Case Report

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Internal Medicine Section

Widespread Grey and White Matter Abnormalities in 15-year-old Female: A Case Report on a Rare Radiological Presentation of Wilson Disease

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ABSTRACT

Wilson disease is a genetic disorder affecting copper metabolism, characterised by the accumulation of excess copper, primarily in the liver and brain, and the liver's inability to excrete copper into the bile. The putamen, lentiform nucleus, thalamus, and brainstem are prominently involved in Magnetic Resonance Imaging (MRI) of the brain in Wilson disease, while lesions affecting grey and white matter are rare. Hereby, the authors present a case of a 15-year-old female patient who presented with postural tremor, dystonia, rigidity, dysarthria, and gait instability, along with bilateral Kayser-Fleischer rings and symmetric grey and white matter T2 hyperintensities in the fronto-temporo-parietal region. Therefore, patients exhibiting clinical signs of neurological involvement and abnormal MRI findings should be thoroughly evaluated for Wilson disease, as it is a disabling yet treatable disorder.

Keywords: Copper, Drooling, Kayser-Fleischer ring, Magnetic resonance imaging brain

CASE REPORT

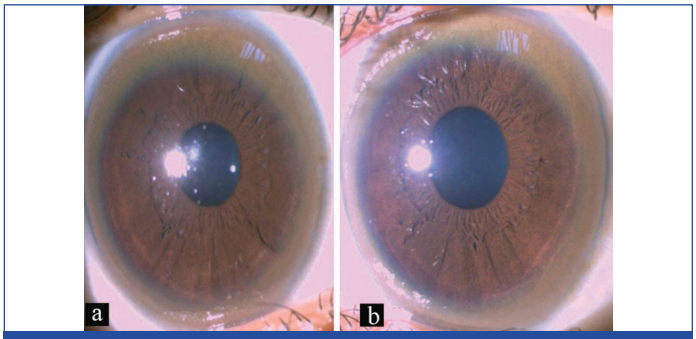
A 15-year-old female student presented to the Neurology Outpatient Department (OPD) with the chief complaint of abnormal body movements for the past 1.5 years and mental abnormalities for the past six months. On detailed history taken from the patient's mother, it was noted that the patient was apparently asymptomatic 1.5 years ago when she developed complaints of tremulousness in both hands and tightness in the left arm, accompanied by reduced movement during activity. This was associated with intermittent drooling of saliva and was followed by progressive difficulty in speech, swallowing, and writing over the next year.

For the past six months, she has experienced a progressive decline in scholastic performance, along with some degree of personality changes, including continuous smiling, lack of interest in daily activities, and the repetition of the same sentences. Additionally, she has had difficulty dressing herself for the past two months. She was born to non consanguineous parents without any significant birth or developmental history, and the family history was negative.

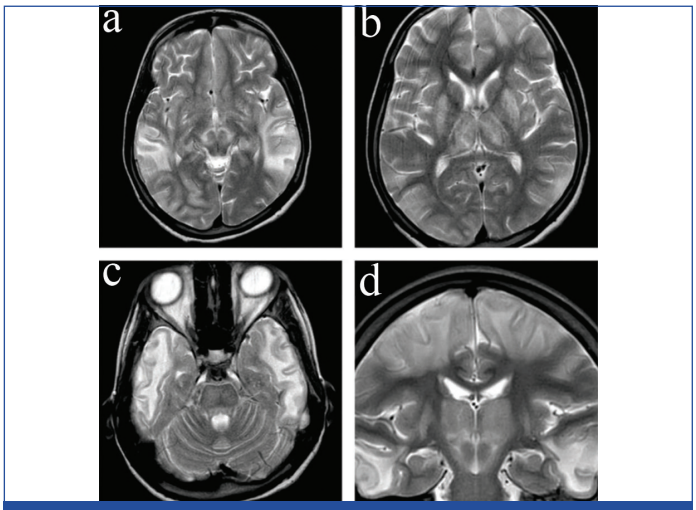
On examination, she exhibited postural tremor, generalised dystonia, dysarthria, and gait instability, with rigidity more pronounced on the left-side. Ophthalmological examination via slit-lamp biomicroscopy confirmed the presence of bilateral hyperdense areas of copper deposits in Descemet's membrane of the cornea, suggesting Kayser-Fleischer rings (K-F rings) [Table/Fig-1a,b].

Further investigations revealed normal liver function tests, but altered liver parenchymal echogenicity on ultrasonography. Serum ceruloplasmin level was recorded at 13.7 mg/dL (normal range: 20-40 mg/dL), and 24-hour urinary copper excretion was 60 mcg/day (normal range: 15-60 mcg/day).

The MRI showed confluent T2 hyperintensity involving the bilateral fronto-temporal lobes in a symmetric fashion. Similar, but less severe, signal changes were also noted in the bilateral parietal lobes. Bilateral symmetrical T2 hyperintensity was observed in the bilateral lentiform nucleus, head of the caudate, and thalami, along with mild signal changes in the external capsule and claustrum. Mild signal changes were also identified in the midbrain, pons, and superior cerebellar peduncle [Table/Fig-2a-d].



[Table/Fig-1]: (a) Showing K-F ring in the right eye; (b) Showing K-F ring in the left eye.



[Table/Fig-2]: MRI brain, showing (a) Confluent T2 hyperintensity in the bilateral parietal lobe; (b) Bilateral symmetrical T2 hyperintensity in bilateral lentiform nucleus, head of caudate, and thalami along mild signal changes in the external capsule/claustrum; (c,d) Confluent T2 hyperintensity involving bilateral frontotemporal lobe in a symmetric fashion. Mild signal changes are also seen in the midbrain, pons, and superior cerebellar peduncle.

The diagnosis of Wilson disease was confirmed, as the patient exhibited symptoms consistent with a K-F ring, a serum ceruloplasmin level of less than 20 mg/dL, and a 24-hour urinary copper excretion exceeding 40 mg/day. She was initially started on the copper chelator

penicillamine at 250 mg once daily, trihexyphenidyl at 2 mg twice daily, and zinc acetate (equivalent to 50 mg of elemental zinc) three times daily, along with a copper-restricted diet. As a result of this treatment, the patient has shown symptomatic improvement and has been under regular follow-up for the past six months for dosage titration of the aforementioned medications based on her clinical condition.

DISCUSSION

Wilson disease is a genetic condition that causes abnormal copper metabolism. It is inherited in an autosomal recessive pattern and is characterised by Central Nervous System (CNS) symptoms, liver cirrhosis, and the deposition of copper in various tissues as a result of the loss of function of the ATP7B gene, which is associated with gains or losses on chromosome 13q14.3-q21.1. The incidence of the disease is estimated to be between 1 in 50,000 and 100,000 individuals [1]. The manifestations at the time of presentation can vary. Common complaints are primarily associated with liver and CNS involvement.

In present case, a young female presented with postural tremor, dystonia, rigidity, dysarthria, and gait instability, along with bilateral Kayser-Fleischer rings and symmetric grey and white matter T2 hyperintensities in the fronto-temporo-parietal region. These are among the presentations of Wilson disease. The disease can present with either liver disease (18-84%), neurological manifestations (18-73%), or psychiatric symptoms (10-100%) [2]. The neurological manifestations experienced by our patient, which included variable presentations of dysarthria, dystonia, tremors, and choreoathetoid movements, are quite common. The present patient also exhibited liver involvement, as indicated by altered echogenicity of the liver parenchyma on ultrasonography. However, her liver function profile during her initial visit and follow-up was within normal limits.

The MRI of the brain in Wilson disease typically shows prominent involvement of the basal ganglia and thalamus, as well as a "giant panda" sign (14.3%), basal ganglia involvement, tectal plate involvement (75%), thalamic lesions, and central pontine myelinolysis-like abnormalities (62.5%), along with brainstem involvement [3]. These areas show high-signal T2 images, which can be attributed to cystic degeneration, gliosis, or oedema [4]. Long repetition time sequences have occasionally shown hyperintensities believed to be caused by the paramagnetic effect of copper deposition [5]. Diffusion restriction on MRI is rarely seen as a result of inflammation or cytotoxic oedema; however, this is generally not observed in chronic cases [6].

The MRI scan of present patient showed confluent T2 hyperintensities involving the bilateral fronto-temporal lobes in a symmetric fashion. Similar, but less severe, signal changes were also noted in the bilateral parietal lobes. The findings of bilateral confluent T2 hyperintensities across both grey and white matter in the cerebrum are observed in a very small number of patients with Wilson disease as reported in the literature [7,8].

White matter changes on MRI were identified in seventeen, nine, seven, and five patients in the frontal, parietal, temporal, and occipital regions, respectively, in a major study conducted by Prashanth LK et al., which involved 56 patients with Wilson disease; however, there was no mention of involvement across multiple lobar regions or simultaneous involvement of both grey and white matter [3]. In a study by Ranjan A et al., involving confirmed cases of Wilson disease, MRI revealed subcortical white matter involvement in 23.5% of cases and cerebral cortex involvement in 26.5% of cases [9]. A combination of demyelination, spongy degeneration, softening, and cavitation could be the cause of these signal alterations [4].

In another study by Zhong W et al., which included 76 patients with Wilson disease, only 5.9% exhibited involvement of both the cerebral cortex and white matter on MRI. A more in-depth analysis indicated that the frontal cortex was most frequently involved among cerebral cortex cases, while the parietal and occipital cortices were affected less frequently [10]. Patients with Wilson disease rarely show white matter abnormalities on MRI brain scans. Nazer H et al., did not find any white matter alterations in their study of six patients with Wilson disease [11]. According to Jha SK et al., it was reported in 10% of cases [12]. White matter lesions in patients with Wilson disease are often asymmetrical, in contrast to the majority of symmetric grey matter lesions [5].

CONCLUSION(S)

The present case demonstrates clinical signs of neurological involvement and the uncommon MRI characteristics associated with Wilson disease. While Wilson disease is a treatable condition, it can be potentially fatal in the absence of prompt diagnosis and treatment. Therefore, the learning objective of present case is that, even though cerebral white matter abnormalities are uncommon, their presence should not preclude the diagnosis of neurological Wilson disease.

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