

Case Report

Unveiling Wilson Disease: Recurrent Seizures as an Initial Presentation

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<https://doi.org/10.59652/0rdig184>

Abstract: Wilson disease is an autosomal recessive disorder caused by pathogenic variants in ATP7B, resulting in impaired copper excretion and progressive copper accumulation in the liver, brain, cornea, and other tissues. Neurologic disease more commonly presents with movement abnormalities, whereas seizures are an uncommon initial manifestation. We report a 32-year-old man with a 2-year history of recurrent generalized tonic-clonic seizures, followed by intention tremor, dysarthria, gait disturbance, and hypersalivation. Serum ceruloplasmin was markedly reduced (6 mg/dL), 24-hour urinary copper excretion was elevated (321 µg/24 h), Kayser-Fleischer rings were present, and brain MRI showed bilateral basal ganglia and midbrain hyperintensities. A Leipzig score of 8 supported the diagnosis of Wilson disease. Treatment with D-penicillamine, zinc acetate, pyridoxine, dietary copper restriction, and levetiracetam was associated with cessation of seizures and improved functional independence over six months. Wilson disease should be considered in young adults with unexplained recurrent seizures accompanied by progressive movement abnormalities or encephalopathy.

Key clinical message: Wilson disease can rarely present with seizures as an initial neurologic manifestation. It should be considered in young patients with otherwise unexplained recurrent seizures, particularly when movement abnormalities or encephalopathy are also present, because early diagnosis allows disease-specific treatment.

Keywords: Wilson disease, ATP7B, seizures, intention tremor, Kayser-Fleischer rings, copper metabolism.

Received: 15 July 2026

Accepted: 20 September 2026

Published: 27 September 2026

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1. Introduction

Wilson disease was first described clinically in the nineteenth century and was later characterized in detail by neurologist Samuel Alexander Kinnier Wilson in 1912 (1,2). It is an autosomal recessive disorder caused by pathogenic variants in the ATP7B gene on chromosome 13, which impair hepatic copper transport and biliary copper excretion (3-5). The resulting copper accumulation can damage the liver, brain, cornea, kidneys, heart, and other tissues (5-7).

Clinical presentation is broadly hepatic or neuropsychiatric. Hepatic disease often appears earlier in life, whereas neurologic involvement more commonly emerges in the second or third decade. Typical neurologic features include tremor, dystonia, bradykinesia, dysarthria, dysphagia, gait disturbance, and hypersalivation (1,3,4,7,8). Less common manifestations include headache, autonomic dysfunction, and seizures (8,12). Seizures are only rarely the initial manifestation of Wilson disease (12,13), although epilepsy occurs more frequently in affected patients than in the general population (9).

This report describes a 32-year-old man who initially presented with recurrent generalized tonic-clonic seizures and later developed intention tremor and progressive neurologic dysfunction. The case illustrates why Wilson disease should remain in the differential

diagnosis of unexplained seizures in young adults, especially when seizures are accompanied by movement abnormalities or encephalopathy.

2. Case Presentation

A 32-year-old man was evaluated in the outpatient department for recurrent seizures that had been occurring for approximately two years. Episodes were characterized by prolonged drooling, upward deviation of the eyes, and generalized tonic-clonic movements lasting two to three minutes. There was no reported tongue biting or urinary or fecal incontinence.

During the preceding year, he had also developed an intention tremor, dysarthria, an unsteady gait, and excessive salivation. These symptoms progressively impaired his ability to perform activities of daily living independently. He had previously been admitted with diagnoses including encephalitis and epilepsy and had received multiple medications without meaningful improvement. The persistence of seizures together with progressive movement abnormalities prompted further evaluation.

Routine laboratory investigations, including complete blood count, thyroid function, liver function, and renal function tests, were within reference ranges. Serum ceruloplasmin was markedly reduced at 6 mg/dL (reference range, 20-60 mg/dL), whereas 24-hour urinary copper excretion was increased to 321 $\mu\text{g}/24\text{ h}$ (reference range, $<60\text{ }\mu\text{g}/24\text{ h}$). Ophthalmologic examination demonstrated Kayser-Fleischer rings. Abdominal ultrasonography showed a normal-sized liver without sonographic evidence of hepatic disease.



Figure 1. Kayser-Fleischer ring: a dark peripheral corneal ring caused by copper deposition in Descemet membrane.

Brain magnetic resonance imaging demonstrated bilateral, symmetrical hyperintensities involving the basal ganglia and midbrain on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences (Figure 2). The Leipzig score was 8, supporting the diagnosis of Wilson disease.

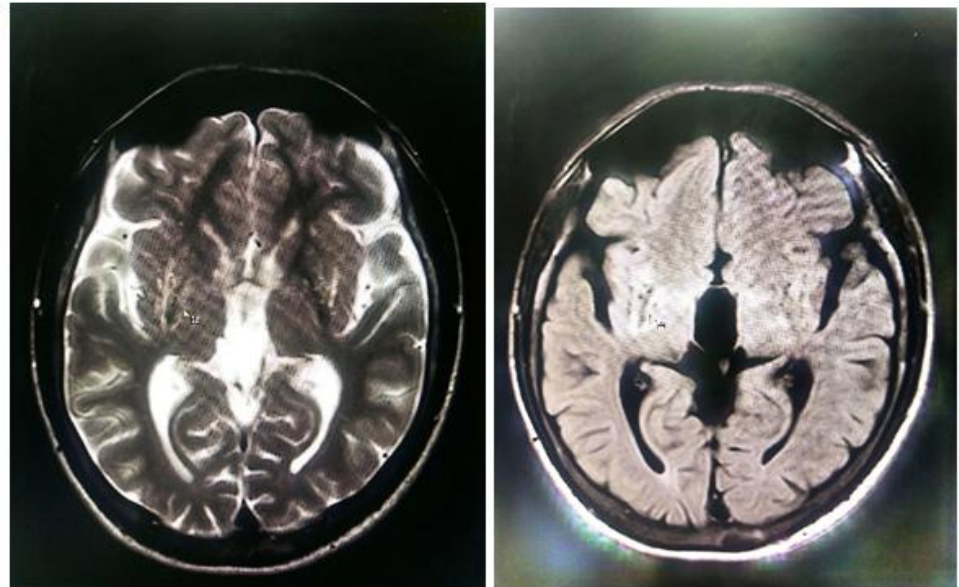


Figure 2. Brain MRI showing bilateral hyperintensities involving the basal ganglia and mid-brain (arrows): (A) T2-weighted image and (B) FLAIR sequence.

3. Differential Diagnosis

The combination of seizures, tremor, and progressive neurologic decline prompted consideration of the following diagnoses:

- Primary epilepsy
- Viral encephalitis
- Mitochondrial or metabolic disease, including Leigh syndrome
- Other neurodegenerative disorders, including Huntington disease and parkinsonian syndromes
- Wilson disease

Wilson disease was established on the basis of markedly low serum ceruloplasmin, increased urinary copper excretion, Kayser-Fleischer rings, characteristic brain MRI abnormalities, and a diagnostic Leipzig score.

4. Treatment and Follow-up

After the diagnosis was established, treatment included dietary copper restriction, with avoidance of high-copper foods such as shellfish, nuts, liver, mushrooms, cocoa, and chocolate. D-penicillamine was started at 250 mg once daily and was gradually increased to 1.5 g/day in divided doses. Zinc acetate was prescribed at 150 mg/day in three divided doses, together with pyridoxine 20 mg/day and levetiracetam 500 mg/day. The levetiracetam dose was adjusted at two-week intervals according to clinical response.

At six months, the patient had experienced marked clinical improvement. Seizures had ceased, and he was again able to perform his daily activities independently. Urinary copper excretion had decreased to 61.26 µg/24 h, close to the laboratory reference range. Written informed consent for publication of the case details and accompanying images was obtained from the patient.

5. Discussion

Wilson disease is a rare autosomal recessive disorder of copper metabolism, affecting approximately 1 in 30,000 people (1). Pathogenic variants in ATP7B impair normal copper transport and biliary excretion, causing progressive copper accumulation, particularly in the liver and brain (10,14). The disease can present across a wide age range, although diagnosis is most common between 5 and 35 years of age (1,3).

Neurologic manifestations are diverse and include behavioral change, dysarthria, tremor, dystonia, bradykinesia, incoordination, hypersalivation, and micrographia (8,11). Seizures are much less typical but are well documented in neurologic Wilson disease (9,12,15). In one clinical-radiologic study, seizures occurred in approximately 15% of patients with neurologic Wilson disease and were associated with cortical and subcortical MRI abnormalities (15). The occurrence of recurrent seizures before the full movement-disorder phenotype is therefore unusual but clinically important.

Epilepsy associated with Wilson disease is often controllable, and seizure burden may improve when the underlying copper disorder is treated (9,15). Antiseizure therapy should be selected with the patient's hepatic status and the potential hepatotoxicity of individual agents in mind (8,9). In the present case, disease-specific therapy together with levetiracetam was followed by cessation of seizures and substantial functional recovery.

Diagnosis relies on the combined interpretation of clinical findings and biochemical testing. Kayser-Fleischer rings, low serum ceruloplasmin, elevated urinary copper excretion, and supportive neuroimaging are important diagnostic features (12,13,18,19). Brain MRI in neurologic Wilson disease commonly demonstrates signal abnormalities involving the basal ganglia, thalamus, brainstem, and related structures (17). Genetic testing for ATP7B variants can confirm the diagnosis, while hepatic copper quantification may be useful in selected diagnostically uncertain cases (13,18).

Treatment is lifelong and aims to reduce copper burden and prevent reaccumulation. Chelating agents such as D-penicillamine or trientine increase copper elimination, whereas zinc reduces intestinal copper absorption (4,13). Dietary copper restriction is used as an adjunct rather than a substitute for pharmacologic therapy. Because Wilson disease is inherited, first-degree relatives should undergo appropriate screening so that presymptomatic disease can be identified and treated early (13).

6. Conclusion

Wilson disease should be considered in young patients with recurrent unexplained seizures, particularly when seizures are accompanied by progressive tremor, dysarthria, gait abnormalities, hypersalivation, or other movement features. In this patient, low serum ceruloplasmin, elevated 24-hour urinary copper excretion, Kayser-Fleischer rings, characteristic MRI abnormalities, and a Leipzig score of 8 established the diagnosis.

Early recognition is clinically important because Wilson disease is treatable. In this case, copper-directed therapy and antiseizure treatment were associated with seizure control and improved functional independence over six months. Timely diagnosis also permits screening of at-risk relatives and may prevent irreversible neurologic injury.

Author Contributions

Asif Islam: Supervision; writing - original draft; writing - review and editing.

Hajirah Nisar: Writing - original draft; writing - review and editing.

Fatima Khurshid: Writing - original draft; writing - review and editing.

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. Patient anonymity and confidentiality were maintained in accordance with ethical standards.

Data Availability Statement

The data supporting the findings of this case report are available from the corresponding author on reasonable request. They are not publicly available because of privacy and ethical restrictions.

Conflict of Interest

The authors declare no conflicts of interest.

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