

THE PSEUDOSCLEROTIC FORM ("WING-BEATING TREMOR") OF WILSON'S DISEASE

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ABSTRACT

Wilson disease is a rare monogenic, autosomal recessive disorder of copper metabolism, leading to progressive accumulation of copper in different organs, essentially in the liver, brain and cornea. We report a case of a 25 years old man, Caucasian, with "wing-beating tremor" in the right arm that started with two month in advance of hospital admission, than evolved to the left arm, a week before hospitalization. The slit-lamp examination showed the presence of Kayser-Fleischer rings in both eyes. The laboratory tests and brain MRI confirmed the diagnostic of Wilson's disease.

Keywords: Wilson disease, copper metabolism, wing-beating tremor

BACKGROUND

Wilson disease is a rare monogenic, autosomal recessive disorder of copper metabolism, leading to progressive accumulation of copper in different organs, essentially in the liver, brain and cornea. Copper starts to accumulate after birth. The disease progresses very slowly, the patient being presymptomatic. Most patients start to have hepatic, neurologic and psychiatric manifestations between ages of 11 and 25 years (1), but the disease should be considered in any person between the age of 3 and 55 years with these signs and symptoms (2). Prevalence is 1: 30,000 with a heterozygote carrier frequency of 1 in 100 persons (3).

CASE PRESENTATION

A 25 years old man, Caucasian, was presented with tremor in the right arm that started two month earlier, which gradually extended to the left arm one

week before hospitalization. His past medical history includes spontaneous left femoral fracture with joint involvement (2007). On neurological examination he presented dysarthria and "wing-beating tremor" in both hands. The tremor was irregularly, jerky with high amplitude. It was best elicited with arms held forward and flexed horizontally. Also, the patient presented psychiatric symptoms such as antisocial behavior as aggression toward family members, sexual preoccupation, and irritability. There was a cognitive impairment, with poor school performance; he was in the last year of high school.

INVESTIGATIONS

The complete blood count revealed thrombocytopenia (109,000/ μ L), while liver function was normal. The abdominal echography found splenomegaly and micronodular liver. The slit-lamp examination showed the presence of Kayser-Fleischer rings in both eyes (Fig. 1). Further laboratory findings that

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support the diagnosis of Wilson's disease include low level of ceruloplasmine (6 mg/dl), low level of serum copper (35.8 $\mu\text{g/dL}$) and high level of 24 hour urinary cooper excretion (272.8 $\mu\text{g}/24\text{h}$). Brain MRI revealed bilateral T2/ FLAIR putamin-al, thalamic and brain stem hyperintensity (Fig. 2B). In the midbrain, characteristic "face of giant panda" sign was present – normal signal intensity in red nucleus against hyperintense signal in tegmentum (Fig. 2A). Bilateral hyperintense signal of fronto-parietal regions was observed (Fig. 2C).

DIFFERENTIAL DIAGNOSIS

The "wing-beating tremor" differentials are: acute disorders, such as stroke, and chronic disorders, such as Huntington disease, tumors or multiple sclerosis. None of these are compatible to our case.

TREATMENT

The aim of the treatment is to reduce the amount of free copper (decoppering). The patient started the treatment with Penicillamine at dose of 250 mg/day (maximum dose 1-3 g/day gradually increased). Also, he received Piridoxine 25 mg/day. We treated the tremor with Primidone 250 mg/day.

OUTCOME AND FOLLOW-UP

The pseudosclerotic form of Wilson's disease has the best chance to favorable outcome – 82% are symptom free or minor neurologic deficit (4).

The patient will perform abdominal echography and laboratory tests (24 hour urinary copper excretion, serum cooper and liver function tests) every 6

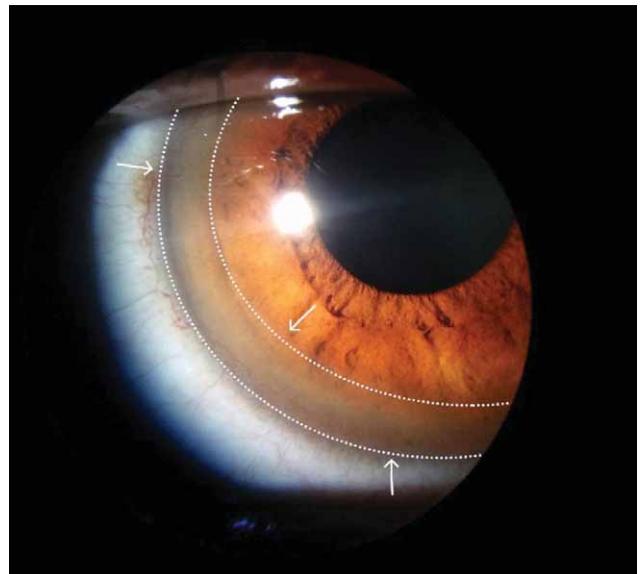


FIGURE 1. Slit-lamp examination – Kayser-Fleischer ring of cornea

month; brain MRI one year from starting the treatment (5).

DISCUSSION

Wilson's disease is an inherited autosomal recessive disorder of copper excretion, caused by mutation in the ATP7B gene.

According to clinical manifestations the disease will start as presymptomatic and at one point in evolution will become symptomatic. The copper is accumulating from birth, determining subclinical liver disease (presymptomatic). In the second decade the patient becomes symptomatic with neurological, psychiatric and hepatic manifestations (4).

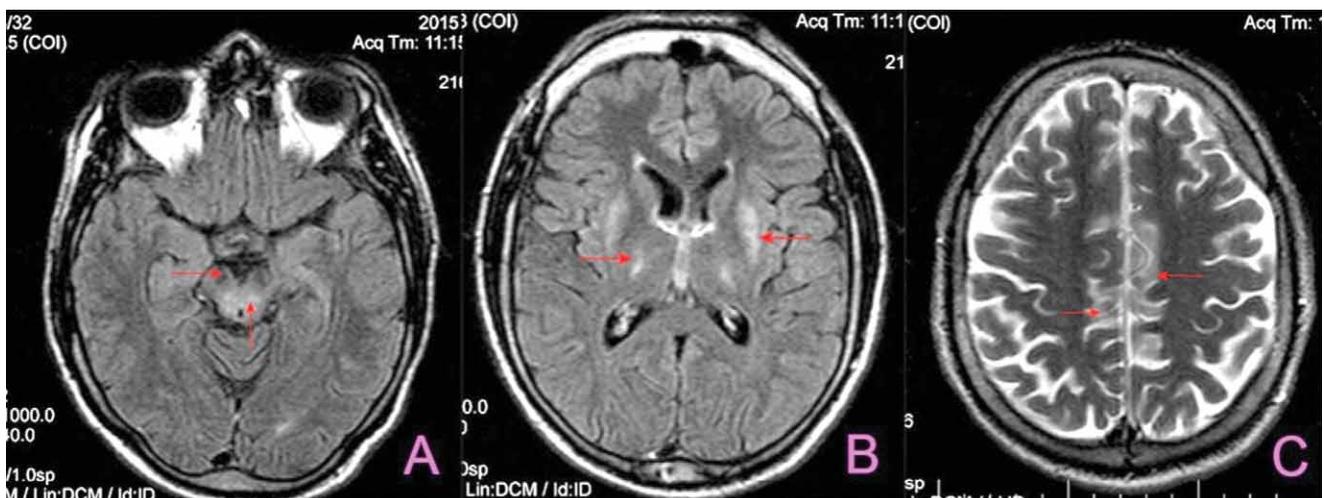


FIGURE 2. Brain MRI. **A** – Face of giant panda (normal red nucleus and hypersignal of tegmentum), FLAIR. **B** – Bilateral hypersignal in putamen and thalamus, FLAIR. **C** – Bilateral hypersignal fronto parietal, T2.

There are three clinical subtypes of neurological Wilson's disease: the pseudosclerotic form (tremor, ataxia and reduced functional capacity); the parkinsonism form (bradykinesia, rigidity and cognitive impairment) and dystonic/choreic syndrome (dystonic posture, chorea and organic personality syndrome). The "the wing-beating tremor" is best elicited with arms facing down and flexed horizontally. This type is less common than other tremor subtypes in Wilson's disease (3).

Psychiatric changes include irritability, anxiety, depression, cognitive impairment, poor school performance.

Kayser-Fleischer ring is the typical ophthalmological manifestation. It represents copper deposits in the Descemet's membrane of cornea (3).

The most common hepatic manifestations are: hepatomegaly, splenomegaly, jaundice, fulminant acute hepatitis, cirrhosis (2).

Combination between clinical manifestations and laboratory test will put the diagnosis of Wilson's disease. Low serum ceruloplasmine, high 24-h urinary copper excretion, low serum copper aided by the presence of Kayser-Fleischer ring at the slit-lamp examination will establish the diagnosis. Brain MRI findings will support the diagnosis for patients with neurologic or psychiatric symptoms: hypersignal T2/FLAIR in the basal ganglia, thalamus, and brain stem and white matter (6).

Starting the decoppering treatment with Penicillamine as soon as the diagnostic was made will prob-

ably improve the neurological and hepatic symptoms, while in the absence of treatment the natural evolution is a severe one. The treatment has two phases: acute decoppering therapy and maintenance therapy. The acute decoppering process is very slowly and it takes 1-3 years to remove the copper from the patient. When Kayser-Fleischer ring disappeared and a neurologic and hepatic recovery is observed, the treatment will switch to the maintenance therapy.

LEARNING POINTS/TAKE HOME MESSAGE

Wilson disease is a genetic, autosomal recessive disorder of copper metabolism, leading to progressive accumulation of copper in different organs, essentially in the liver, brain and cornea.

It should be considered in any person between the age of 3 and 55 years with movement disorder with early-onset or atypical presentation of hepatic manifestations. (2)

Screening diagnostic: low ceruloplasmin level; high 24-h urine copper test; low level of serum copper; slit-lamp examination for Kayser-Fleischer rings; brain MRI: high T2/FLAIR signal in the basal ganglia, thalamus, brain stem and white matter (6)

The treatment with Penicillamine as soon as the diagnostic was confirmed will save the patient life.

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