed cases were collected from patients' files. At time of MRI, liver function tests and 24 hours urinary copper were repeated.

Magnetic resonance images were obtained on a GE Optima MRI scanner with a super-conducting magnet of 1.5T field strength after receiving informed consent from subjects. Spin Echo (SE) T1 weighted (TR 210ms, TE 13ms) images in axial planes were taken, with an acquisition time of 46.8 second, matrix of 256 X 256 pixels and a 230mm field of view. Axial and coronal images of T2 weighted images were acquired (TR 3300ms, TE 99ms). FLAIR sequences were obtained in the axial plane (TR 9000ms, TE 119ms). The slice thickness was 5mm. MRI observations were interpreted by an expert radiology consultant.

A signed informed consent was obtained from the parents of all patients before enrollment in this study. The study was approved by the Research Ethics Committee of National Liver Institute.

Statistical methods:

Data were analyzed using the SPSS (Statistical Package for Social Science) program version 21, SPSS Inc., Chicago, Illinois, USA. Qualitative data were expressed as frequency and percentage. Quantitative data were shown as mean \pm Standard Deviation (SD).

Results

In WD group the age of presentation was (10.03 ± 3.02) years. Also in the same group, 51.4% were

presented by picture of CLD, 22.8% presented by acute hepatitis and 3% with neurologic presentation, while 22.8% were diagnosed during family screening of siblings of patients(presymptomatic). Dysarthria and abnormal gait were the most common neurological symptoms in WD patients.

When we compared disease severity at time of MRI between WD group and CLD group using Child Pugh score, there was no significant statistical difference between the two groups ($p>0.05$). We reported that MRI abnormality was significantly statistically higher in WD group than CLD group ($p=0.003$).

Within CLD group, 8.5% of patients had abnormal MRI. MRI abnormality was in the form of T1 hyperintensity in the globuspallidus and anterior midbrain.

Among WD group, we reported 15 patients (42.8%) had abnormal MRI. T1 weighted images showed bilateral symmetrical hyperintensity signal of globuspallidus in two patients (5.7%), hypointensity signal of left globuspallidus in one patient (2.8%) and bilateral symmetrical hyperintensity in thalami in one patient (2.8%). T2 and FLAIR hyperintensity signals mainly involving basal ganglia were present in 11 patients (31.4%). Ventricular system was affected in two patients (5.7%), it was prominent in one patient and the other patient had hydrocephalus.

We reported that globuspallidus was the most common affected site in T1 weighted images in WD group. T2 bilateral basal ganglionic lesions were the commonest changes. Among basal ganglia nuclei, caudate nucleus was the most affected in T2 weighted images followed by lentiform nucleus then putamen. Lesions in FLAIR images were similar to T2 weighted images. We reported periaqueductal hyperintensity in T2 & FLAIR images in only one case (6.6%).

We reported that MRI brain lesions were bilateral and symmetrical in all patients except in one patient who had signal abnormality affecting only left globuspallidus. Bilateral symmetrical hyperintensity of caudate nucleus in T2 weighted & FLAIR images was the commonest lesion in patients who had dysarthria and abnormal gait. Brain MRI of the patient who had dystonia showed bilateral symmetrical hyperintensity of caudate nucleus and putamen in T2 & FLAIR.

It is still not clear when brain involvement in WD becomes symptomatic. We reported that 60% of WD patients, who had abnormal MRI, were

neurologically free at time of MRI. Searching for risk factors of brain involvement in children with WD, we compared between normal MRI and abnormal MRI WD subgroups as regard type of presentation, liver function tests, 24 hours urinary copper at time of MRI, duration of illness and Child Pugh score at time of MRI and we found that, there was no significant statistical difference between the two groups as regard liver function ($p<0.05$) except AST/ALT ratio which was significantly statistically higher in abnormal MRI WD subgroup than normal MRI subgroup ($p<0.05$).

We reported that all presymptomatic patients had normal MRI. Patients were followed-up over a period of six months to one year and half and we reported that three WD patients (20%) from those who had abnormal MRI deteriorated rapidly and were candidates for LT, while none of other patients needed LT.

Table (1): Comparison between WD group and CLD group as regard T1 weighted images findings.

T1	WD n=35 n (%)	CLD n=35 n (%)	p- value
<i>Caudate nucleus:</i>			
• Normal	35 (100%)	35 (100%)	
<i>Putamen:</i>			
• Normal	35 (100%)	35 (100%)	
<i>Globus pallidus:</i>			
• Normal	32 (91.43%)	32 (91.43%)	
• Bilateral symmetrical hyperintensity	2 (5.71%)	3 (8.57%)	1.000
• Hypointensity of left glopuspallidus	1 (2.86%)	0 (0.00%)	
<i>Lentiform nucleus:</i>			
• Normal	35 (100%)	35 (100%)	
<i>Anterior midbrain:</i>			
• Normal	35 (100%)	33 (94.29%)	0.473
• Hyperintense	0 (0.00%)	2 (5.71%)	
<i>Thalami:</i>			
• Normal	34 (97.14%)	35 (100%)	1.000
• Bilateral symmetrical hyperintensity	1 (2.86%)	0 (0.00%)	
<i>Periaqueductal region:</i>			
• Normal	35 (100%)	35 (100%)	
<i>Posterior high parietal region:</i>			
• Normal	35 (100%)	35 (100%)	
<i>Ventricular system:</i>			
• Normal	33 (94.29%)	35 (100%)	
• Prominent	1 (2.86%)	0 (0.00%)	
• Hydrocephalus	1 (2.86%)	0 (0.00%)	0.500
Total affected patients	5 (14.29%)	3 (8.57%)	0.452

Table (1): This table shows that there was no significant statistical difference between the two groups as regard T1 weighted images findings ($p>0.05$).

Table (2): Comparison between WD group & CLD group as regard T2 weighted images findings.

T2	Groups	WD n=35 n (%)	CLD n=35 n (%)	p-value
<i>Caudate nucleus:</i>				
• Normal		27 (77.14%)	35 (100%)	0.009*
• Bilateral symmetrical hyperintensity		8 (22.86%)	0 (0.00%)	
<i>Putamen:</i>				
• Normal		31 (88.57%)	35 (100%)	0.122
• Bilateral symmetrical hyperintensity		4 (11.43%)	0 (0.00%)	
<i>Globus pallidus:</i>				
• Normal		33 (94.29%)	35 (100%)	0.500
• Bilateral symmetrical hyperintensity		1 (2.86%)	0 (0.00%)	
• Hyperintensity of left globuspallidus		1 (2.86%)	0 (0.00%)	
<i>Lentiform nucleus:</i>				
• Normal		30 (85.71%)	35 (100%)	0.063
• Bilateral symmetrical hyperintensity		5 (14.29%)	0 (0.00%)	
<i>Anterior midbrain:</i>				
• Normal		35 (100%)	35 (100%)	
<i>Thalami:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Bilateral symmetrical hyperintensity		1 (2.86%)	0 (0.00%)	
<i>Periaquiductal region:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Hyperintense		1 (2.86%)	0 (0.00%)	
<i>Posterior high parietal region:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Bilateral symmetrical hyperintensity		1 (2.86%)	0 (0.00%)	
<i>Ventricular System:</i>				
• Normal		33 (94.29%)	35 (100%)	0.500
• Prominent		1 (2.86%)	0 (0.00%)	
• Hydrocephalus		1 (2.86%)	0 (0.00%)	
Total affected patients		15 (42.86%)	0 (0.00%)	<0.001*

Table (2): This table shows that abnormalities in T2 weighted images were significantly higher in WD group than CLD group ($p<0.001$).

Table (3): Comparison between WD group & CLD group as regard FLAIR images findings.

FLAIR	Groups	WD n=35 n (%)	CLD n=35 n (%)	p-value
<i>Caudate nucleus:</i>				
• Normal		27 (77.14%)	35 (100%)	0.009*
• Bilateral symmetrical hyperintensity		8 (22.86%)	0 (0.00%)	
<i>Putamen:</i>				
• Normal		31 (88.57%)	35 (100%)	0.122
• Bilateral symmetrical hyperintensity		4 (11.43%)	0 (0.00%)	
<i>Glopuspallidus:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Bilateral symmetrical hyperintensity		1 (2.86%)	0 (0.00%)	
<i>Lentiform nucleus:</i>				
• Normal		30 (85.71%)	35 (100.0%)	0.063
• Bilateral symmetrical hyperintensity		5 (14.29%)	0 (0.00%)	
<i>Anterior midbrain:</i>				
• Normal		35 (100%)	35 (100%)	
<i>Thalami:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Bilateral symmetrical hyperintensity		1 (2.86%)	0 (0.00%)	
<i>Periaquiductal region:</i>				
• Normal		34 (97.14%)	35 (100%)	1.000
• Hyperintense		1 (2.86%)	0 (0.00%)	
<i>Posterior high parietal region:</i>				
• Normal		35 (100%)	35 (100%)	
<i>Ventricular system:</i>				
• Normal		33 (94.29%)	35 (100%)	
• Prominent		1 (2.86%)	0 (0.00%)	
• Hydrocephalus		1 (2.86%)	0 (0.00%)	0.500
Total affected patients		14 (40%)	0 (0.00%)	<0.001*

Table (3): This table shows that abnormalities in FLAIR images were significantly higher in WD group than CLD group ($p<0.001$).

Table (4): Relation of MRI abnormality to the presence of neurological signs in WD subgroups.

Neurological signs	Abnormal MRI group n=15 n %	Normal MRI group n=20 n %
Positive	6 (40%)	0 (0.00%)
Negative	9 (60%)	20 (100%)

Table (4): This table shows that 60% of WD patients with abnormal MRI were neurologically free at time of MRI.

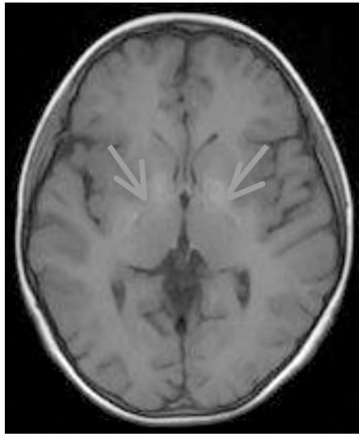


Fig. (1A): T1.

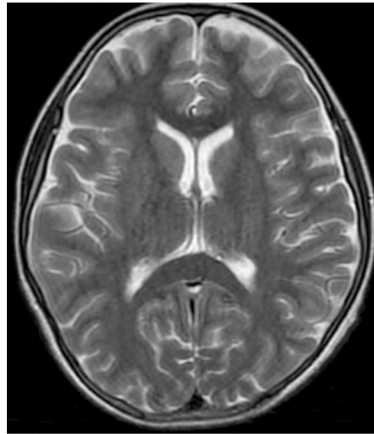


Fig. (1B): T2.

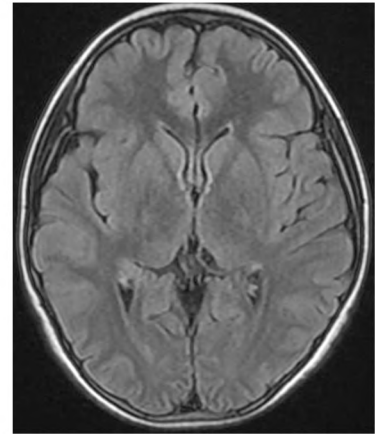


Fig. (1C): FLAIR.

Fig. (1): (A,B,C): Show axial views of brain MRI (without contrast) of a 14 years old male with AIH with bilateral symmetrical hyperintensity signals of globus pallidus in T1 weighted images (1A) (arrows) and normal T2 weighted & FLAIR images (B,C).

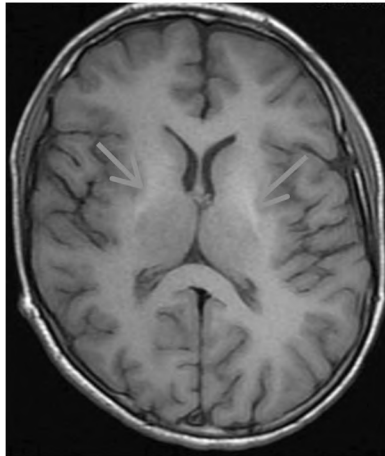


Fig. (2A): T1.

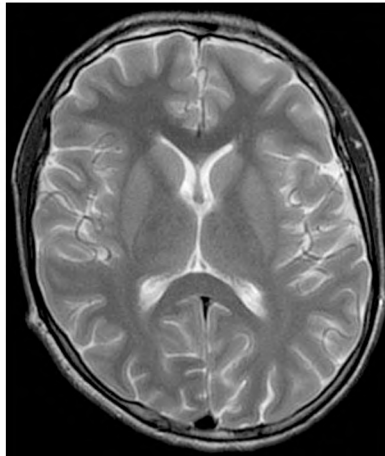


Fig. (2B): T2.

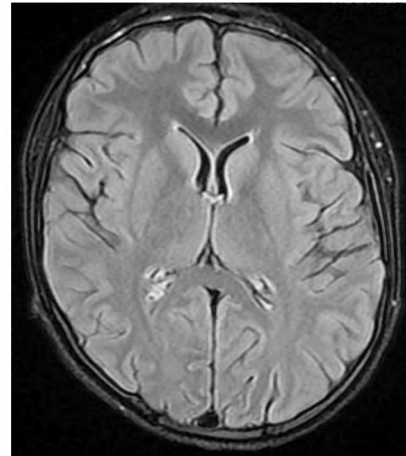


Fig. (2C): FLAIR.

Fig. (2): (A,B,C): Show axial views of brain MRI (without contrast) of a 12 years old male with WD with T1 bilateral symmetrical hyperintensity signals of globus pallidus (A) (arrows) & normal T2 weighted and FLAIR images (B,C).

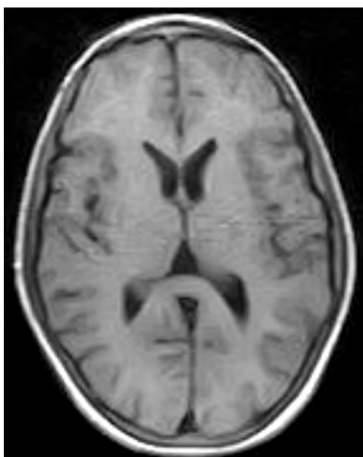


Fig. (3A): T1.

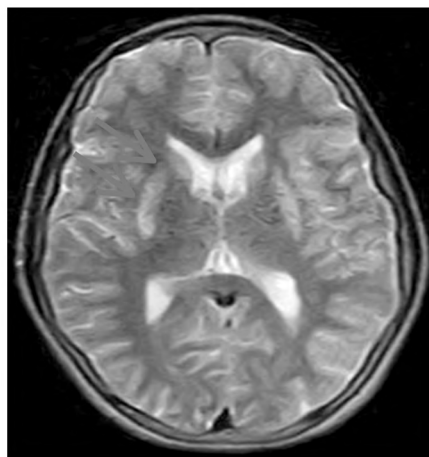


Fig. (3B): T2.

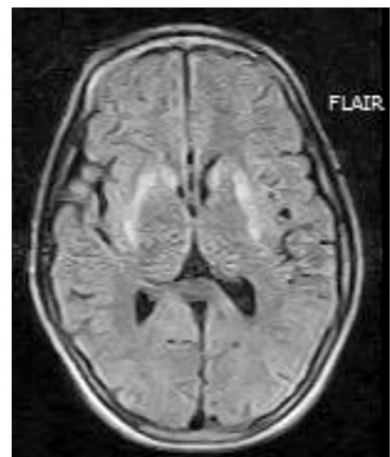


Fig. (3C): FLAIR.

Fig. (3): (A,B,C): Show axial views of brain MRI (without contrast) of a 13 years old male with WD with bilateral symmetrical hyperintensity signals of caudate nuclei and lentiform nuclei in T2 weighted & FLAIR images (B,C) (arrows) and normal T1 weighted image (A).

Table (5): Comparison between normal and abnormal MRI WD subgroups.

	Normal MRI group n=20 n (%)	Abnormal MRI group n=15 n (%)	P-value
<i>Type of presentation:</i>			
• Presymptomatic	8 (40%)	0 (0%)	0.020*
• Picture of acute hepatitis	5 (25%)	3 (20%)	
• Picture of CLD	7 (35%)	11 (73.33%)	
• Neurologic presentation	0 (0%)	1 (6.67%)	
<i>Duration of illness (months):</i>			
• Min-max	0.5-108.0	1.0-84.0	0.184
• Mean ± SD	39.5±40.3	24.2±26.1	
<i>24 hours urinary Copper at time of MRI (µg/24 hours):</i>			
• Min-max	27.00-1012	51.00-760	0.986
• Mean ± SD	232.05±268.60	230.54±208.15	
<i>Child Pugh score:</i>			
• Class A	16 (80%)	9 (60%)	0.061
• Class B	0 (0.00%)	4 (26.67%)	
• Class C	4 (20%)	2 (13.33%)	

Table (5): There was significant statistical difference between the two groups as regard type of presentation ($p < 0.05$).

Discussion

Wilson's disease is an inherited disorder of hepatic copper metabolism with considerable variation in clinical presentations, the most common ones being liver disease and neuropsychiatric disturbances [9].

In this study, 51.4% presented by picture of CLD, 22.8% presented by acute hepatitis and 3% with neurologic presentation, while 22.8% were diagnosed presymptomatic during family screening of siblings of patients. In hand with our results, Gheorghe et al., 2004 reported that 52.8% presented by CLD picture and 25.4% were presymptomatic. This maximizes the importance of family screening, as it is a main step for the diagnosis of WD to allow treatment of asymptomatic patients in order to avoid hepatic and neurological complications [11]. In agreement with our results about neurologic symptoms in WD group, Machado et al., 2006 reported that dysarthria and abnormal gait were the most common neurological symptoms. While Noureen and Rana, 2011 reported that dystonia and dysarthria were the most common neurological symptoms. We reported that MRI abnormality was significantly statistically higher in WD group than CLD group ($p = 0.003$). We reported that there was

no significant statistical difference between CLD group and WD group as regard T1 weighted images finding ($p > 0.05$). This is due to that WD as a CLD can produce brain abnormalities similar to that produced by other CLDs. In CLD, the most characteristic findings of T1-weighted images are a bilateral and symmetric high signal in the region of basal ganglia mostly globus pallidus. This is attributed to manganese accumulation secondary to failed hepatobiliary clearance and portosystemic shunting [14]. Indeed, pallidal manganese concentrations are elevated in cirrhotic patients dying with hepatic coma. Other brain areas can also accumulate manganese, albeit to a lesser extent. Elevated CSF manganese levels have been documented in patients with liver failure, consistent with more widespread manganese accumulation [15]. Manganese is a paramagnetic metal that shortens the T1 relaxation time sufficient to produce T1 hyperintensity. In contrast, copper typically results in increased T2 signal abnormalities only, because copper does not have the paramagnetic properties to generate T1 hyperintensity [16]. Among WD group, we reported 15 patients (42.8%) had abnormal MRI. While Li et al., 2019 detected abnormal MRI in only 4.4% of WD patients. This may be due to younger age at diagnosis (5.9 years) and higher percent of presymptomatic patients (86%) in their study. We reported that globus pallidus was the most common affected site in T1 weighted images in WD group. Our result is in agreement with Bayram et al., 2016 who reported that globus pallidus is the most affected in T1 weighted images in WD patients. In this study, T2 bilateral basal ganglionic lesions were the commonest changes. Consistent with our result, Ranjan et al., 2015 reported that T2 bilateral basal ganglia lesions were the commonest and suggestive of WD. Among basal ganglia nuclei, caudate nucleus was the most affected in T2 weighted images followed by lentiform nucleus then putamen. This disagree with Salari et al., 2018 who reported that putamen was the most affected site followed by pons followed by midbrain in T2 weighted images. Lesions in FLAIR images were similar to T2 weighted images except in one patient. Hyperintense signal of caudate nucleus was the most common followed by lentiform nucleus then putamen. This result is in agreement with that reported by Ranjan et al., 2015. We reported that MRI brain lesions were bilateral and symmetrical in all patients except in one patient who had signal abnormality affecting only left globus pallidus, this in agreement with Ranjan et al., 2015 and Zhong et al., 2019 who reported that brain lesions in MRI of WD patients were bilateral and symmetric. In our study,

bilateral symmetrical hyperintensity of caudate nucleus in T2 weighted & FLAIR images was the commonest lesion in patients who had dysarthria and abnormal gait. In hand with our result, Sinha et al., 2006 reported that caudate lesions have a significant association with dysarthria. In our study, brain MRI of the patient who had dystonia showed bilateral symmetrical hyperintensity of caudate nucleus and putamen in T2 & FLAIR images. Consistent with our result, Svetel et al., 2001 reported correlation of dystonia with putamen lesion. It is still not clear when brain involvement in WD becomes symptomatic. We reported that 60% of WD patients, who had abnormal MRI, were neurologically free at time of MRI. In hand with our result, Güngör et al., 2018 reported that 42.1 % had abnormal MRI without any clinical sign. There was no significant statistical difference between the two WD subgroups as regard liver function ($p < 0.05$) except AST/ALT ratio also there was no significant statistical difference between the two WD subgroups as regard 24 hours urinary copper at time of MRI. In accordance to our results, Sinha et al., 2006 reported that MRI changes did not correlate with duration of illness. But these results disagree with Zhong et al., 2019 who reported that disease duration in MRI-abnormal patients was significant longer than that in patients who were MRI normal. We reported that all presymptomatic patients had normal MRI. In hand with our result Sinha et al., 2006 reported that all presymptomatic patients had normal MRI.

Conclusions:

All CLD patients had normal T2 weighted and FLAIR images. Bilateral symmetrical hyperintense signals in T2 weighted and FLAIR images mainly involving basal ganglia are specific for WD and represent CNS involvement of WD. Caudate nucleus was the most common affected site in T2 weighted and FLAIR images followed by lentiform nucleus. Bilateral symmetrical hyperintensity of caudate nucleus in T2 weighted and FLAIR images was the most common lesion in WD patients who had dysarthria and abnormal gait. Abnormal MRI may be a bad prognostic factor as 20% from abnormal MRI WD subgroup deteriorated rapidly and were candidates for LT.

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تشوهات تصوير الدماغ بالرنين المغناطيسي لدى الأطفال المصابين بمرض ويلسون؛ هل هي مؤشر على زراعة الكبد؟

إن مرض ويلسون (WD) هو اضطراب وراثي جسمي مقهور من النحاس حيث التمثيل الغذائي مع إنتشار حوالي ١ في ٣٠٠٠٠ شخص. إنه أكثر شيوعاً مع قرابة الوالدين. تم الإبلاغ عن أن جين الأدينوزين ثلاثي الفوسفات (ATP7B)، الذي يرمز للنحاس الذي ينقل النحاس من النوع P، يحتوي على ٢٨٠ نوعاً مختلفاً. يؤدي النحاس إلى تلف الأنسجة عن طريق التراكم في العديد من الأعضاء بما في ذلك الكبد والدماغ بشكل رئيسي. تُعزى المظاهر العصبية ل WD إلى الترسب غير الطبيعي للنحاس في أنسجة المخ، وخاصة المادة الرمادية العميقة (العقد القاعدية والمهاد) والمادة البيضاء تحت القشرية. يمكن أن يظهر مرض ويلسون سريريًا عن طريق أمراض الكبد أو الاضطرابات العصبية أو الأمراض النفسية. في الطفولة، تسود المظاهر الكبدية مع طيف متغير للغاية يتراوح من التهاب الكبد الذاتي إلى الفشل الكبدي الخاطف. وتهدف هذه الدراسة إلى الكشف عن التغيرات الدماغية بواسطة التصوير بالرنين المغناطيسي لدى الأطفال المصابين بمرض ويلسون وعلاقتها بالنتائج السريرية والبيوكيميائية. حيث شملت هذه الدراسة ٧٠ مريضاً. ٣٥ مريضاً مع WD و٣٥ مريضاً يعانون من أمراض الكبد المزمنة الأخرى (CLD) كعنصر تحكم. ضمت مجموعة ٢٠ WD من الذكور و١٥ من الإناث. كان متوسط أعمارهم (٢٠.٨٦±١٢.٧٣) سنة. تضمنت المجموعة الضابطة ٣٥ مريضاً مصاباً بمرض CLD ٢٠ مصاباً بالتهاب الكبد المناعي الذاتي (AIH)، وإثنان مصابان بالتهاب الأقفنية الصفراوية المصلب و١٣ مصاباً بفيروس التهاب الكبد المزمن. وقد أسفرت هذه الدراسة عنه من بين مجموعة WD، أبلغنا عن إصابة ١٥ مريضاً (٤٢.٨٪) بتصوير غير طبيعي بالرنين المغناطيسي. أظهرت الصور الموزونة T1 إشارة فرط كثافة متناظرة ثنائية من Globuspallidus في مريضين (٥.٧٪)، وإشارة شدة شدة الشاحبة اليسرى في مريض واحد (٢.٨٪) وفرط تماثل في المهاد في مريض واحد (٢.٨٪). كانت إشارات فرط الشدة T2 و FLAIR التي تشتمل بشكل أساسي على العقد القاعدية موجودة في ١١ مريضاً (٣١.٤٪). تأثر الجهاز البطني في مريضين (٥.٧٪)، وكان بارزاً في مريض واحد وكان الآخر مصاباً بإستسقاء الرأس. تمت متابعة المرضى على مدار فترة تتراوح من ٦ إلى ١٨ شهراً وأبلغنا أن ثلاثة مرضى مصابين بداء السكري (٢٠٪) من أولئك الذين لديهم تصوير بالرنين المغناطيسي غير الطبيعي قد تدهوروا بسرعة وكانوا مرشحين لزراعة الكبد، بينما لم يكن أي من المرضى الآخرين بحاجة إلى زراعة الكبد، ومما سبق إستنتجنا أن إشارات فرط الشدة الثنائية المتناظرة في صور T2 المرجحة وصور FLAIR التي تتضمن بشكل أساسي العقد القاعدية خاصة ب WD وتمثل مشاركة الجهاز العصبي المركزي ل WD. قد يكون التصوير بالرنين المغناطيسي غير الطبيعي عاملاً إنذارياً سلباً حيث أن ٢٠٪ من المجموعة الفرعية للتصوير بالرنين المغناطيسي غير الطبيعية تدهورت بسرعة وكانت مرشحة لزراعة الكبد.