

Wilson's disease presenting as resistant rickets without Fanconi syndrome

Bhavin Patel¹, Vijay Sardana²

From ¹Senior Resident, ²Senior Professor and Head, Department of Neurology, Government Medical College, Kota, Rajasthan, India

Correspondence to: Dr. Vijay Sardana, Department of Neurology, Government Medical College, Kota, Rajasthan, India.

E-mail: vsard13@gmail.com

Received - 14 January 2020

Initial Review - 30 January 2020

Accepted - 18 February 2020

ABSTRACT

Wilson's disease is a disorder of copper metabolism which usually presents with neurological or hepatic manifestation. Wilson's disease presenting as a musculoskeletal disorder is rare. We are reporting the case of a 12-year-old male boy presented with resistant rickets followed by dysarthria. The patient was diagnosed as having Wilson's disease based on Kayser–Fleischer ring on examination, high 24 h urinary copper level, and magnetic resonance imaging brain changes. This case highlights that in the case of resistant rickets, a high index of suspicion for Wilson's disease should be kept. Early recognition of this entity results in timely treatment and prevention of significant disability.

Key words: *Arthropathic manifestation, Dysarthria, Resistant rickets, Wilson's disease*

Wilson's disease (hepatolenticular degeneration) is an autosomal recessive disorder of biliary copper excretion due to mutation in the ATP7B gene on chromosome 13. Worldwide, its prevalence is approximately 1 case in 30,000 live births. There is impaired biliary copper excretion which leads to the accumulation of copper in various body tissues predominantly in the liver, brain, and cornea. An arthropathic manifestation of Wilson's disease occurs in a later stage and that too in 25–50% of patients [1]. The patient presenting with musculoskeletal symptoms is rare in Wilson's disease. Fanconi syndrome is characterized by an impairment of the proximal renal tubule function that leads to glycosuria, phosphaturia, and aminoaciduria. Fanconi syndrome is one of the reasons for the musculoskeletal manifestation in Wilson's disease.

Here, we are reporting the case of a child who presented as resistant rickets and subsequently diagnosed as having Wilson's disease. In our case, resistant rickets is not associated with Fanconi syndrome which thought to be a common reason behind musculoskeletal involvement. Nutritional rickets is a common musculoskeletal condition affecting children in developing countries when it is resistant to usual treatment, other diagnoses should be thought including Wilson's disease.

CASE REPORT

A 12-year-old Hindu male child born by non-consanguineous marriage with a normal birth history and developmental milestone presented with complaint of bilateral knee joint pain. It was insidious in onset, gradually progressive in intensity, and almost continuous throughout the day for the past 3 years. Due to the pain, he had difficulty in standing from a squatting

position. There was no history of joint swelling or tenderness. After 4–5 months of knee joint pain, the patient's relative noticed deformity in the bilateral lower limb in the form of knock knee which was also gradually progressive since onset. For the past 6 months, relative also noticed mild difficulty in a speech in the form of effortful speech with an intermittent pause in between which was insidious in onset and slowly progressive. There was no history of weakness, sensory paresthesia, other cranial nerve abnormality, and imbalance while walking, any abnormal movement including seizures and tremulousness, skin rashes, fever, or other joint pain. There was no history of jaundice or ascites. Family history was non-significant. His diet was deficient for adequate calcium requirement and sun exposure was good. He was treated as having nutritional rickets for 1.5 years with an adequate dose of Vitamin D and calcium, but the illness was progressive despite good compliance.

On general examination, the patient was malnourished and moderately built. His vitals were normal. No signs of jaundice were present. Musculoskeletal examination revealed rachitic rosary and genu valgus in the bilateral lower limbs. Mild hepatomegaly was present on the abdominal examination. Neurological examination was suggestive of normal mental status with spastic dysarthria and normal cranial nerve examination. Motor system examination revealed normal tone with power 4/5 in both lower limbs and normal reflex. There were no signs suggestive of extrapyramidal involvement. Sensory and cerebellar examination was normal with no meningeal signs. On slit-lamp examination, Kayser–Fleischer (KF) ring was present in both the eyes.

Investigations revealed microcytic hypochromic anemia, normal renal function, and liver function except elevated serum alkaline phosphate level. Serum calcium and phosphorus levels

were normal. Vitamin D level was 26.57 ng/ml which is in the insufficient range. Serum parathyroid hormone, Vitamin B12, antinuclear antibody, and serum C-reactive protein levels were normal. Urine routine microscopy report showed no pus cells with nil sugar and proteins. The 24 h urinary copper level was 267.40 mg/l (3–80 mg/l). X-ray of bilateral knee joint and wrist was suggestive of widened growth plate with splaying and cupping of metaphysis which has reduced density along with thin bony spur extending from the metaphysis to surrounding uncalcified growth plate. These changes were suggestive of rickets. Ultrasound abdomen was showing an altered echotexture of the liver with mild hepatomegaly. Magnetic resonance imaging (MRI) brain showed hyperintensity in T2 and fluid-attenuated inversion recovery images with hypointense T1 image without any diffusion restriction in bilateral thalamus (Fig. 1), basal ganglia, dorsal midbrain, and pons (Fig. 2). The patient could not afford genetic testing and gave a negative consent for the liver biopsy.

Given the presence of KF ring with high 24 h urinary copper and MRI brain changes, a diagnosis of Wilson's disease was kept and the patient was treated with D-penicillamine. The patient showed significant improvement in knee pain and able to stand from a sitting position. Repeat urine routine and microbiology report was also nil for sugar and amino acid.

DISCUSSION

Wilson's disease is a relatively rare genetic disorder which commonly present as neuropsychiatric or liver disorder. Musculoskeletal involvement as a presenting feature is quite rare in Wilson's disease. Morgan *et al.* [2] were first to report the case of Wilson's disease with a rachitic presentation in 1962. From the Indian subcontinent, Mehta and Shinde [3] reported a similar case in 1965 after which there are few case reports published by Kabra *et al.* [4], Goyal *et al.* [5], and Joshua [6], etc. In 2014, Basu [7] from Sri Lanka published a case report of Wilson's disease with resistant rickets. In all these case reports, the cause of resistant rickets in Wilson's disease patient was Fanconi syndrome, leading to renal tubular acidosis. In our case, the patient was having resistant rickets without Fanconi syndrome. A similar case presented by Ghosh *et al.* [8], in which the patient was having rickets without Fanconi syndrome.

Rickets in the Indian population is considered secondary to nutritional deficiency unless proved otherwise. Our patient was also treated as having the same for a long time with adequate supplements but did not respond to it. Considering the appearance of dysarthria, the possibilities of connective tissue disorder with vasculitis, hypoparathyroidism with basal ganglia involvement, and Wilson's disease were considered. KF ring on slit-lamp examination followed by laboratory data showing high 24 h urine copper level leads to the diagnosis of Wilson's disease.

In Wilson's disease, the occurrence of rickets is thought to be secondary to hypoparathyroidism or Fanconi syndrome. In a rare instance, it can also occur due to the deposition of copper in the synovial membrane and cartilage. Kramer *et al.* [9] demonstrated

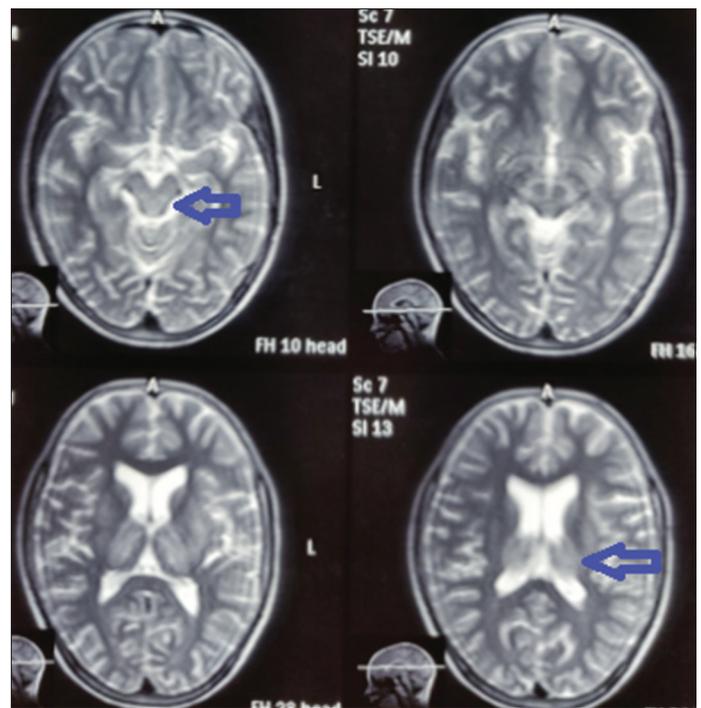


Figure 1: T2-weighted images showing hyperintensity in bilateral thalamus and basal ganglia

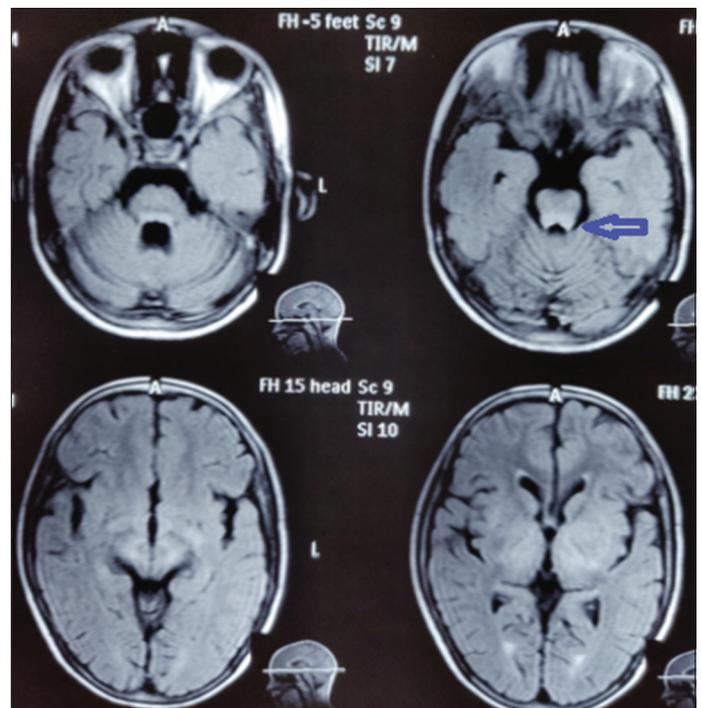


Figure 2: Fluid-attenuated inversion recovery images showing hyperintensity in dorsal midbrain

a high concentration of copper and iron in the synovial membrane of joints in patients with Wilson's disease by X-ray energy spectroscopy and postulated that the synovial copper deposition can be a possible explanation of arthropathy. Although a cartilage matrix glycoprotein exhibiting marked homology with ceruloplasmin has recently been described, there remains scant evidence to directly implicate copper accumulation in the pathogenesis of osteoarticular changes observed in Wilson's disease [10].

In our case, the patient had a low phosphorus level with normal calcium and elevated alkaline phosphatase that was favoring hypophosphatemic rickets caused by Fanconi syndrome. However, on urine examination, there were no glycosuria, aminoaciduria, or phosphaturia, which were against Fanconi syndrome. Repeat urine examination to rule out the possibility of Fanconi syndrome was done which also came out to be normal. Given the normal parathyroid hormone level, we considered the possibility of copper deposition in the synovial membrane as a possible cause of rickets in our case. However, it could not be confirmed due to the unavailability of X-ray energy spectroscopy.

Overall, arthropathic manifestations are less common in Wilson's disease, but as compared to the Western world, the Indian population had a different scenario in this regard. Usually, nutritional deficiency rickets which is a more common entity responds well to proper treatment. Olsen *et al.* [11] reported recurrent arthritis in a child as presenting a complaint of Wilson's disease and they stressed that clinicians should consider Wilson's disease in case of repetitive unexplained joint symptoms in the pubertal period as in case of unexplained liver and neurological involvement. In any case of rickets who do not respond to usual treatment, the possibility of Wilson's disease should be considered and the patient should be thoroughly examined and investigated for the same.

CONCLUSION

A high index of suspicion for Wilson's disease should be kept in case of resistant rickets. Heightened awareness in clinicians of possible rachitic presentation of Wilson's disease results in the

early diagnosis and timely treatment. Delay in treatment increases morbidity in Wilson's disease.

REFERENCES

1. Golding DN, Walshe JM. Arthropathy of Wilson's disease. Study of clinical and radiological features in 32 patients. *Ann Rheum Dis* 1977;36:99-111.
2. Morgan HG, Stewart WK, Lowe KG, Stowers JM, Johnstone JH. Wilson's disease and the Fanconi syndrome. *Q J Med* 1962;31:361-84.
3. Mehta RS, Shinde VA. Wilson's disease with rickets. *Neurol India* 1965;13:67-73.
4. Kabra SK, Bagga A, Malkani I. Wilson's disease presenting with refractory rickets. *Indian Pediatr* 1990;27:395-7.
5. Goyal JP, Kumar N, Rao SS, Shah VB. Wilson's disease presenting as resistant rickets. *Gastroenterology Res* 2011;4:34-5.
6. Joshua GE. Hepatolenticular degeneration (Wilson's disease) and rickets in children. *Indian J Med Res* 1973;61:1876-84.
7. Basu M. Wilson disease presenting as a case of resistant rickets. *Sri Lanka J Child Health* 2014;43:106-7.
8. Ghosh JB, Chakrabarty S, Singh AK, Gupta D. Wilson's disease--unusual features. *Indian J Pediatr* 2004;71:937-8.
9. Kramer U, Weinberger A, Yarom R, Zoldan J, Bahar A, Godoth N. Synovial copper deposition as a possible explanation of arthropathy in Wilson's disease. *Bull Hosp Jt Dis* 1993;52:46-9.
10. Menerey KA, Eider W, Brewer GJ, Braunstein EM, Schumacher HR, Fox IH. The arthropathy of Wilson's disease: Clinical and pathologic features. *J Rheumatol* 1988;15:331-7.
11. Olsen BS, Helin P, Mortensen HB. Recurrent arthritis in a child. A rare manifestation of Wilson's disease. *Ugeskr Laeger* 1996;158:4305-6.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Patel B, Sardana V. Wilson's disease presenting as resistant rickets without Fanconi syndrome. *Indian J Case Reports*. 2020;6(2):90-92.

<https://doi.org/10.32677/IJCR.2020.v06.i02.016>