

How to Cite:

Kumar, D., Kaur, G., & Gupta, A. (2022). Rare presentation of neurometabolic disorder (Wilson's disease): A case report and review of literature. *International Journal of Health Sciences*, 6(S6), 10545–10549. <https://doi.org/10.53730/ijhs.v6nS6.12820>

Rare presentation of neurometabolic disorder (Wilson's disease): A case report and review of literature

Dinesh Kumar

Assistant professor, Sri Guru Ram Das Institute of Medical Sciences & Research, Amritsar, Punjab, India

*Corresponding author email: manishksharma27@gmail.com

Gursimran Kaur

Student, Sri Guru Ram Das Institute of Medical Sciences & Research, Amritsar, Punjab, India

Ashima Gupta

Intern, Sri Guru Ram Das Institute of Medical Sciences & Research, Amritsar, Punjab, India

Abstract--Introduction: Wilson's disease (WD) is a disorder of copper metabolism leading to the accumulation of this metal in different organs. Hepatic manifestations tend to occur in the first decade and neurological symptoms in the third decade. Neurological manifestations are said to worsen with chelation therapy. Case report: A 16-year-old male presented to our institution with recurrent episodes of seizures since last 3 months despite being on multiple anti-epileptic medications. Patient eventually progressed to having problems while moving all his four limbs which further progressed to speech arrest and extraocular muscle palsy. MRI scan confirmed typical features of Neurometabolic disorder. Metabolic parameters like Ceruloplasmin level were also evidently low. Conclusion: Wilson's disease is an inherited metabolic disorder. Early diagnosis and appropriate management help to prevent the systemic complications. Siblings needed to be screened to prevent manifestations. It also points out the need to suspect Wilson's disease in any young patient presented with the unexplained liver disease.

Keywords--Wilson's disease, copper accumulation, liver cirrhosis.

Introduction

Neurometabolic diseases are rare, complex disorders, but overall they account for a remarkable number of diseases of the central nervous system (CNS) in children. The underlying pathomechanism is highly variable and the clinical presentation is often non-specific. Neuroimaging plays a key role in the investigation of children with neurometabolic diseases: It is helpful to (1) distinguish neurometabolic disorders from other more common diseases of the pediatric brain, (2) guide the further diagnostic workup, and (3) suggest a specific diagnosis. In some neurometabolic disorders, early diagnosis and institution of the appropriate therapy is mandatory to prevent death or ameliorate long-term neurological sequelae, while misdiagnosis or a delayed diagnosis can result in a devastating, irreversible injury to the developing brain.

It is therefore important that pediatric radiologists are familiar with the neuroimaging findings of pediatric neurometabolic disorders. Neurometabolic diseases are rare, complex disorders, but overall they account for a remarkable number of diseases of the central nervous system (CNS) in children. The underlying patho-mechanism is highly variable and the clinical presentation is often non-specific. Neuroimaging plays a key role in the investigation of children with neurometabolic diseases: It is helpful to (1) distinguish neurometabolic disorders from other more common diseases of the paediatric brain, (2) guide the further diagnostic workup, and (3) suggest a specific diagnosis. In some neurometabolic disorders, early diagnosis and institution of the appropriate therapy is mandatory to prevent death or ameliorate long-term neurological sequelae, while misdiagnosis or a delayed diagnosis can result in a devastating, irreversible injury to the developing brain.

It is therefore important that paediatric radiologists are familiar with the neuroimaging findings of paediatric neurometabolic disorders. Neurometabolic disorders may be classified in various groups depending on the predominantly involved tissue (e.g., white matter in leukodystrophies or leukoencephalopathies), the involved metabolic processes (e.g., organic acidurias and amino-acidopathies) and primary age of the child at presentation (e.g., neurometabolic disorders of the newborn). Classification according to patho-mechanism causing the symptoms and clinical findings, which includes: (1) intoxication diseases, (2) energy production diseases, (3) diseases of the biosynthesis and catabolism of complex molecules and (4) neurotransmitter diseases. Wilson disease (WD) is an autosomal recessive inherited disorder caused by dysfunction of the copper transporter ATP7B, which is expressed mainly in hepatocytes and is critical for hepatic copper homeostasis.¹⁻³ Defective ATP7B function causes impaired biliary copper excretion and pathological accumulation of copper in the liver and central nervous system.

WD has a prevalence of approximately 1 in 30,000 live births. Most patients present with symptoms in their first or second decades of life, with 5% developing acute liver failure; in rare cases, however, symptoms occur up to and including the eighth decade of life.⁴ The natural history of untreated WD is disease progression. Patients presenting with liver disease may subsequently develop neurologic or psychiatric symptoms, and conversely, liver failure may develop in

patients presenting with neurologic or psychiatric symptoms. Medical therapy can treat disease or prevent its development, and liver transplantation can be curative.

Case Report

A 16-year-old male presented to our institution with recurrent episodes of seizures since last 3 months despite being on multiple anti-epileptic medications. Patient showed typical Wilson facies (Vocascious smile, facial grimace). Patient eventually progressed to having problems while moving all his four limbs which further progressed to speech arrest and extraocular muscle palsy. MRI scan confirmed typical features of Neurometabolic disorder. (Figure 1) Metabolic parameters like Ceruloplasmin level were also evidently low. After confirmation of diagnosis, patient was put on regular treatment as well as management under our Neuromedicine department.

Discussion

Neurometabolic disorders are rare diseases, but overall, they account for a significant number of disorders of the paediatric brain. They can present at any age and with very different symptoms. They can affect the white matter, grey matter or both. Few are treatable, and an early diagnosis is paramount to prevent death or permanent long-term neurological sequelae. Neuroimaging has been shown to provide key information in the diagnostic workup of children with neurometabolic disorders. MRI not only provides biochemical information on heavy metal distribution in brain tissue but also gives an insight into the pathologic and anatomic correlates of clinical signs and symptoms in Wilson's disease. Interval changes seen on follow-up MR imaging have good correlation with clinical symptoms and can be useful in evaluating the clinical response to treatment of children with Wilson's disease.⁵

The midbrain “face of the giant panda” sign⁶ consists of high signal intensity in the tegmentum, preservation of signal intensity of the lateral portion of the pars reticulata of the substantia nigra and red nucleus (arrowhead), and hypointensity of the superior colliculus. In addition, a “face of panda cub” is seen within the dorsal part of pons. “Eyes of the panda” are formed from the relative hypointensity of the central tegmental tracts (CTT) (arrowhead) in contrast with the hyperintensity of the aqueduct opening into the fourth ventricle (“nose and mouth of the panda”) bounded inferiorly by the superior medullary velum. The panda's “cheeks” are formed from the superior cerebellar peduncles.⁷ Life-long medical therapy is required in patients with WD. Treatment should be considered in two phases: removing or detoxifying the tissue copper that has accumulated, and preventing its reaccumulation.^{2,3,8} Copper removal is achieved by the administration of potent chelators.

The primary chelator that has been used is D-penicillamine; however, approx.30% of patients do not tolerate long-term therapy because of side effects, and some with neurologic symptoms may develop worsening and irreversible changes. Trientine, an alternative chelator introduced as a second-line agent for those intolerant to D-penicillamine, is a reasonable option for primary therapy because

of its lower incidence of side effects. The prognosis for WD is excellent in all but those with advanced liver or neurological disease at presentation.^{2,3,9} The neurologic, psychiatric, and hepatic abnormalities may gradually improve with medical treatment or following LT in most patients, but currently LT is mainly recommended for WD patients with hepatic failure. A multidisciplinary team approach to diagnosis and treatment at experienced centers and longitudinal monitoring of treatment and adherence improves outcomes for these individuals.

Conclusion

As Wilson's disease is a rare disease the diagnosis is likely to be missed. There should be a high index of suspicion in all cases of liver cirrhosis with no clear-cut etiology or an isolated neurological symptom such as tremor.

References

1. Ala A, Borjigin J, Rochwarger A, Schilsky M. Wilson disease in septuagenarian siblings: raising the bar for diagnosis. *Hepatology* 2005;41:668-670.
2. Beinhardt S, Leiss W, St€attermayer AF, Graziadei I, Zoller H, Stauber R, et al. Long-term outcomes of patients with Wilson disease in a large Austrian cohort. *Clin Gastroenterol Hepatol* 2014;12:683-689.
3. Ferenci P, Czlonkowska A, Stremmel W, Houwen R, Rosenberg W, Schilsky M. European Association for Study of Liver. EASL clinical practice guidelines: Wilson's disease. *J Hepatol* 2012;56:671-685.
4. Hitoshi S, Iwata M, Yoshikawa K. Midbrain pathology of Wilson's disease: MRI analysis of three cases. *J Neurol Neurosurg Psychiatry*. 1991;54:624-6.
5. Jacobs DA, Markowitz CE, Liebeskind DS, Galetta SL. The double panda sign in Wilson's disease. *Neurology*. 2003;61:969.
6. Kim TJ, Kim IO, Kim WS, Cheon JE, Moon SG, Kwon JW, et al. MR imaging of the brain in Wilson disease of childhood: Findings before and after treatment with clinical correlation. *AJNR Am J Neuroradiol*. 2006;27:1373-8.
7. Roberts EA, Schilsky ML, American Association for Study of Liver Diseases (AASLD). Diagnosis and treatment of Wilson disease: an update. *Hepatology* 2008;47:2089.
8. Rosencrantz R, Schilsky M. Wilson disease: pathogenesis and clinical considerations in diagnosis and treatment. *Semin Liver Dis* 2011;31:245-259.
9. Weiss KH, Gotthardt DN, Klemm D, Merle U, Ferenci-Foerster D, Schaefer M, et al. Zinc monotherapy is not as effective as chelating agents in treatment of Wilson disease. *Gastroenterology* 2011;140:1189-1198.

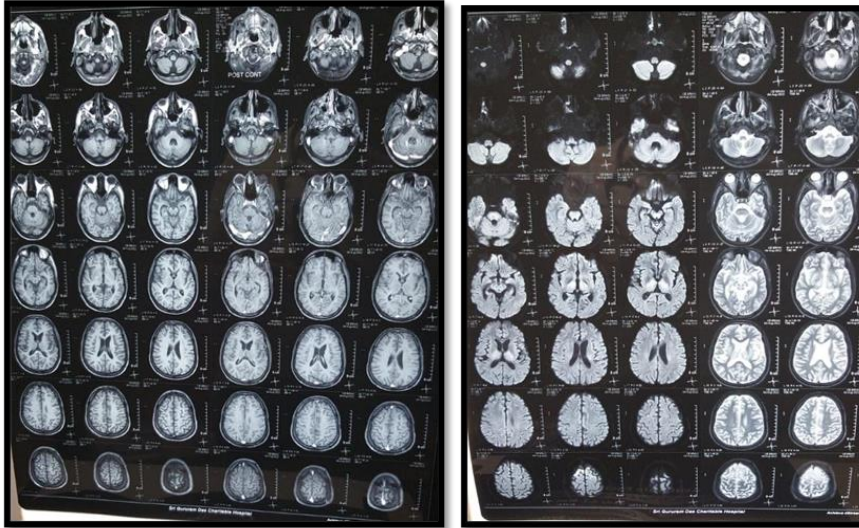
Figures

Figure 1. Magnetic resonance (MR) imaging showed T2 and FLAIR hyperintense lesions involving bilateral thalami, midbrain, and pons. Double panda sign is also evident