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# Proximal myopathy in an untreated case of Wilson's disease – A case report

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## Abstract

Wilson's disease (WD) is a genetic disease of autosomal recessive inheritance resulting in the mutation of the adenosine triphosphate 7B (ATP7B) gene. The estimated prevalence of WD is one in 30,000 to 100,000, with a wide age of presentation between 3 to 55 years. Initial manifestations of WD are mainly neurologic, hepatic, or a combination of both. Proximal myopathy, however, is a rare presenting feature, with only a limited number of cases described in the literature. Presenting features such as rhabdomyolysis, hypokalemic muscle paralysis, and spasmodic contractions have been documented, but, as per our knowledge, only one case of proximal myopathy as the initial complaint has been reported. The underlying mechanism of this phenomenon in untreated cases remains unclear and warrants further investigation. We report the case of a 9-year-old female who presented with difficulty in walking, difficulty standing from a sitting position, and jaundice, subsequently diagnosed as WD with proximal myopathy.

**Keywords:** Muscle weakness; myopathy; Wilson's disease.

## Introduction

Wilson's disease (WD) is a rare, inherited autosomal recessive disorder of copper metabolism, resulting in the accumulation of copper in various organs, primarily the liver, brain, and cornea.[1] The estimated prevalence of WD ranges from 1 in 30,000 to 1 in 100,000 individuals.[2] WD typically manifests between the ages of 3 and 55 years.[3] Although hepatic and neurological dysfunction are the most commonly reported presenting symptoms, involvement of other organs has also been documented.[4] Myopathy is reported in patients on penicillamine therapy, but it is rarely observed as an initial presenting symptom of WD.[5] We present the case of a 9-year-old female who initially presented with difficulty in walking and transitioning from a sitting to a standing position, later diagnosed with WD.

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## Case Report

A 9-year-old female presented with a two-month history of generalized swelling, initially involving the abdomen and progressively extending to the face and both lower limbs, accompanied by jaundice and intermittent episodes of epistaxis. Another prominent complaint was difficulty in walking and standing up from a squatting or sitting position, which had also persisted for the past two months. A detailed medical history revealed no familial history of chronic liver disease or Wilson's disease (WD). Additionally, there was no reported history of recent drug use.

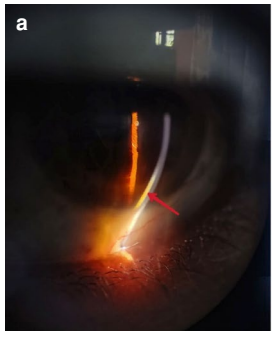
On examination, the patient was hemodynamically stable. Pallor, icterus, bilateral pitting pedal edema, and anasarca were noted. Abdominal examination revealed moderate ascites and mild splenomegaly with a firm consistency. The liver was non-palpable, with a liver span of 8 cm. Neurologically, higher mental functions were age-appropriate, and no cranial nerve deficits were observed. Motor examination demonstrated normal muscle bulk and tone in all four limbs. Strength was graded as 4/5 in the proximal muscles of the upper limbs and 3/5 in the proximal muscles of both lower limbs, according to the Medical Research Council (MRC) grading system. Distal muscle strength was normal, with a grade of 5/5 in all four limbs. Reflexes were intact bilaterally, and a waddling gait was present.

Further investigations revealed anemia (Hb=10.1 g/dL) and thrombocytopenia (62,000/mm³) on complete blood count. Liver function tests indicated mildly elevated direct serum bilirubin levels. Impaired synthetic liver function was evident from a deranged coagulation profile, decreased albumin levels, and a reversal of the albumin-to-globulin ratio (1:2) (Table 1). Ultrasonography showed a liver with heterogeneous echotexture, while the portal Doppler examination was normal. Serum ceruloplasmin levels were found to be low, and 24-hour urinary copper excretion was elevated. Ophthalmic slit-lamp examination revealed the presence of a Kayser-Fleischer (KF) ring (Fig. 1a). According to the Leipzig criteria for the diagnosis of Wilson's disease, the patient met the diagnostic threshold for established Wilson's disease, with a score of 5 (criteria ≥4).[6]

To investigate the muscle weakness further, additional tests were conducted. Given the potential for electrolyte imbalances contributing to the weakness, serum levels of potassium, phosphate, and magnesium were assessed and found to be within normal limits. However, creatine phosphokinase (CPK) levels were elevated (430 U/L, reference range: 26–192 U/L). Nerve conduction studies (NCS) were normal, while electromyography (EMG) demonstrated a myopathic pattern (Fig. 1b). Muscle biopsy could not be performed, as the patient's relatives declined the invasive procedure. Additionally, the patient's coagulogram was deranged. In the absence of other focal neurological deficits, a magnetic resonance imaging (MRI) scan of the brain was not conducted. Although an MRI of the muscles was considered, it was deferred due to financial constraints.

**Table 1.** Biochemical investigations of the patient with reference levels

| Parameter | Patient's value (at admission) | Patient's value (at 6 months follow up) | Reference range |
|---|---|---|---|
| Haemoglobin | 10.1 g/dL | 11.2 g/dL | 12-15 g/dL |
| Platelet | 62000/mm$^3$ | 52000/mm$^3$ | 150000–450000/mm$^3$ |
| Aspartate transaminase | 82.4 U/L | 58.5 U/L | 0–45U/L |
| Alanine transaminase | 27.5 U/L | 26.1 U/L | 0–45 U/L |
| Bilirubin total | 3.16 mg/dL | 1.63 mg/dL | 0.2–1.2 mg/dL |
| Bilirubin direct | 0.95 mg/dL | 0.90 mg/dL | 0–0.3 mg/dL |
| Albumin | 2.23 g/dL | 3.41 g/dL | 3.2–4.5 g/dL |
| Prothrombin time | 30 sec | 26.9 sec | 11–13.5 sec |
| Activated partial thromboplastin time | 60.5 sec | 50.5 sec | 21–35 sec |
| International normalised ratio | 2.2 | 1.99 | <1.1 |
| Serum ceruloplasmin | 10.40 mg/dL | – | 18–45 mg/dL |
| 24-hour urinary Copper | 733.59 mcg/day | – | <50 mcg/day |
| Creatine phosphokinase total (CPK) | 430 U/L | 378 U/L | 26–192 U/L |
| Serum potassium | 3.8 mmol/L | 4.1 mmol/L | 3.5–5.5 mmol/L |
| Serum phosphate | 4.1 mg/dL | 4.4 mg/dL | 3.7–5.4 mg/dL |
| Serum magnesium | 2.0 mg/dL | 2.06 mg/dL | 1.6–2.4 mg/dL |
| Serum uric acid | 3.2 mg/dL | 2.1 mg/dL | 2.3–5.7 mg/dL |
| Vitamin D | 9.75 ng/mL | 14.47 ng/mL | >30 ng/mL |
| PELD score (paediatric end-stage liver disease) | 14.7 | 6.7 | |




b

| EMG Summary Table | Spontaneous | | | MUAP | | | Recruitment |
|---|---|---|---|---|---|---|---|
| Muscle | Fib | PSW | Fasc | Amp | Dur. | PPP | Pattern |
| L. Biceps brachii | - | - | - | 0.5-1µV | 2-5s | + | Early and full |
| L. First dorsal interosseous | - | - | - | 0.5-1µV | 1-5s | + | Early and full |
| R. Vastus lateralis | - | - | - | 0.5-1µV | 5-10s | - | Early and full |
| R. Tibialis anterior | - | - | - | 0.5-1µV | 5-15s | - | Early and full |

**Figure 1.** Features of Wilson's disease **(a)** Slit lamp examination showing Kayser-Fleischer ring (red arrow) indicating copper deposition in Descemet's membrane. **(b)** Electromyography report on admission showing small duration, short amplitude polyphasic Motor Unit Action Potential with early and full recruitment pattern suggestive of myopathic pattern.

EMG: Electromyography; MUAP: Motor unit action potential; Fib: Fibrillation; PSW: Positive sharp waves; Amp: Amplitude; Dur: Duration; PPP: Polyphasic potential; L: Left; R: Right.

Oral vitamin D supplementation was initiated due to low vitamin D levels of 9.75 ng/mL (reference range: >30 ng/mL). The patient was also started on oral fat-soluble vitamins and parenteral vitamin K therapy. Chelation therapy with D-penicillamine was commenced. After receiving treatment, the patient was discharged and continues to follow up for Wilson's disease management. At the 6-month follow-up, the patient remained stable, with notable improvements in gait and muscle strength. However, follow-up EMG continued to demonstrate a persistent myopathic pattern. The biochemical investigations at admission and at follow-up, along with their respective reference ranges, are summarized in Table 1.

## Discussion

Wilson's disease, also known as hepatolenticular degeneration, is an autosomal recessive genetic disorder caused by mutations in the adenosine triphosphate (ATP) 7B gene, which is located on the long arm of chromosome 13 (13q).[7]

Major studies conducted worldwide have shown that the clinical presentation of Wilson's disease primarily involves the liver, brain, and eyes.[4] Musculoskeletal involvement in Wilson's disease is relatively rare.[5] Some authors have reported manifestations such as arthralgia, arthritis, proximal muscle weakness due to hypokalemia, rhabdomyolysis, and spasmodic muscle cramps.[4,5]

Geissinger et al.[8] (1981) first described copper-induced skeletal myopathy in rabbits. In 1996, a case was reported of a patient who experienced recurrent hypokalemic muscle weakness from the age of 13, ultimately being diagnosed with Wilson's disease at the age of 18.[9] Taly et al.[4] evaluated 282 patients with Wilson's disease over three decades and found that 2.1% (6 patients) had musculoskeletal involvement, including arthralgia, arthritis, or proximal myopathy. In 2013, Rosen et al.[10] reported a case of a 10-year-old boy who experienced intense spasmodic lower limb muscle cramps over a period of 3 months and was subsequently diagnosed with Wilson's disease.

Padmanabha et al.[5] described proximal myopathy as a presenting manifestation in an 8-year-old boy who was later diagnosed with Wilson's disease. In this case, the patient's CPK level (89 IU/L) and nerve conduction velocity (NCV) were normal, while electromyography (EMG) revealed a myopathic interference pattern in the quadriceps femoris. In contrast, in our case, the CPK level was elevated, and EMG findings were consistent with a myopathic pattern.

Although generalized muscle wasting is commonly observed in adults with chronic liver diseases, isolated proximal myopathy is not a well-recognized feature, particularly in the pediatric population. Therefore, in our patient, Wilson's disease was suspected as the likely cause of myopathy, prompting further investigations. Had a muscle biopsy been performed in our case to identify copper deposition in the affected muscles, it could have provided additional support for this intriguing initial presentation of Wilson's disease.

The pathophysiology underlying muscle weakness in Wilson's disease remains unclear. It is hypothesized that copper accumulation in skeletal muscles may lead to oxidative stress, the formation of free radicals, secondary mitochondrial dysfunction, and ultimately cell death.[5] This case report highlights a rare and intriguing manifestation of Wilson's disease in the form of myopathy, the underlying mechanisms of which have yet to be fully elucidated. Further investigation and studies are needed to better understand this association.

## Conclusion

The presentation of Wilson's disease with myopathy is rare, and such an association should be considered when encountering a patient exhibiting features of Wilson's disease alongside myopathy. The pathophysiology underlying this presentation remains unclear and warrants further investigation.

**Ethics Committee Approval:** This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

**Informed Consent:** Written informed consent was obtained from participants.

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## References

1. Hedera P. Wilson's disease: A master of disguise. Parkinsonism Relat Disord 2019;59:140–145. [CrossRef]
2. Scheinberg IH, Sternlieb I. Wilson's Disease. Philadelphia: W.B. Saunders; 1984.
3. Wiernicka A, Dądalski M, Jańczyk W, Kamińska D, Naorniakowska M, Hüsing-Kabar A, et al. Early Onset of Wilson Disease: Diagnostic Challenges. J Pediatr Gastroenterol Nutr 2017;65(5):555–560. [CrossRef]
4. Taly AB, Meenakshi Sundaram S, Sinha S, Swamy HS, Arunodaya GR. Wilson disease: Description of 282 patients evaluated over 3 decades. Medicine (Baltimore) 2007;86:112–121. [CrossRef]
5. Padmanabha H, Sethuraman A, K Sarma GR. Proximal myopathy as a presenting manifestation of Wilson's disease. Neurol India 2019;67:1152–1153. [CrossRef]
6. Ferenci P, Caca K, Loudianos G, Mieli-Vergani G, Tanner S, Sternlieb I, et al. Diagnosis and phenotypic classification of Wilson disease. Liver Int 2003;23(3):139–142. [CrossRef]
7. Chang IJ, Hahn SH. The genetics of Wilson disease. Handb Clin Neurol 2017;142:19–34. [CrossRef]
8. Geissinger HD, Robinson GA. Copper induced skeletal myopathy in rabbits. Can J Comp Med 1981;45(1):97–102.
9. Chu CC, Huang CC, Chu NS. Recurrent hypokalemic muscle weakness as an initial manifestation of Wilson's disease. Nephron 1996;73(3):477–479. [CrossRef]
10. Rosen JM, Kuntz N, Melin Aldana H, Bass LM. Spasmodic muscle cramps and weakness as presenting symptoms in Wilson disease. Pediatrics 2013;132(4):e1039–e1042. [CrossRef]