CASE REPORT

Atypical neuroimaging in Wilson's disease

Rushad Patell,¹ Rupal Dosi,¹ Harshal K Joshi,¹ Dennis Storz²¹Department of Medicine, Medical College Baroda, Vadodara, India²Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany**Correspondence to**
Dr Rushad Patell,
rushadpatell@gmail.com

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SUMMARY

Wilson's disease is a rare metabolic disease involving copper metabolism. Neuroimaging plays an important part in evaluation of patients with a neuropsychiatric presentation. We present a case of a 14-year-old girl with atypical confluent white matter disease and cystic degeneration on MRI, with a rapidly progressive course, who succumbed to complications despite treatment with trientine. Wilson's disease should be considered as a differential for leucoencephalopathy in young patients with progressive neurological disease for its early recognition and optimum outcome.

BACKGROUND

Wilson's disease is a rare autosomal recessive disease involving copper transport leading to its deposition in various tissues, chiefly the liver, brain and cornea.¹ Accumulation of copper in the basal ganglia and brainstem is predominant but not exclusive. Leucoencephalopathy has been rarely reported early in the course of the disease. We present a case of a 14-year-old girl with unusually rapid neurological progression and atypical confluent white matter degeneration with cystic changes on imaging. Clinicians and radiologists should be aware of less common manifestations of diseases to avoid delays in diagnosis and for institution of timely treatment.

CASE PRESENTATION

A 14-year-old girl presented with a 6-month history of insidious onset and gradually progressive decline in scholastic performance, loss of motor skills, difficulty in ambulation, abnormal posturing, speech disturbances and behavioural abnormalities accompanying a steady cognitive decline. There was no evidence of jaundice or portal hypertension on clinical history of the patient or similar illnesses in the family.

Examination revealed slow, dysarthric and non-fluent speech, impaired attention, abstract thinking and judgment along with rigidity, dystonia (lead pipe) bradykinesia and bilateral positive Babinski's sign. There was no history of seizures, myoclonus or neuropathy. MRI of the brain was suggestive of abnormal hyperintense signals on T2-weighted scans in the basal ganglia, thalamus and midbrain (figure 1). Bilateral, symmetrical, confluent white matter hyperintensities were also noted within the frontal lobes and a subcortical cyst was detected on the right suggestive of leucodystrophy (figure 2).

INVESTIGATIONS

Investigations revealed microcytic hypochromic anaemia (haemoglobin of 10.4 g/dL; reference range 14–17 g/dL) with mild thrombocytopaenia (110 000/mm³; reference range 150 000–4 500 000). Peripheral smear showed presence of target cells and thrombocytopaenia. Liver function tests were suggestive of mild hyperbilirubinaemia (serum

Figure 1 T2-weighted axial MRI demonstrates: 'face of the giant panda' in the midbrain with hyperintense signal in tegmentum and normal red nuclei (arrow). Symmetric hyperintense signals in the putamen, posterior internal capsule and thalami.

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Figure 2 T2-weighted axial MRI demonstrates: bilateral, symmetrical, confluent white matter hyperintensities within the frontal region. A subcortical cystic lesion in the right frontal lobe (arrow).

bilirubin of 1.6 mg/dL; reference range <1 mg/dL); alkaline phosphatase was raised at 250 U/L (reference range 20–140 U/L); alanine transaminase and aspartate transaminase levels were 51 mcg/L (reference range <49 mcg/L) and 49 mcg/L (reference range <49 mcg/L), respectively. Hypoalbuminaemia (serum albumin 1.9 g/dL; reference range 3.4–4.9 g/dL) and elevated prothrombin time (INR 2.4; reference range 0.8–1.2) were also noted. A diagnosis of Wilson's disease was made based on the presence of Kayser-Fleisher rings (figure 3), low serum ceruloplasmin (7.78 mg/dL; reference range 20–60 mg/dL) and increased urinary copper excretion (356 µg/day; reference range 18–100 µg/day). A shrunken liver with altered echotexture, mild splenomegaly (on ultrasound) and laboratory evaluation supported the diagnosis of chronic liver disease. A liver biopsy was not performed due to coagulopathy.

TREATMENT

Treatment was started with a copper-chelating agent, trientine (20 mg/kg, in three divided doses), and zinc (75 mg, in three divided doses), ensuring that both medications were taken 3–4 h

apart from each other. However, over the course of the next 2 months the patient worsened neurologically and was bedbound with minimal speech and response to external stimulus. She succumbed in the intensive care unit to aspiration pneumonia soon thereafter. Screening of the siblings was normal.

DISCUSSION

Wilson's disease is an inherited disorder of mutations involving copper-transporting peptide ATP7B on chromosome 13.² Neuropsychiatric or hepatic manifestations are common for most patients although other systems are also rarely involved.^{3–4} Neurological abnormalities have been described as (1) akinetic-rigid syndrome; (2) pseudosclerosis (predominant tremor); (3) ataxia and (4) dystonic syndrome.⁴ Hepatic disease is often diagnosed on laboratory evaluation, imaging or histology, although some patients may be symptomatic.³

Neurological imaging in Wilson's disease commonly reveals abnormalities in the grey matter of the basal ganglia and brainstem⁴ including the characteristic 'giant panda sign'.⁵ White matter changes have also been studied in patients of Wilson's disease⁶ including reports of atypical confluent white matter changes.^{7–8} Verma *et al*⁸ described a case who developed leucoencephalopathy within 1 year of the diagnosis. In another similar case reported by Hedera *et al*,⁷ leucoencephalopathy was accompanied by a rapid clinical progression with neurological deterioration, similar to our case. Cystic changes indicate severe or prolonged disease, such changes as seen in the case reported, have been described only exceptionally rarely before in children with Wilson's disease. A single case reported from India⁹ describes a 12-year-old boy with prominent cystic changes on neuroimaging and a poor outcome despite treatment for Wilson's disease. A retrospective study correlating seizures with neuroimaging and pathological findings also noted that subcortical white matter changes were statistically more common in patients with seizures and severe changes suggestive of necrosis or cystic degeneration were also noted in a subgroup.¹⁰ Leucoencephalopathy has been associated with severe progressive disease and treatment resistance.¹¹

Wilson's disease is universally fatal if untreated, and progression to death can be rapid.³ Starting effective treatment early is imperative as it can reverse neurological and hepatic manifestations. Trientine and ammonium tetrathiomolybdate are

Figure 3 Slit-lamp examination revealed a golden brown Kayser-Fleisher ring in the cornea.

preferred chelators in neurological presentations because paradoxical worsening on treatment is often seen with penicillamine;^{1 3 4} however, both these agents are orphan drugs not readily available in India. In this case, several financial and bureaucratic hurdles had to be overcome to procure trientine from the UK for our patient at the cost of valuable time.

A delay in diagnosis has been recognised in Wilson's disease.¹¹ In India, preventable mortality and morbidity and a lack of access to medications to the poor patients remain a key area of concern.¹² Neuroimaging is a valuable tool in the evaluation of patients. White matter changes are less well known and when confluent are easily confused with other leucodystrophies. These diseases have remarkably different prognostic and therapeutic implications. This case report stresses the importance of the clinician and the radiologist recognising the presence of white matter disease early, along with the better-known basal ganglia and brainstem findings, to ensure an early diagnosis and subsequent treatment.

Learning points

- ▶ Wilson's disease is an uncommon disease with myriad possible presentations.
- ▶ White matter changes, especially with cystic degeneration, are not as well known as classic brainstem abnormalities on neuroimaging.
- ▶ Awareness of the less common aspects of this treatable condition can lead to better outcomes with earlier recognition and institution of treatment.

Contributors All authors were involved in caring for the patient as well as researching and writing the paper.

Competing interests None.

Patient consent Obtained.

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