

Neuropsychiatric presentation of Wilson's disease

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Abstract

Wilson's disease is a rare autosomal inherited disorder with various manifestations. Initial manifestations could be hepatic, neurological or psychiatric and there is invariable delay coming to the correct diagnosis. Exact frequency of children and adolescents presenting with psychiatric complaint as the initial manifestation is not known. It is recommended that detailed medical evaluation be done in any child presenting with psychiatric complaints. We hereby present a case of an eight- year old girl who presented with anxiety and subsequently diagnosed to have Wilson's disease.

Keywords: Wilson's disease, neuropsychiatric presentation, children

Introduction

Wilson's disease (WD) is a rare autosomal inherited disorder affecting both the liver and the central nervous system. Because it affects both liver and central nervous system, it is sometimes also called hepatolenticular degeneration. The lifetime prevalence is estimated at around 1:30,000, but a recent study of abnormal gene frequency point to a possible higher prevalence of 1:7026. WD is attributed to a defect of the gene ATP7B on chromosome 13, which encodes an ATP-dependent copper transporting transmembrane protein mainly expressed in the liver. A defect in ATP7B function leads to the accumulation of copper, primarily in the liver and subsequently in the brain. Without treatment, WD is progressive and fatal, with patients dying of liver failure or complications of their neurological illness.¹⁻⁵

It has been suggested that the hepatic, neurologic, and psychiatric presentations of Wilson's disease occur in roughly equal proportions.⁶⁻⁸ An accurate estimate of the presenting proportions is challenging because many of the large case series have ascertainment bias based on clinical specialty, and likely under represent the psychiatric presentation.⁸ Psychiatric manifestations of WD can be categorized into five groups: personality changes, affective disorders, psychosis, cognitive impairment, and others. Lishman reported that behavioral and personality changes and affective disorders, including depression are the most common psychiatric manifestations.⁶ Because of the varied and sometimes subtle way in which the psychiatric features of Wilson's disease can present, Wilson's disease should be considered and excluded in any young person who develops unexplained psychiatric dysfunction, especially when any signs of neurological

dysfunction are also present.⁹

We present a case of an anxious young girl whose medical workup in the psychiatric setting ultimately revealed Wilson's disease as the final diagnosis.

Case Report

An eight year old female child from a remote area who was studying in class one presented in Psychiatry outpatient department (OPD) as a referral from Pediatric OPD. She had presented with complaints of fearfulness, palpitations, restlessness and tremors of upper limbs followed by bitemporal headache of three months duration. The patient had refused going to school for one month prior to presentation owing to increased fearfulness. Mental status examination revealed an anxious child with fine tremors of both upper limbs. She was provisionally diagnosed as anxiety disorder and admitted in psychiatry ward; and started on oral sertraline 25mg/day. Further evaluation revealed history dating back to four months when she had started with drooling of saliva, difficulty swallowing, and difficulty speaking, with progressive increase in all symptoms.

Drooling of saliva had gradually become more severe leading to soaking of her pillow and wetting of her clothes. She had progressive increase in difficulties in chewing and swallowing of solid foods. She also had difficulty in expressive language. She couldn't speak long and complex sentences. However, she could communicate with great difficulties with unclear, few words, written language and gestures. Difficulty in speaking was not associated with language comprehension and problem in vocabulary and it was not situation specific. She had marked impairment in her socio-occupational functioning associated with difficulties in speaking. Her interaction

with her peers and neighborhood had decreased. Her fearfulness gradually increased to the extent that she refused going to school in the later days. There were also twitching of tongue and low- amplitude tremors of upper limbs present even during sleep separate from episodes of fearfulness. Biological functions, however, were not altered.

Treatment history revealed that she had been taken to multiple physicians out of Kathmandu valley with symptomatic treatment but no improvement followed by visits to pediatricians in Kathmandu, where she had received multivitamins and antibiotics. She was then brought to pediatric department of Tribhuvan University Teaching Hospital from where she was referred to psychiatry OPD for her anxiety symptoms. Past history, family history and personal history were not significant. Mental state examination revealed a cooperative and well- oriented but anxious looking child sitting on her bed. Relevant findings during mental state examination included fine tremors of bilateral upper limbs with difficulty initiating speech which was difficult to comprehend. Relevant physical findings included increased tone and rigidity of limbs with slight drooling of saliva. There was mild facial asymmetry with weakness of facial nerve and motor weakness of both lower limbs. Bilateral knee and ankle reflexes were exaggerated.

Routine hematological parameters were within normal limits except that she had mild degree of anemia with hemoglobin (Hb) of 10.8 g/dl. Biochemistry revealed some impairment of liver functions (SGOT 51 U/L, SGPT 28 U/L, Alkaline phosphatase 112 U/L, bilirubin 8 micromol/litre). Electrolytes, renal function tests, and blood sugar levels, thyroid function tests, all were within normal limits. C- reactive protein (CRP) was elevated to 6 mg/dl. Serology for HIV 1-2, HBsAg, and VDRL tests all were negative. Ultrasound abdomen revealed coarse echotexture of liver parenchyma with increased echogenicity. At this point, possibility of Wilson's disease was considered and ophthalmological evaluation along with investigation of serum ceruloplasmin levels and 24- hour urinary copper excretion were planned. Slit-lamp examination of eyes revealed Kayser Fleischer (K-F) rings in both corneas. Serum ceruloplasmin level was decreased to 2 mg/dl; and 24-hour urinary copper excretion was elevated to 102 µg/day. Diagnosis of Wilson's disease was confirmed and she was then transferred to neurology unit of medicine ward. Treatment was started with d- Penicillamine 250 mg orally three times a day. She then showed gradual improvement in her symptoms of twitching of tongue and speech difficulty; and was finally discharged on 23rd day of transfer with advice for follow- up in OPD. She showed gradual improvement in all her symptoms on subsequent follow-ups.

Discussion

This case highlights the importance of detailed physical examination and persistence in the diagnostic process. The hypothesis that the psychiatric symptoms of any given child or adolescent may be caused or exacerbated by a concurrent medical condition should always be considered, and the psychiatrist involved should not hesitate to perform a detailed physical examination.^{2,6,10,11} Literature suggests that patients who first present with neurological or psychiatric signs in Wilson's disease tend to be older than those with hepatic features alone.⁹ One third of these patients may initially present with behavioral abnormalities and failure to recognize this may lead to misdiagnosis, institution of ineffective symptomatic therapy or unwarranted treatment e.g. electroconvulsive therapy (ECT), increased morbidity, delay in starting specific treatment, and on occasion disastrous outcome of primary illness.⁶

Studies have shown that most of these patients are usually seen by a number of doctors from different disciplines before being referred and there is great delay making the final diagnosis. Reasons cited are Wilson's disease itself is a rare disorder, has broad clinical manifestations and initial manifestations are different in patients and may be non- specific.¹²

Our patient had presented at eight years of age. She had presented with symptoms of anxiety and there were tremors noted during examination. History of drooling of saliva, difficulty swallowing and difficulty speaking were brought into light after a thorough work-up. Physical examination revealed dystonia, rigidity and facial asymmetry. Based on these findings, provisional diagnosis of Wilson's disease was entertained and final diagnosis was made after findings of decreased serum ceruloplasmin level and increased 24-h urinary copper excretion on biochemical investigation and presence of K-F rings on eye examination. She had presented to multiple physicians and even to pediatricians prior to being referred to our facility. Admitting her in ward for thorough evaluation was a good judgment. Had it been an outpatient work- up, she could just have been dismissed as having anxiety. This case also highlights the significance of detailed evaluation in a child by pediatricians even when presentation is primarily due to psychiatric complaints.

Conclusion

Psychiatric presentation of any kind in children must be taken seriously. Detailed multidisciplinary approach is essential so as not to miss the rare diagnosis of Wilson's diseases.

Conflict of interest: None declared**References**

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