

TO THE EDITOR

Wilson's Disease only Presenting with Isolated Unilateral Resting Tremor

Wilson's disease (WD) is an autosomal recessive disorder of copper transport that results in the accumulation of copper, primarily in the liver, brain and cornea.¹ Although WD is treatable, the great variability of its clinical manifestations makes it difficult to diagnose at an early stage, and diagnostic delay can lead to irreversible damage of the affected organs, resulting in poor outcome.^{2,3}

We report a case of WD presenting with a combination of three atypical manifestations: neurological WD without any Kayser-Fleischer ring, isolated resting tremor of the right foot and absence of hepatic involvement.

CASE

A 34-year-old male presented in our movement disorder clinic with a five month history of a new onset unilateral resting tremor of low frequency. There was no remarkable past and family history. Physical examination did not reveal any findings indicative of liver disease.

On neurological examination, a resting tremor involving the right foot was observed. The tremor had a frequency of 2-3 Hz, and did not change when the patient was asked to tap his left foot, but was resolved when he was walking. (See video on-line) The tremor did not involve any other body parts, nor did the patient exhibit other parkinsonian symptoms or cerebellar signs. Only mild hesitancy on gait initiation was observed.

Laboratory tests revealed some abnormalities suggestive of WD: low ceruloplasmin level (<0.1 g/L [ref. 0.23-0.40 g/L]), markedly elevated urinary 24 hour Cu (918.19 μ g [ref. 38-70 μ g/day]) and low serum Cu (24.9 μ g/dL [ref. 70-155 μ g/dL]). However the patient had normal liver enzyme levels and no

Kayser-Fleischer rings on slit-lamp examination by a skilled worker. Abdominal CT and liver biopsy were performed but gave no evidence of inflammation or fibrosis. Magnetic resonance imaging of the brain revealed diffuse brain atrophy and T2 hypointensity involving bilateral caudate nuclei and putamen. (Figure)

Although the clinical findings, laboratory tests and imaging study were suggestive of WD, the absence of Kayser-Fleischer ring and the atypical manifestations for WD made diagnosis unclear. Therefore, genetic testing was performed to confirm the diagnosis of WD, and an ATP7B gene mutation (c.2333G>T) was detected.

A final diagnosis of Wilson's disease was made and the patient was treated with D-penicillamine and zinc acetate.

DISCUSSION

The patient in our case presented with three atypical features of WD. First, he showed only one neurological sign and no hepatic involvement. Presentation with neurological manifestations but without any clinical involvement of the liver or abnormalities in liver function test is very unusual for WD.

Second, the initial manifestation was isolated resting tremor of the right foot. In a study of 119 cases, postural tremor was the most prevalent (55%), and isolated resting tremor was relatively rare (5%).⁴

Most neurological symptoms in the limbs present unilaterally, and involvement of the upper limbs is more common than that of the lower limbs; also, when resting tremor exists, it is usually accompanied by postural and kinetic tremors as a mixed type, which can be more severe.²⁻⁴ The characteristics of tremor in the present case were unilateral resting presentation relieved by walking, and involvement of a lower limb. The features of tremor in our patient were not typical of WD and may be regarded as atypical tremor.

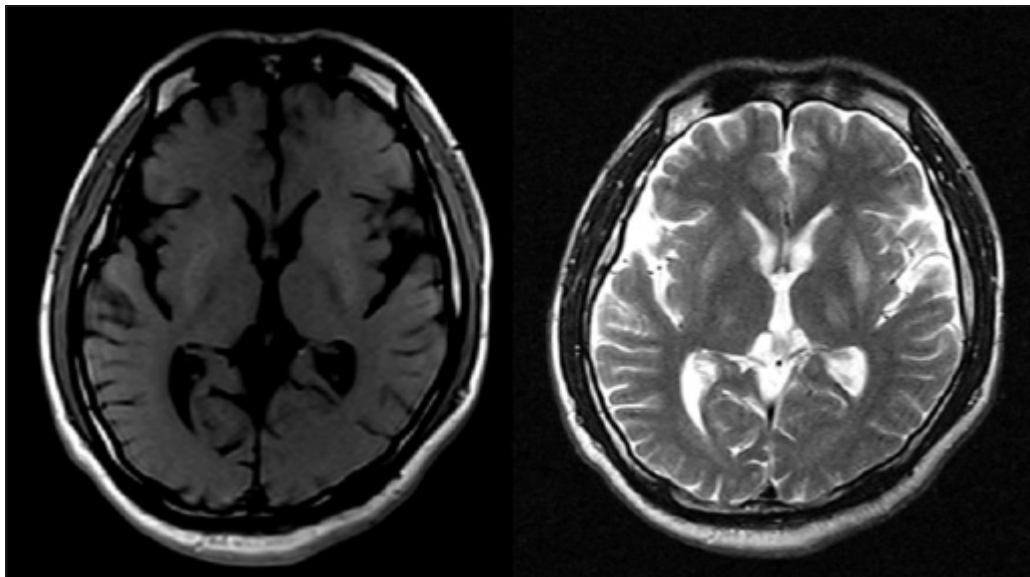


Figure: T1 and T2 weighted MRI reveals high signal intensity in both thalamus and putamen compatible with Wilson's disease.

Finally, Kayser-Fleischer rings are hallmarks of WD that require identification by a skilled observer. Kayser-Fleischer rings are almost always observed in patients who present with neurological manifestations, and are observed in about 50% of patients presenting with only hepatic features.³

Diagnostic error is a challenging problem due to the wide variety of clinical manifestations of WD.

Prashanth et al suggested the following possible causes of error: lack of awareness, low prevalence in the community, absence of family history and history of liver disease, relatively late onset of disease, and absence of markers such as Kayser-Fleischer rings.⁵ Our patient had no family history of liver disease, atypical neurologic manifestations, absence of Kayser-Fleischer rings, and relatively late onset of symptoms. These factors correspond to the proposed reasons for diagnostic error.

In summary, atypical features such as absence of Kayser-Fleischer rings and hepatic symptoms and unusual neurologic manifestations do not rule out the possibility of WD and may cause diagnostic errors or misdiagnosis. The possibility of WD should be considered in all young adults with movement disorders, and careful investigation should be undertaken.

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