WILSON'S DISEASE

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ABSTRACT

A disturbance of copper metabolism causes hepatolenticular degeneration (Wilson's disease), an autosomal recessive disorder whose genetic locus lies on the long arm of chromosome 13. The concentration of the copper transport protein ceruloplasmin is abnormally low and, as a result, the serum free copper concentration is high and an abnormally large amount of copper is eliminated in the urine. Free copper is deposited in the liver, the edge of the cornea, the brain. We present a case who debuted by tremors and thrombocytopenia. Continuous therapy with Trientine hydrochloride and Mega zinc, and elimination of copper rich foods were improved cognitive, behavioral and motor dysfunctions.

Key words: Wilson's disease (WD), treatment, Global Assessment Scale for WD (GAS for WD)

INTRODUCTION

Wilson's disease is a genetic metabolic disorder with autosomal recessive transmission (1, 2, 7). The Wilson's disease gene has been mapped to chromosome 13q14 linkage to esterase D locus, and it is called ATP7B. There are 2 main dysfunction in copper metabolism: decrease in carrying function of copper by ceruloplasmin and decrease of copper excretion in bile (2). Copper deposits in tissue leads to clinical manifestation of disease (3,4,6.11): hepatic cirrhosis (13), cerebral manifestations, hemolytic anemia, renal tubular dysfunction, Kayser Fleischer ring and osteomuscular manifestations.

MATERIAL AND METHOD

We present a case of 28 years old patient who was diagnosed with essential tremors (brain CT scan and EEG are normal) and idiopathic autoimmune thrombocytopenia (abdominal ultrasound and sternal puncture were normal) in 2005. Symptoms worsen progressively, after 3 years there were action and postural tremors at the level of upper limbs (right hand more than left), dysarthria and gait abnormalities and easy postural instability (dystonic gait with forced backward position of arms during walking). The handwriting was near impossible, the patient had inability to do daily activity without someone help.

RESULTS

In 2008 global assessment scale for Wilson Disease (3) was: L (liver) 3, C (cognitive) 2, M (motor) 4, O (osteomuscular) 0. L3C2M4O0.

Biological examinations reveal: serum copper: 71μg% (NV 70-140μg %), decreased ceruloplasmin level 0,05g/l (NV 0,16–0,36g/l) an increased 24 hours urine copper level-1280μg/24ore (NV 15-70 μg/24h).

Ophthalmologic examination confirmed the presence of right eye incomplete Kayser-Fleischer ring.

Cerebral MRI (5,9) (2008) reveals the presence of symmetric hypersignal bands of T2 weighted (Fig. 2 and Fig. 3) and FLAIR images (Fig. 1) at the level of bilateral spinothalamic tracts without contrast enhancement.

The diagnosis was of hepatic cirrhosis after internal medicine exam, abdominal ultrasound exam and liver tests.

Continuous therapy (from 2008) with Trientine hydrochloride 2 tablets three times a day and Mega zinc 150 mg tid, elimination of copper rich foods (10,11,12): liver, mushroom, cabbage, beans, choc-

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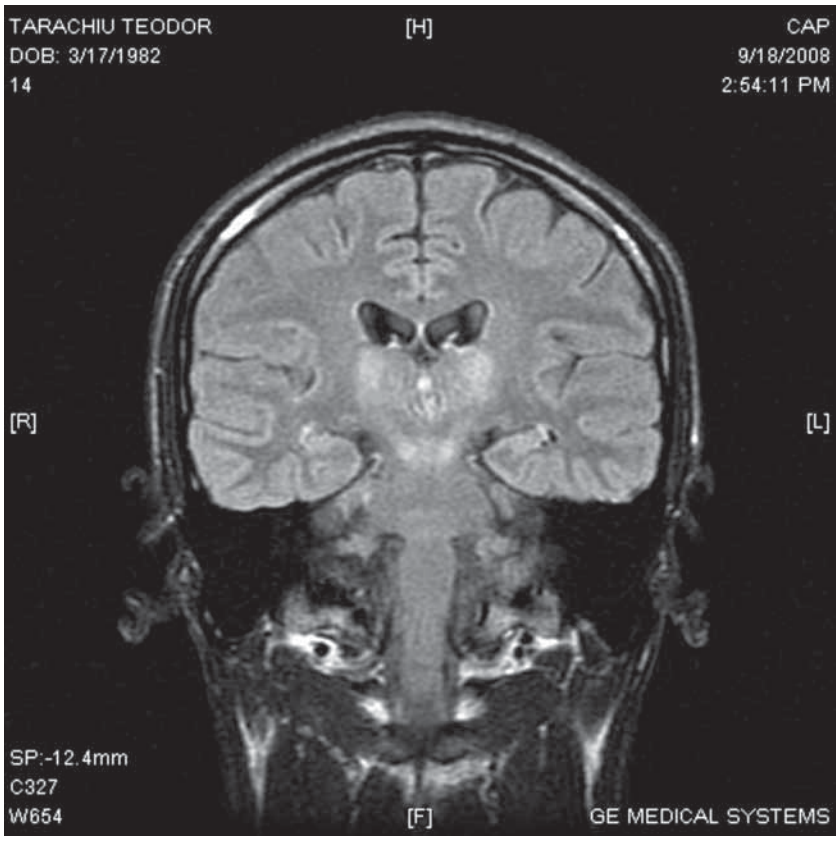

Figure 1. *Cerebral MRI reveals FLAIR bilateral hypersignal bands of spino-thalamic tracts*

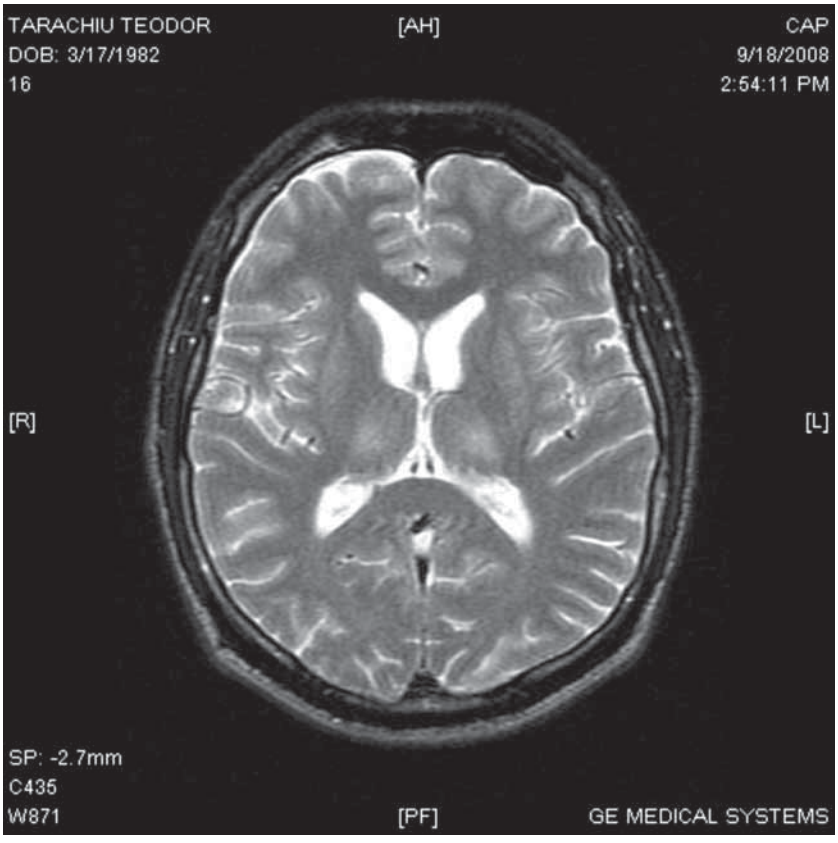

Figure 2. *T2 weighted reveals bilateral thalamic hypersignal*

olate, sea foods, nuts and interdiction of preparing food in any copper dishes. After 2 weeks treatment urinary copper was 1280 μg/24h, cognitive and behavioral and also motor dysfunctions were improved. One and half year latter ophthalmic examination confirmed the absence of Kayser Fleischer ring. From May 2010 lowered the Trientine dose to 3 tablets a day and Mega zinc 150 mg/day.

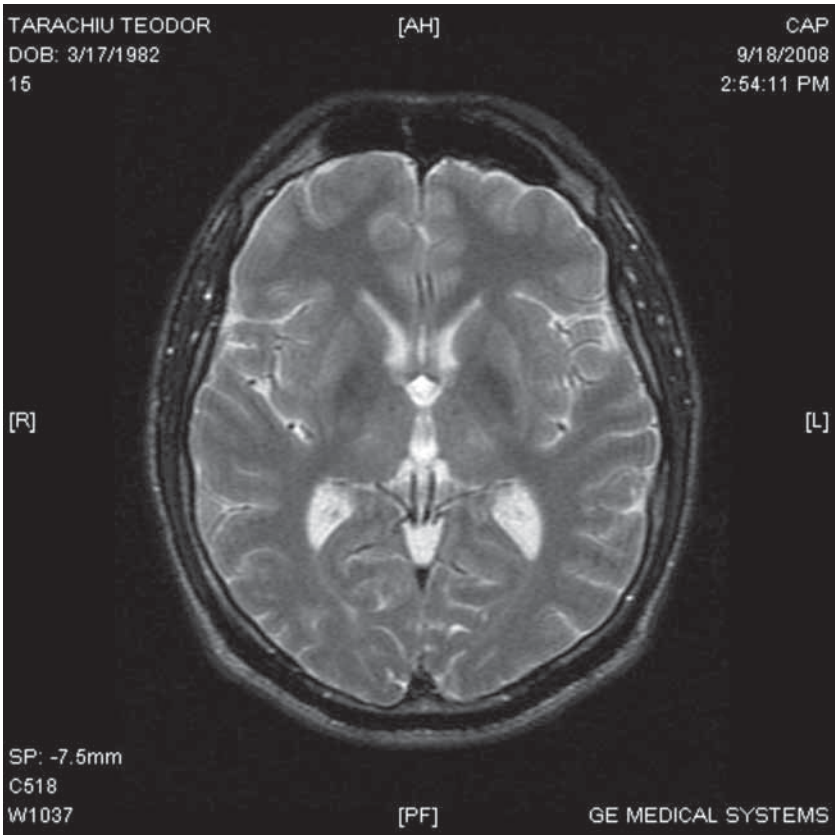

Figure 3. *T2 weighted reveals bilateral thalamic hypersignal.and globus pallidus hyposignal*

In May 2011 patient had GAS score of: L (liver) 3- compensated hepatic cirrhosis, C (cognitive) 0-normal, M (motor) 1- minors clinical sign, patient can do his daily activity alone, O (osteomuscular) 0-normal.

Score is L3C0M1O0.

On neurological evaluation of GAS scale patient presents a fine postural tremor of right upper limb -1, mild dysarthria -1, emotional liability -1, so score is 3 out of 56 total score that can be obtained in very severe cases.

At present patient has copraemia of 94,74μg/dl, cupruria 252,3 μg/24h, thrombocytes 117.000/mm3, TGO – 29UI, TGP – 37UI, urine exam normal, CEA (carcinoembrionic antigen) 2.9 ng/ml (NV <3.4).

Abdominal ultrasound: liver left lobe 6.8cm (enlarged), right lobe 12.2cm (normal), portal vein 15mm (dilated), liver with irregular border and non-homogenous structure (hepatic cirrhosis). Gall bladder with thin walls and without lythiasis. Right kidney with bipolar diameter of 11.2 cm (normal), cortex 10 mm hyperechogen. Normal pancreas. Absence of ascites, empty urinary bladder. Conclusion: hepatic cirrhosis and portal hypertension.

Gastric endoscopy: normal esophagus with absence of varices. Edematous and hyperemic gastric mucosa. Normal D1 and D2. Hepatic fibroscan: F3 (there are 4 stages of gravity).

Fibro Test: F1-F2 (F4 meaning severe hepatic cirrhosis).

Conclusion: significant hepatic fibrosis with slow evolution under copper chelation therapy.

Cerebral MRI scan: FLAIR images reveal bilateral thalamic hypersignal (Fig. 4), hypersignal globus pallidum on T2* (Fig. 5), thalamic hypersignal on T2 (Fig. 6).

CONCLUSIONS

An interesting case which would be easily wrong diagnosed due to the lack of hereditary background characteristic of Wilson's disease, initial normal cerebral images and abdominal ultrasound examination which also led to delay for specific tests, diagnosis and appropriate treatment.

Any kid or young adult with hepatic affections and neurological dysfunction must be investigated for Wilson's disease.

Despite actual possibilities for diagnosis and treatment patients with Wilson's disease remain with sever disabilities due to diagnosis delay and difficulties in treatment monitoring.

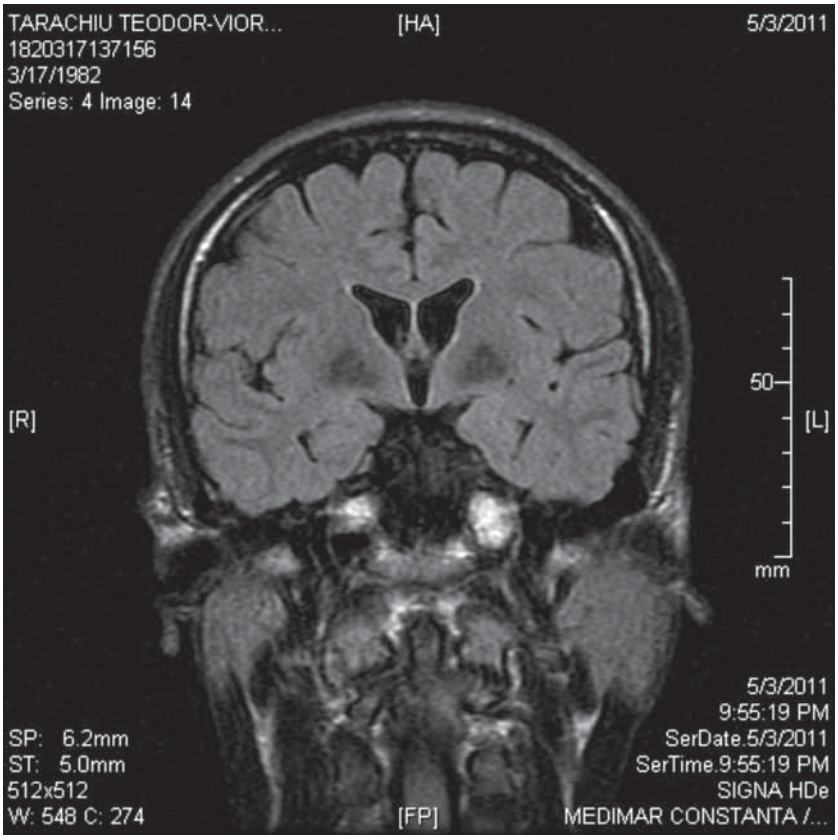

Figure 4. *Cerebral MRI FLAIR reveals bilateral thalamic hyposignal*

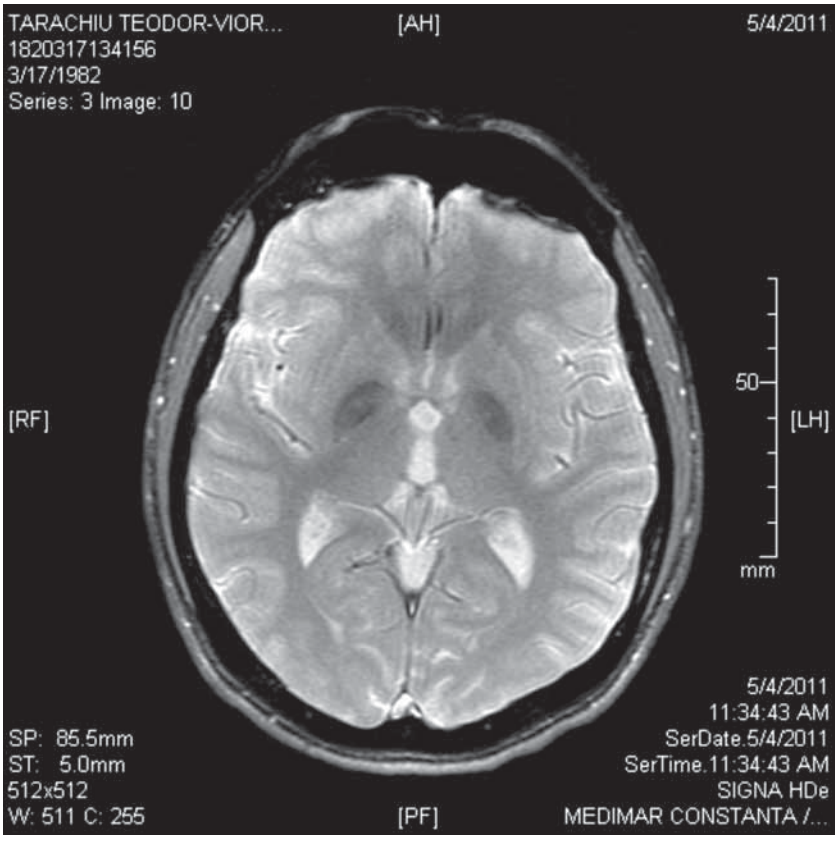

Figure 5. *MRI cerebral T2* weighted reveals bilateral globus pallidus hyposignal*

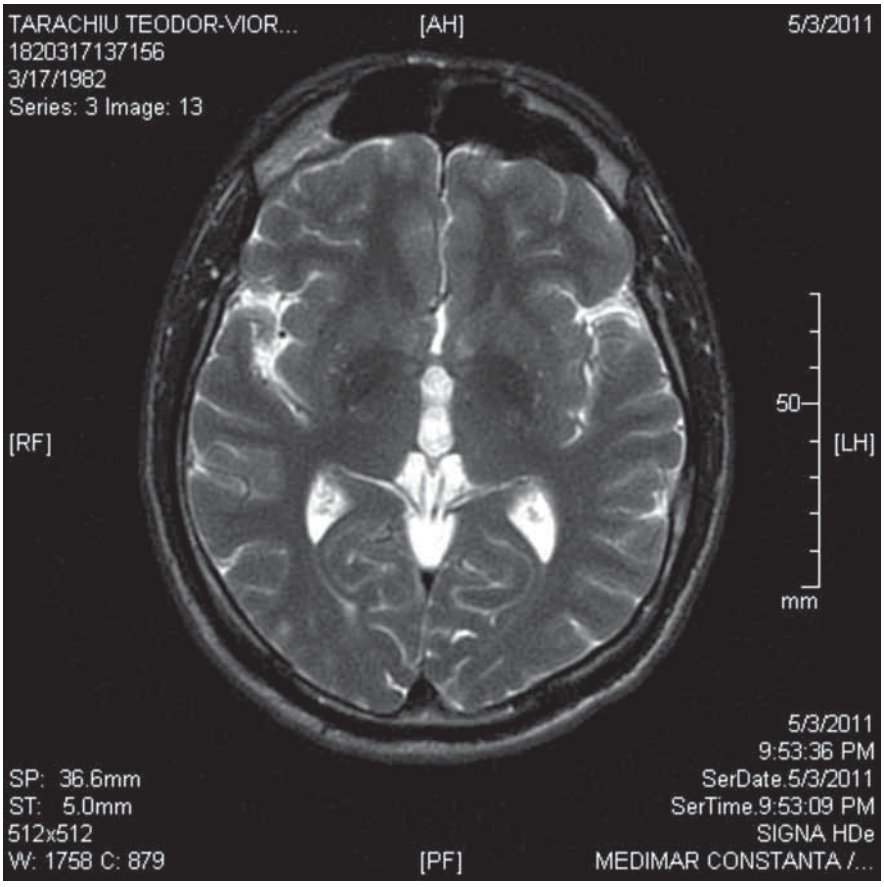

Figure 6. *MRI cerebral T2 weighted reveals bilateral thalamic hyposignal*

Cognitive and behavioral disturbances answer well to copper chelation therapy, hepatic affections stopped and therapeutic response of osteoarticular affections is not well known.

GAS scale is use for quantification of Wilson's disease and monitoring of therapeutic response.

GAS (global assessment scale) of Wilson's disease is formed of two parts: first part reflects global disabilities and the second neurological abnormalities.

Global disabilities focus on four main points (liver -L, cognitive and behavioral -C, motor –M and osteomuscular -O) each of them being independent, on a scending six point scale (0-5). Their scores are not summed.

Neurological abnormalities scale: searches for

- Wilson's facials
- cognitive and behavioral functions: intellectual performance, depression, psychosis
- extrapyramidal signs: dystonia, tremors, chorea and parkinsonian syndrome
- Kaiser Fleischer rings
- presence or not of following signs rarely seen in this disease: emotional lability, epileptic seizure, myoclonus, stereotypy, tics, pyramidal signs and eye movements' abnormalities.

The score is obtained by the sum of all individual scores, total score varies between o and 56, the more the score the severe the disease.

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