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# Neurological Wilson Disease in a Young Brazilian Adult: A Case Report

Igor Pereira Matos de Oliveira

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## Abstract

We report a rare case of Wilson's Disease with neurologic features in a 31-year-old man. This disease consists of a disturbance of copper metabolism secondary to a mutation in the gene responsible for encoding the tissue transporter and the enzyme that incorporates the excess element into bile, generating toxic accumulation in the liver, cornea, and central nervous system. According to his wife, the patient had been treated for an unspecified mood disorder. The clinical picture was characterized by depressive mood, anhedonia, and anxiety. He had his first seizure episode on December 3rd, 2021. He progressed with dysarthria, ataxic gait, dystonia of the right-hand flexor muscles, and intermittent urinary incontinence. Marked worsening was observed after the diagnosis of COVID-19 in February 2022. At the clinical evaluation on March 24th, risorius muscle dystonia (risus sardonicus), resting tremor, and Kayser Fleischer rings at slit-lamp examination was also noted.

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*Index terms*— wilson disease. inborn errors in metal metabolism. dystonia.

## 1 Introduction

Wilson's Disease (WD) is a metabolic disorder resulting from biallelic mutations in the ATP7B gene on chromosome 13, characterized by the toxic accumulation of this element in the liver, cornea, and central nervous system.

The incidence of these mutations in newborns was estimated at 1:7,000 in Sardinia, Italy and 1.7:100,000 in the Republic of Ireland, in contrast, the prevalence of the disease has been estimated to be between 1:250,000 and 1:300,000 in Sweden and between 1:30,000 and 1:40,000 in other populations.

Copper is an essential cofactor for several enzymes and is present in foodstuffs such as seafood, pulses, and nuts. Its metabolism is dependent on the ATP7B gene, which is responsible for encoding ceruloplasmin, and on the ATPase, which incorporates it into the bile and allows its exteriorization with the feces.

Due to the absence of these mechanisms, copper accumulates in the liver until it spills over into the bloodstream. High levels of cupremia cause disruption of the blood-brain barrier and deposition with a cytotoxic effect in the striatum, globus pallidus, locus coeruleus, substantia nigra, and cerebral cortex.

## 2 II.

## 3 Case Report

A 31-year-old male, mixed race, bricklayer, residing in Paraisópolis, Minas Gerais State, Brazil. History of alcoholism and drug use. Diagnosis of previous unspecified mood disorder and using Fluoxetine 40mg/day. No other relevant environmental exposures were reported. Report of a male adult family member diagnosed with liver failure of unknown etiology.

Magnetic Resonance Imaging (MRI) of the brain on December 1st, 2021, showed involvement of the putamen, associated with hemosiderin residue, and crus posterius bilaterally, in addition to the midbrain and pons, without restriction to diffusion (images 1A-1D), and an extra-axial parietal left paramedian contrast-enhanced lesion suggestive of meningioma (images 1E-1F). On December 3rd, 2021, the patient suffered the first generalized

## 6 CONCLUSION

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43 clonic tonic seizure while sleeping, and in a follow-up visit on December 21st, he started to use Levetiracetam  
44 orally.

45 He was diagnosed with Covid 19 on February 3rd, 2022, with a mild evolution without the need for ventilatory  
46 support or complications. The wife noted that the development of the disease was accentuated after the infection.  
47 From February 9th, he appeared to have speech and gait disturbance, difficulty mobilizing the right hand, and  
48 urinary incontinence. During outpatient follow-up, a new MRI of the brain was requested on April 1st, 2022,  
49 which denoted better characterization of foci of signal alteration in cerebellar peduncles (images 2).

50 On June 2022, he had moderate dysarthria, hypomimia, right-hand flexor dystonia, tetraparesis, bradykinesia,  
51 and postural instability, but without rigid or resting tremors.

52 The specific treatment was started on May 2022 with pyridoxine chlorhydrate 50 mg daily and zinc sulfate  
53 heptahydrate 4 mg/mL 15mL three times a day orally. Due to the cost of the drug, the patient delayed starting  
54 penicillamine.

## 55 4 III.

## 56 5 Discussion

57 Incipient neurological symptoms are subtle and nonspecific, such as difficulty concentrating and motor coord-  
58 ination and handwriting changes (for example, micrograph) [13][14][15][16][17][18][19] and begin on average  
59 between 20 and 40 years [20][21][22]. As it progresses, more prominent symptoms appear, whose order of  
60 incidence is dysarthria (57.6%), dystonia (42.4%), abnormal gait (37.8%), tremor (36.2%), parkinsonism (17.3%),  
61 choreoathetosis (15.3%) and convulsion (4.7%) 16,17. Neurological impairment occurs about a decade after liver  
62 failure and, therefore, signs of advanced disease 23. Cognitive impairment is considered rare and was reported  
63 by Machado, Chien, Deguti, et al. (2006) 16 in 4.2% of cases.

64 Given the heterogeneity of clinical manifestations, the neurological phenotype of WD can be grouped for  
65 didactic purposes into dystonic, pseudosclerotic, parkinsonian, and hyperkinetic subtypes 4. The patient  
66 discussed in this study had a predominance of the dystonic subtype manifested by multifocal dystonia affecting  
67 both the risorius muscle (sardonic laughter) and the flexor muscles of the right hand fingers. As reported by  
68 Lorincz (2010) 24, bilateral putaminal lesions were found on an MRI of the brain.

69 Dysarthria can result from any condition that damages the motor control structures necessary for speech  
70 production, such as cranial nerves IX, X, XII, cerebellum, and basal ganglia 12. In this case, it was noted  
71 evident bilateral impairment of the basal ganglia.

72 Seizures are not uncommon and are reported variably in 4.7% 16,17 to 14.5% 25 of WD cases. The patient  
73 in question presented, at the initial manifestation, a single episode of generalized tonic-clonic seizure without  
74 recurrence.

75 We also detected the presence of brownish Kayser Fleischer rings, more evident in the lower region of the iris  
76 bilaterally. Such a semiological sign is due to copper deposition in the Descemet's membrane of the cornea 26  
77 and is present in approximately 100% of neuropsychiatric WD cases 10.

78 Psychiatric symptoms are reported by about 30% to 60% of individuals affected by WD 26. In this case, the  
79 disorder for which the patient had been using Fluoxetine was not specified. However, the familiar states that at  
80 the time of initiation of therapy, he had a depressive mood, anhedonia, and anxiety.

81 It is possible that such symptoms were already an incipient manifestation of central nervous system  
82 involvement.

83 Cognitive impairment is initially mild and recognized only by family members. It is categorized into frontal  
84 lobe syndrome, which involves impulsivity, promiscuity, apathy, hypotenacity, impaired social judgment, planning  
85 dysfunction, and emotional lability, and subcortical dementia characterized by slowed thinking amnesia, and  
86 executive dysfunction, but without aphasia, apraxia, or agnosia 10. In this case, it was impossible to attribute  
87 a clinical syndrome related to the metabolic disorder, given the history of alcoholism and use of narcotics.

88 IV.

## 89 6 Conclusion

90 This case report represents the importance of a detailed neurological clinical evaluation and the association of  
91 findings with Imaging and laboratory workup. It is a rare disease whose epidemiology in Brazil lacks data, and  
92 complementary tests have reduced specificity.

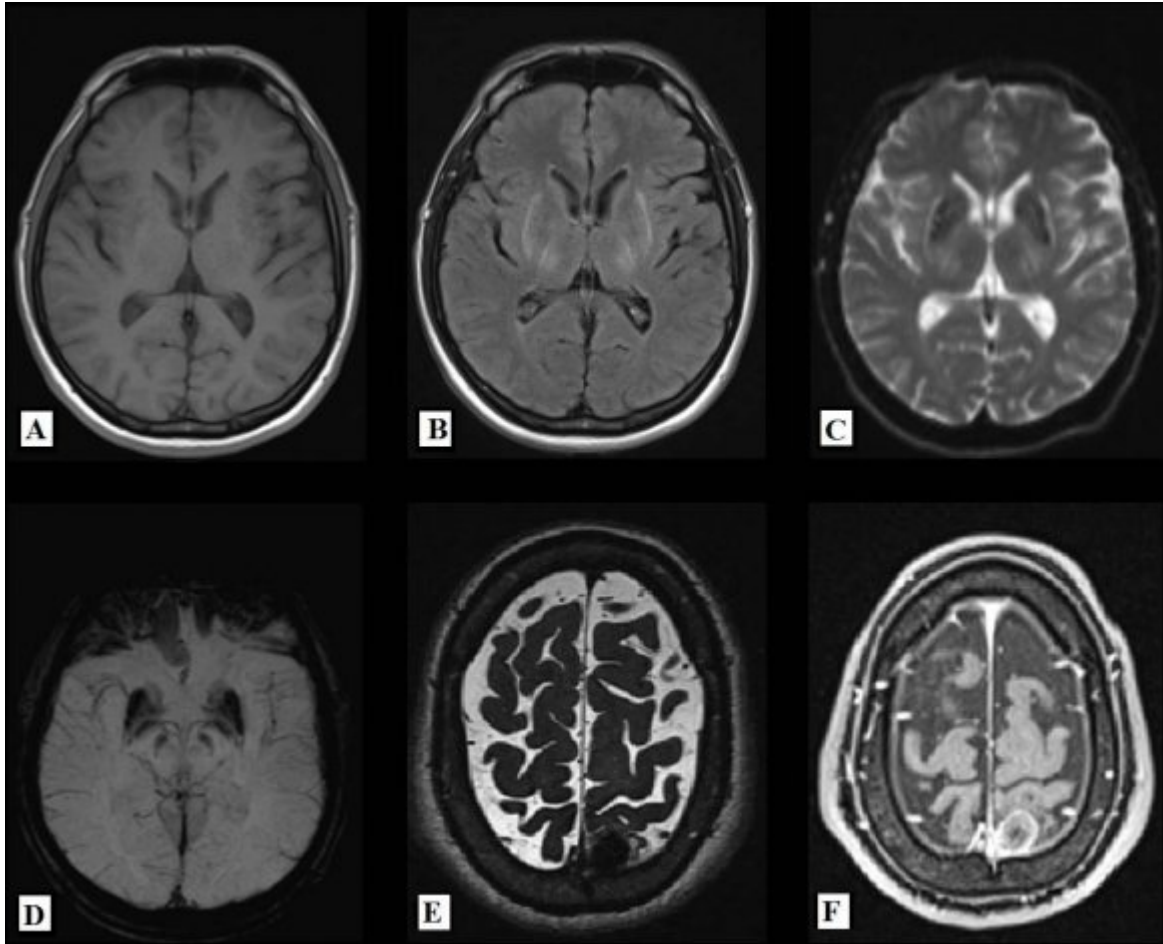


Figure 1: W

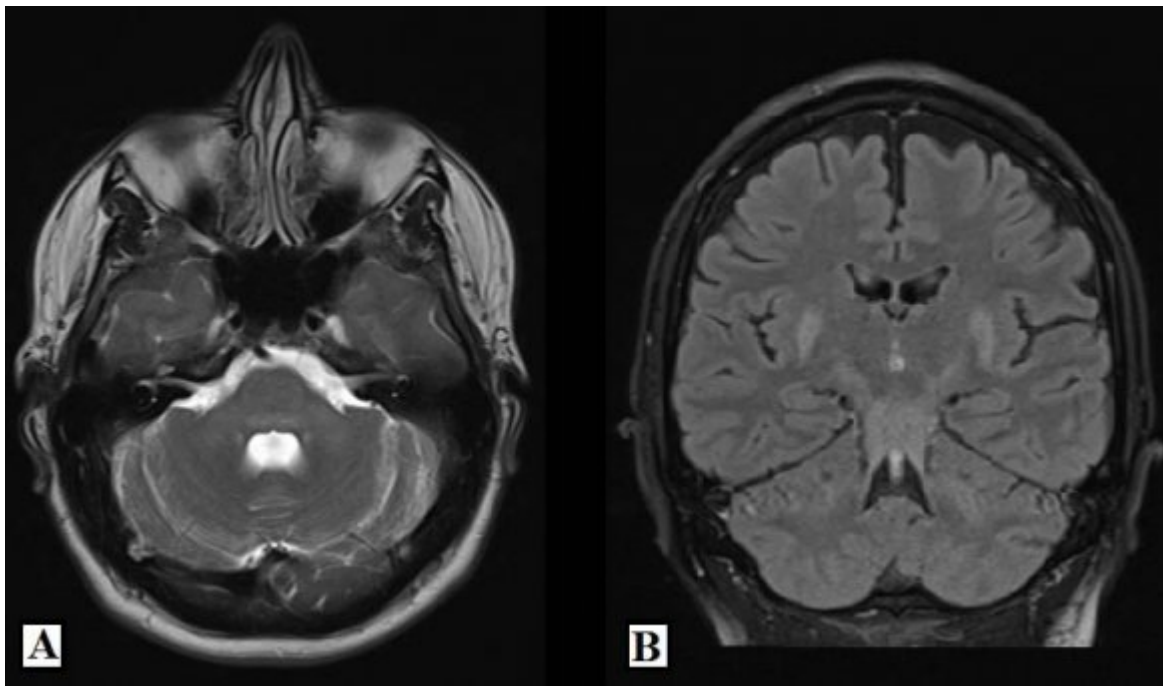


Figure 2:



## .1 Disclosure statement

No potential conflict of interest was reported by the authors.

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