

The neuropathologic abnormalities observed in this case are those usually seen in AHCD, including prominent astrocytic changes, white matter spongy degeneration, and pseudo-laminar cortical necrosis.⁶ The spongy degeneration was marked, particularly in the cerebellar white matter and the internal capsule. Petechial hemorrhages and microabscesses were considered as a terminal event caused by sepsis.

Since the original report of van Woerkom,⁷ most cases of AHCD have been diagnosed in patients with well-established liver disease. Our patient had no historic or clinical evidence of hepatic disease, and the diagnosis of hepatic vein thrombosis and portal-systemic shunting was only considered after MRI and the development of neurologic dysfunction.

In conclusion, this case report suggests that AHCD should be considered when typical neuroradiologic findings are seen in patients with chronic progressive neurologic disorders, even in the absence of overt liver disease or previous episodes of hepatic encephalopathy. A careful search for evidence of liver disease should be made whenever the suggestive AHCD clinical or neuroradiologic findings are found.

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Strokelike presentation of Wilson disease with homozygosity for a novel T766R mutation

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Wilson disease is an inherited autosomal recessive disorder in which there is copper accumulation particularly in the liver and brain. The onset is usually insidious, although acute liver or hematologic,^{1,2} but not neurologic, syndromes have been described. We report a case of Wilson disease in which the patient had sudden onset of neurologic symptoms and signs leading to an initial misdiagnosis of stroke.

Case report. A 17-year-old boy sought treatment at the emergency department; he had been well until that morning, when he had awoken with slurred speech, difficulty swallowing solids, and problems walking. He had also noticed intermittent involuntary movement of his thumbs across his palms. There was no remarkable medical or family history, although he had lost weight during the preceding year. He denied drug use and was taking no medication. The patient, his family, and the team members with whom he played football several times a week were adamant that he had been asymptomatic until the day of presentation and that there had been no personality change, unusual behavior, or decline in school performance.

Examination revealed normal eye movements, severe dysarthria with barely comprehensible speech, slow tongue movements, and a brisk jaw jerk. There was increased tone in the limbs, reflexes were normal, and his gait was severely ataxic. No dyskinesias were seen. Brain CT showed low signal in the right putamen and caudate. In view of the sudden onset of symptoms and the CT findings, a diagnosis of ischemic stroke was made, and he was transferred to the neurology ward, where examination confirmed the previous findings and intermittent dystonic posturing of the arms.

Brain MRI revealed abnormalities bilaterally in the basal ganglia and midbrain (figure) that were suggestive of Wilson disease. Kayser-Fleischer rings were seen on slitlamp examination. Ceruloplasmin was 3 mg/dL (normal, ≥ 16 mg/dL), and urinary copper was 83.37 $\mu\text{mol}/24$ hours (normal, < 0.937 $\mu\text{mol}/24$ hours). Ultrasound of the liver revealed early cirrhotic changes, and γ -glutamyl transpeptidase was mildly increased at 60 U/L, but liver function was otherwise normal. He was treated with penicillamine and zinc, resulting in improvement of his symptoms and resolution of the basal ganglia abnormalities on repeat brain CT, but he was left with residual dysarthria.

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DNA sequencing showed that the patient was homozygous for T766R, a novel mutation in *ATP7B*, the gene associated with Wilson disease. The mutation lies in transmembrane domain 4, a region in which several missense mutations have previously been reported.³ There was no known consanguinity between the parents, but both came from the same small village in central England. Both parents were heterozygous for the T766R mutation. Neither of his two brothers was affected, although genotyping showed that one was a carrier.

Discussion. This case illustrates that Wilson disease may present with a sudden onset of severe neurologic syndrome. The

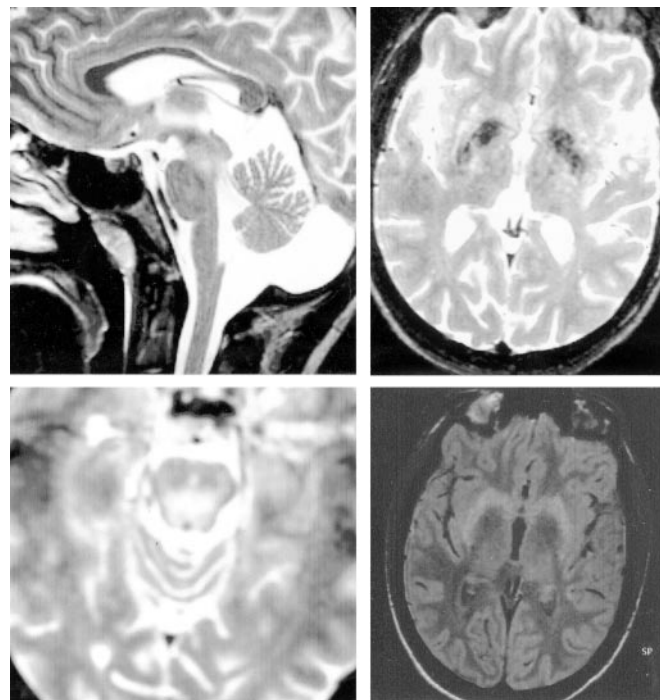


Figure. T2-weighted brain MRI showing hyperintensity in the midbrain, caudate, and putamen and hypointensity in the pallidum with a T1-weighted image (bottom right) for comparison.

fact that our patient was homozygous for a novel mutation in the Wilson gene might suggest a link between the unusual clinical syndrome and his genotype.

The Wilson gene produces a copper-transporting protein of the adenosine triphosphatase family. There are >200 mutations described in the gene, and most patients are compound heterozygotes, making determination of phenotype/genotype associations difficult. To date, no clear associations between a given mutation and clinical phenotype or disease course have been observed. Some authors have reported later onset of neurologic presentations in patients with the most common mutation, His1069Gln, but this is disputed by others.⁴ Different phenotypes are seen with identical mutations and in identical twins,^{2,4,5} suggesting that other genetic and environmental factors are important. For example, the APOE-ε3 genotype delays disease onset by 5 to 11 years.⁶ Dietary copper intake and the ability to counter copper stress at the cellular level might also be expected to play a role.⁵

Although specific genotype/phenotype associations have not been found conclusively in Wilson disease, homozygosity for less common mutations is rare. Therefore, it remains possible that homozygosity for T766R may be associated with a sudden onset of neurologic syndrome, and its rarity may explain the lack of previous reports of this phenotype.

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Frequency-specific mal de débarquement

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After a prolonged period of passive motion, a nonvertiginous sense of dizziness may be experienced when the subject returns to a stationary environment. Patients with this syndrome, referred to as mal de débarquement (MDD), describe a sensation of rocking, tilting, or swaying that may last from hours to years and that is generally most marked when they are stationary.^{1,2} Possible explanations for MDD have included abnormal adaptation to motion, otolith dysfunction, migraine, or psychogenic mechanisms.^{1,3} I describe a patient whose symptoms closely mimicked the subjective head motion dynamics associated with travel in two different cars. This case supports the contention that MDD results from an aberrant adaptive response to passive motion.

Case report. A 55-year-old woman sought treatment for a 4-year history of dizziness. She described her symptoms as a sense of rocking and pitching. These symptoms invariably followed prolonged driving trips, typically occurred in episodes lasting for hours, and were relieved by riding in her automobile. Similar symptoms also occurred after travel in an airplane. While driving her large sedan, she noted a slow, low frequency sense of movement that was reproduced by the abnormal sensation of motion that occurred for hours after her car trip ended. She subsequently purchased a sports car with a much more rigid suspension, such that the head motion she perceived while driving changed substantially, containing a higher frequency and acceleration content. After she began driving the new car, she found that the symptoms that followed car trips changed such that they mimicked the sense of motion experienced in the new car. Although her husband noted similar percepts of motion while driving in the two vehicles, he did not experience any sense of movement after exiting the car.

On examination, eye movements were normal, as was the vestibulo-ocular reflex (VOR). There was no spontaneous or gaze-holding nystagmus, and no nystagmus was provoked with tragal compression, Valsalva maneuver, head shaking, or positional testing. Further diagnostic evaluation included an audiogram, brain MRI, and vestibular testing (calorics, sinusoidal rotation, posturography, vestibular evoked myogenic potentials, and subjective visual vertical). All results were unremarkable, including the time constant of the VOR (17 seconds).

To investigate her symptoms further, we rotated the patient sinusoidally at a frequency of 0.1 Hz for 1 hour. After the motion ended, she experienced a continued sense of sinusoidal movement and estimated its frequency (using hand movements to illustrate perceived rotation) to be between 0.08 and 0.14 Hz.

Discussion. Although the basis for MDD is uncertain, one hypothesis suggests that it is a manifestation of aberrant adapta-

tion. During passive motion there may be a mismatch between the vestibular inputs that encode head motion and other sensory and motor cues that do not correlate with the labyrinthine signals.⁴ Central adaptation may minimize the symptoms provoked by this mismatch, but when the movement ends, the brain must readapt to the stationary environment. It has been suggested that patients with MDD undergo a physiologic adaptive process during passive motion, but for unknown reasons they do not readily adapt back to the stable environment. This impaired return to baseline results in a perception of motion when the subject is stationary.

We describe a subject whose illusionary sense of motion closely mimicked the subjective head movement dynamics produced by travel in two different cars. These percepts of motion presumably reflected transient shifts in the orientation of the gravito-inertial force (produced by linear acceleration) and brief angular movements of the car (produced by irregularities in the road).

This case suggests that her adaptation while driving was tailored to the specific frequency and acceleration characteristics experienced in each car and that this adaptation became symptomatic when she failed to readapt promptly to a stationary environment. Therefore, the symptoms in this subject appear to be a manifestation of impaired adaptation after passive motion, suggesting that this may be the operative mechanism underlying MDD syndromes. Furthermore, her symptoms suggest that percepts of motion may undergo a form of frequency-specific adaptation similar to that observed in the VOR.⁵ This hypothesis is supported by the observation that patient's illusion of motion after prolonged sinusoidal rotation closely approximated the frequency of the preceding rotation.

The central "velocity storage" mechanism that prolongs the VOR response during low frequency movements may contribute to the genesis of motion sickness,⁶ and it is reasonable to postulate that MDD may result from an aberrant increase in velocity storage.¹ In our subject, however, velocity storage (reflected in the VOR time constant) was normal, suggesting that abnormalities in velocity storage are not essential for MDD.

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