Isolated Neuropsychiatric Manifestation in Wilson Disease :A Case Report

Abstract :

One of the rare genetic disorders of copper metabolism is Wilson disease (WD) which presents with various clinical manifestations at the time of diagnosis. Usually it involves the liver during the early course of the disease and later with neuropsychiatric involvement. Most patients WD presents with advanced degree of liver disease or neuropsychiatric disease during early decades of life esp. 2nd decade and 3rd decade. For diagnosis of WD, a high degree of suspicion is required. Here we are presenting a case of a 21-year-old lactating woman who presented with only neuropsychiatric manifestation without any hepatic manifestations and family history of any neuropsychiatric illness.

Keywords: Wilson disease (WD), Neuropsychiatric, Lactating woman.

Introduction

Wilson's disease is a rare autosomal recessive disorder which is known to cause . It was first describe by Samuel Alexander Kinnier Wilson in 1912 [1]. The incidence of Wilsons Disease is estimated to be one in 30,000 births [2]. It is caused by a mutation in the ATPase copper-transporting beta (ATP7B) gene that code for a membrane-bound copper-transporting ATPase. In human body under normal physiology, the liver produces and secretes apoceruloplasmin, which binds with copper and form Ceruloplasmin and it eradicate the excess amount of copper (Cu) through bile[4]. The gene mutation in Wilsons Disease leads to a failure of incorporation of Cu with Apoceruloplasmin. This result in decreases excretion of copper into the bile. It results in accumulation of Cu in liver and lead to Hepatic manifestation[4,5]. Defective copper incorporation into apoceruloplasmin leads to excess catabolism and low blood levels of ceruloplasmin. Serum copper levels are usually lower than normal because of low blood levels of ceruloplasmin, which normally binds >90% of serum copper. In Wilson Disease, due to reduced half-life of apoceruloplasmin there is decreased blood level of the serum ceruloplasmin. Copper from the blood eventually gets deposited in other organs, including the brain, kidneys, and cornea and its toxic effect lead to variety of clinical symptoms [4] .Wilsons Disease typically presents with hepatic manifestation in childhood and

neuropsychiatric presentation in adults. At the time of diagnosis, about 60% shows liver function abnormalities, 40% to 60% exhibit neurological symptoms, and up to 10% to 25% present with psychiatric symptoms [5]. When Cu is deposited in the cornea, then Kayser-Fleischer (K-F) ring is observed. In 90% to 100% of the patients with pronounced neurological signs and 20% to 30% of asymptomatic patients K-F Ring is present. Even though the neurological and psychiatric symptoms can manifest at any stage of the disease, it usually exhibits signs in the later stages of the condition after the occurrence of the liver symptoms[5,6,7]. Here we present an atypical case of WD presenting with neuropsychiatric signs as the primary presenting sign before exhibiting any significant symptoms of liver dysfunctions.

Case Summary

A 21 years old lactating woman presented with slurring of speech for 4 months, which was insidious in onset and gradually progressive in nature. It was associated with drooling of saliva from the angle of mouth. She had no difficulty in understanding language. She also had difficulty in swallowing which was more to liquid than solid. She had difficulty in walking and it was gradually progressive. She also complains of weakness of her whole body for 3 months with no distal or proximal predominant. Initially she noticed that she had difficulty in writing and holding objects and difficulty in walking with history of frequent fall. Her face retained a wry smile and she was emotionally labile. She cried or become angry if anyone does not give attention to her or to her activities. There was no any history of visual disturbance, diplopia, memory loss, headache, fever or tingling and numbness. There was also no history of bladder and bowel disturbance and sleep.

On examination, her tongue was found to retracted posteriorly. On examination of the eyes, a brown ring was seen in the bilateral cornea, which was confirmed to be Kayser-Fleischer Ring on slit lamp examination. On higher mental examination patient had speech impairment which was dysarthric with normal intellect and no hallucination, delusion and illusion. On examination of her cranial nerves functions were intact. On motor and sensory examination were within normal limits with bat wing type of tremor present.

On MRI of Brain shows T2/FLAIR hyper intensities in Bilateral Caudate Nucleus, Lentiform Nucleus, Ventrolateral Thalami and Tectum of Midbrain showing subtle diffusion restriction on DWI suggestive of

Wilsons Disease. On Laboratory investigation show Serum cerulopasmin 8mg/dl and urine copper of 116 µg in 24 hour urine sample. She was diagnosed to be Wilson Disease based on Leipzig criteria (score 4). However liver biopsy couldnot be done.

She was treated with D-Penicillamine and Zinc. Her symptoms and signs were improved on medications and who is on regular follow up.

Discussion

This patient presented with Neuropsychiatric manifestation without any hepatic disorder. She was diagnosed as a case of Wilsons Disease on the basis of Serum ceruluplasmin, presence of Kayser-Fleischer ring and MRI findings. Usually WD present with Hepatic Manifestation prior to Neurological Manifestation. Neuropsychiatric manifestations may precede neurological signs in the early stages of Wilsons Disease. About 20% of psychiatric manifestation precede hepatic and neurological dysfunction[6]..

Her symptoms were improved on treatment with Penicillamine and Zinc. No major side effects were noticed during the treatment. This case illustrate neuropsychiatric manifestations in Wilsons Disease.

Conclusion

In summary, not all patients of WD with neuropsychiatric symptoms present with coexisting clinical problems of the liver at the time of diagnosis. It is important to emphasize the critical aspect of diagnosing, as neuropsychiatric symptoms without typical clinical liver abnormality involvement can be fatal if not treated appropriately. Since, timely diagnosis and management of WD hold prognostic value to reduce disease impact, and clinicians should be vigilant to identify similar atypical scenarios.

Authors

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Figures

Fig 1;- Brown ring in the cornea, which was confirmed to be Kayser-Fleischer Ring on slit lamp examination.

Fig 2;- T2/FLAIR hyper intensities in Bilateral Caudate Nucleus, Lentiform Nucleus, Ventrolateral Thalami and Tectum of Midbrain showing subtle dffusion restriction on Diffusion Wetted Imaging

Fig 3;- Posterior retraction of the tongue.