CASE REPORT
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WILSON'S DISEASE- ATYPICAL RADIOLOGICAL PRESENTATION WITH FRONTAL LOBE INVOLVEMENT

Neurology

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ABSTRACT

Background: Wilson's disease is a rare autosomal recessive disorder of copper metabolism resulting from mutations in the ATP7B gene. The consequent toxic accumulation of copper primarily affects the liver and brain. While neuroimaging commonly reveals basal ganglia and thalamic involvement, atypical findings such as frontal lobe and white matter tract lesions may indicate early or aggressive disease forms. **Case Report:** A 17-year-old female presented with progressive neurological symptoms and characteristic Kayser–Fleischer rings. Brain MRI demonstrated symmetrical hyperintensities in the frontal lobes, basal ganglia, and brainstem, along with pathognomonic features of Wilson's disease. Laboratory investigations revealed decreased serum ceruloplasmin and increased 24-hour urinary copper excretion. Initiation of D-penicillamine, zinc acetate, and pyridoxine therapy led to partial neurological improvement. **Discussion:** This case illustrates an uncommon neuroimaging pattern of Wilson's disease with prominent frontal cortical and brainstem involvement accompanied by iron deposition. Recognition of such atypical presentations expands the known radiological spectrum and aids differentiation from other white matter disorders. Frontal lobe lesions, in particular, may correlate with executive dysfunction and cognitive impairment. Early diagnosis through clinical suspicion, biochemical evaluation, and MRI is crucial to prevent irreversible neurological damage. **Conclusion:** Unusual neuroimaging features, including frontal lobe and white matter involvement, should prompt consideration of Wilson's disease in pediatric or adolescent patients presenting with unexplained dystonia or neurological deficits. Timely initiation of chelation therapy can significantly improve outcomes and mitigate long-term morbidity. Enhanced awareness and the use of advanced imaging modalities are vital for early detection and management.

KEYWORDS

Wilson's disease, copper metabolism, MRI, frontal lobe, basal ganglia, white matter, Kayser–Fleischer rings, neuroimaging, chelation therapy, pediatric neurology

INTRODUCTION:

Wilson's disease (WD) is a rare autosomal recessive disorder caused by mutations in the ATP7B gene, leading to defective copper metabolism. This results in excessive copper accumulation, primarily in the liver, which eventually spills into the bloodstream and deposits in various organs, including the brain [1]. Approximately 40% of patients initially present with hepatic manifestations, 40%-50% exhibit neurological symptoms, and 10% primarily display psychiatric symptoms [2]. Biochemically, WD is marked by reduced serum ceruloplasmin levels and increased urinary copper excretion, aiding in diagnosis. This case report presents an atypical imaging spectrum, including bilateral symmetrical deep grey nuclei involvement, brainstem signal abnormalities, and uncommon frontal lobe changes [3]. Importantly, the presence of Kayser-Fleischer rings reinforces clinical suspicion of Wilson's disease[4]. These findings suggest early or aggressive disease activity, contributing to expanding the known radiological spectrum of WD.

Case Report:

A 17-year female presented to neurology department in Dr. Pinnamaneni Siddhartha institute of medical sciences and research foundation with complaints of difficulty in walking, tremors, dysarthria, dysphagia, excessive drooling of saliva and loss of appetite over past 3 years which was aggravated in last 2 months. Upon ophthalmic examination the patient had Kayser-Fleischer (KF) ring.

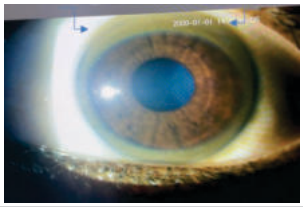

Fig-1: Slit lamp examination showing Kayser-Fleischer (KF) ring.

Routine blood investigations were done and which came out normal. A Magnetic resonance imaging (MRI) scan of brain was done and it revealed bilateral symmetrical T2 & FLAIR hyperintensities noted involving frontal lobes, basal ganglia, internal capsule and long tracts in mid part of pons. Bilateral symmetrical involvement of middle cerebellar peduncles noted. Excess iron deposition seen in basal ganglia region, claustrum and also substantianigra in a layered pattern.

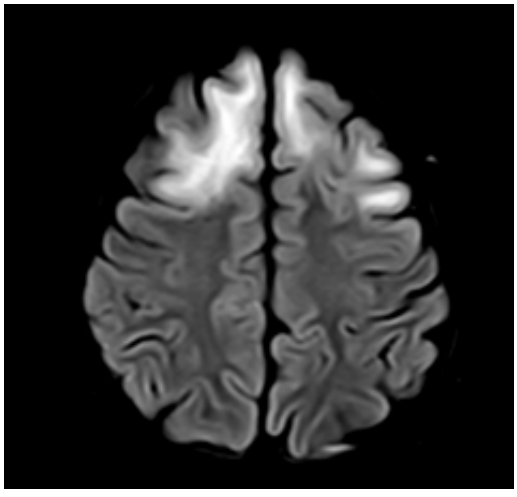

Fig. 2 MRI showing, Axial FLAIR - confluent hyperintensity in the bilateral frontal subcortical white matter, representing cortical/white matter involvement.

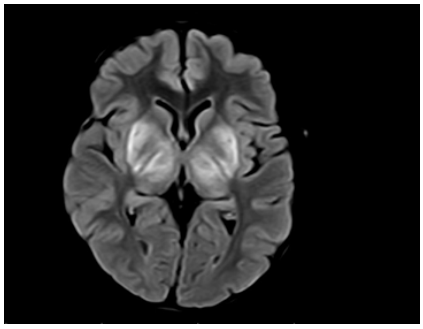

Fig. 3 MRI showing, Axial FLAIR at the level of the basal ganglia demonstrates symmetric hyperintensity of the putamina and thalami, - favor Wilson disease.

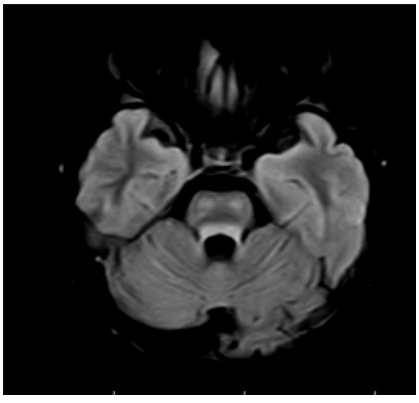

Fig. 4 MRI showing, Axial FLAIR demonstrating central pontine hyperintensity with relative sparing of corticospinal tracts - Trident sign.

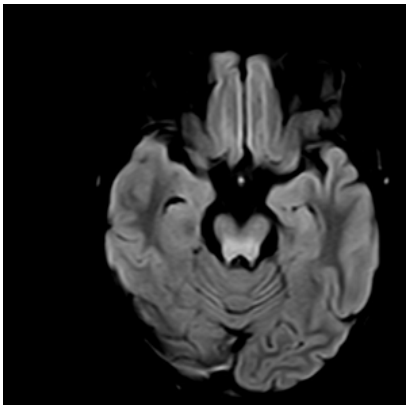

Fig. 5 MRI showing, Axial FLAIR at the level of the midbrain - hyperintensity in the tegmentum with preserved red nuclei and substantia nigra, consistent with the classic "face of the giant panda sign."

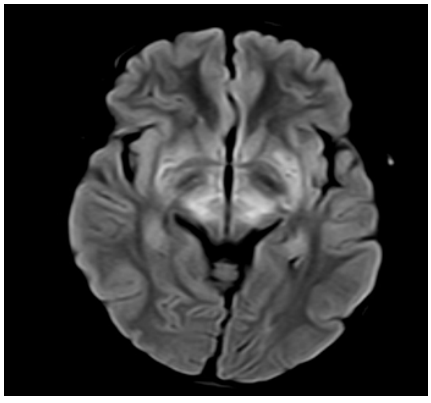

Fig. 6 MRI showing, Axial FLAIR image through the caudate nuclei shows bilateral symmetric hyperintensity extending into the periventricular white matter, reflecting advanced disease.

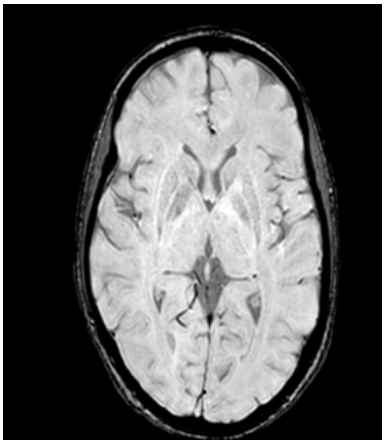

Fig. 7 MRI showing, Axial susceptibility-weighted image (SWI) shows blooming in the basal ganglia and thalami, indicating copper and associated iron deposition.

Further laboratory investigations like serum ceruloplasmin, serum copper and 24-hour urinary copper were supportive of the diagnosis of Wilson's disease. Additional investigation of ultrasonography of abdomen and pelvis was done which was reported normal. A diagnosis of Wilson's disease was made using radiological and laboratory investigations, and treatment with penicillamine, along with anticonvulsants and other supportive measures, was initiated. Following the diagnostic evaluation, the patient was advised to take gradually increasing doses of D-penicillamine, with a daily dosage of 250 mg, Pyridoxine 25mg once daily at the time of discharge, aimed at preventing sudden exacerbation of neurological symptoms. Additionally, zinc acetate at a dosage of 50 mg three times a day and pyridoxine were included in the treatment regimen. Notably, there was no observed deterioration in the neurological symptoms throughout the course of treatment, and the patient did not manifest any adverse reactions to the prescribed medications. Subsequently, family members of the patient were screened and were reported normal. The patient was discharged from the hospital and a follow-up appointment was scheduled to monitor the progress and adjust the treatment plan as necessary. This comprehensive approach highlights the importance of continuous monitoring and individualized treatment strategies in the management of Wilson's disease across different age groups.

DISCUSSION:

Wilson's disease primarily affects the extrapyramidal structures (e.g., basal ganglia, thalamus, brainstem), but white matter tract involvement (e.g., dentatorubrothalamic, pontocerebellar, corticospinal tracts) remains underrecognized[5]. Subcortical white matter changes, although uncommon, can occur and have been associated with disease severity [6]. The bilateral frontal lobe involvement in this case represents a rarer neuroimaging pattern, potentially signifying early or aggressive disease activity [7].Additionally, brainstem signal changes observed here further reinforce metabolic or cytotoxic injury patterns, which are rarely documented in WD [8]. While Kayser-Fleischer rings are a well-recognized ophthalmic marker, their presence in conjunction with diffusion restriction in the fronto-parietal region further supports the diagnosis [9]. These findings underscore the importance of MRI in identifying atypical WD presentations, facilitating early therapeutic intervention [10]. Understanding these inflammatory pathways could open avenues for targeted neuroprotective therapies.Advanced MRI techniques, such as magnetic resonance spectroscopy (MRS), could help in assessing metabolic changes in WD [11]. MRS studies show alterations in choline and N-acetyl aspartate (NAA) levels, potentially serving as biomarkers for disease progression [12]. Including insights on alternative therapies highlights evolving treatment approaches.A detailed differential diagnosis was undertaken to exclude other causes of white matter abnormalities, including HIV encephalopathy, acute disseminated encephalomyelitis (ADEM), extrapontinemyelinolysis, and post hypoxic encephalopathy [13]. These were meticulously ruled out through clinical history, laboratory tests, and imaging review.Importantly, initiation of chelation therapy with penicillamine and zinc, along with symptomatic management, led to partial neurological recovery and normalization of laboratory parameters over a three-month follow-up, underscoring the potential reversibility of WD with early treatment [14].

CONCLUSION:

Wilson's disease is a rare yet treatable condition that can present with a wide spectrum of neurological symptoms, particularly in pediatric patients. This case highlights the importance of maintaining clinical suspicion for Wilson's disease in children with unexplained dystonia or other neurological abnormalities, especially when accompanied by atypical neuroimaging findings such as white matter changes and basal ganglia lesions. Early diagnosis, achieved through a combination of clinical evaluation, biochemical tests, and MRI findings, plays a critical role in preventing irreversible damage to vital organs like the liver and brain. Timely initiation of chelation therapy and appropriate supportive care can lead to significant clinical improvement. Increased awareness among healthcare professionals and further research into neuroimaging patterns can enhance early detection, improve outcomes, and reduce disease-related morbidity.

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