Indian Journal of Clinical Psychiatry
An Official Journal of **Association of Clinical Psychiatry**
(Indian Psychiatric Society- Uttar Pradesh State Branch (IPS-UPSB))

CASE REPORT
ISSN- 2583-8873
doi: 10.54169/ijocp.v3i02.81

Atypical Presentation of Neuropsychiatric Variant of Wilson's Disease and Clinical Improvement with Elemental Zinc Monotherapy

Simranjit Kaur, Utkarsh K. Tripathi, Abhishek Chakladar*, Zaid Ahmed, Gaurav Verma, Alexander M. Alphonse, Ankan Paul

Department of Psychiatry, Varun Arjun Medical College and Rohilkhand Hospital, Banthra, Shahjahanpur, Uttar Pradesh, India.

ARTICLE INFO

Correspondence:
Abhishek Chakladar
avcal89@gmail.com
Department of Psychiatry, Varun Arjun Medical College and Rohilkhand Hospital, Banthra, Shahjahanpur, Uttar Pradesh, India.

Dates:
Received: 22-08-2023
Accepted: 01-10-2023
Published: 08-11-2023

How to Cite:
Kaur S, Tripathi UK, Chakladar A, Ahmed Z, Verma G, Alphonse AM, Paul A. Atypical Presentation of Neuropsychiatric Variant of Wilson's Disease and Clinical Improvement with Elemental Zinc Monotherapy. Indian Journal of Clinical Psychiatry.2023;3(2):34-36.
doi: 10.54169/ijocp.v3i02.81

Introduction

Wilson's disease has been referred to as "the great masquerader" because it has a plethora of clinical manifestations based on the organ system involved.[1] Current understanding is that neuropsychiatric WD develops after years of subclinical hepatic dysfunction.[1] Neurologic dysfunction typically begins at approximately 20 years of age but can present earlier or later.[2] In WD, the predominant neurologic manifestations (60%) are dysarthria, tremor and ataxia, followed by dystonia (15%) and parkinsonism (11%).[3,4] In WD, pure psychiatric presentations are typically seen in patients in their teens. However, symptoms are often non-specific and frequently misdiagnosed as behavioral problems.[5] Therefore, in many cases, when the clinical suspicion is low, the diagnosis of Wilson's disease is often delayed or missed.

Case Report

A 13-year-old male child, studying in the eighth standard, belonging to a Muslim joint family of lower socioeconomic status presented with fearfulness, restlessness, irritability and crying for no apparent reason, decreased food intake and sleep, along with seeing indescribable images for two months. The onset of the symptoms was sub-acute and the course was continuous and steady; during this course, the patient had sought treatment from a local practitioner, and the details were unavailable. During the physical examination, there was rigidity in both upper limbs and in the trunk; there was a lack of facial expressions with obliteration of both nasolabial folds. Mental state examination revealed restlessness and inability to sit at a place throughout the examination; there was poverty of speech with the decrease in rate, tone and productivity; the effect was blunt. The patient was well-orientated with respect to time, place and person. The BPRS score at the time of the first evaluation was 45, and the Modified Simpson Angus Scale (MSAS) score for extra-pyramidal symptoms was 25, indicating a severe degree of movement disorder. A provisional diagnosis of acute transient psychotic disorder, with a possibility of drug-induced extra-pyramidal

Table 1: Diagnostic scoring system for Wilson's disease

Clinical and laboratory presentation	*Points*	*Present in the index case*
Kayser-Fleischer ring		Present (2 points)
Present	2	
Absent	0	
Neurologic symptoms or typical abnormalities of MRI brain		MRI brain was normal
Severe	2	
Mild	1	
Absent	0	
Serum ceruloplasmin (g/L)		0.15 g/L (1 point)
Normal (>0.2)	0	
0.1–0.2	1	
<0.1	2	
Coomb's negative hemolytic anaemia		Absent
Present	1	
Absent	0	
Liver copper (in the absence of cholestasis)		Not done (invasive procedure was avoided).
>5 x ULN (>4 micromol/g)	2	
0.8–4 micromol/g	1	
Normal (<0.8 micromol/g)	-1	
Rhodamine positive granules*	1	
24-hour urinary copper (in the absence of acute hepatitis)		85.41 microgram; 1.7 times of upper limit of normal (1 point)
Normal	0	
1–2 x ULN	1	
>2 times ULN	2	
Mutation analysis		Not done as the facility of genetic analysis is not available in the study centre
Mutations detected on both chromosomes	4	
Mutation detected on a single chromosome	1	
Mutation absent	0	
TOTAL SCORE: 4 or more: Diagnosis established 3: Diagnosis possible; more tests needed 2 or less: Diagnosis very unlikely		

symptoms, was made. Treatment was started with oral trihexyphenidyl 2 mg twice daily, built up to 2 mg thrice daily, and quetiapine 25 mg once daily for movement disorder and behavioral symptoms, respectively. Even after 1-week of treatment, the extra-pyramidal symptoms persisted with MSAS score of 20 and a BPRS score of 42. At this stage, an organic cause for the symptoms was considered. Complete blood count with erythrocyte sedimentation rate, thyroid function tests, liver function tests, renal function tests and MRI were normal. A possibility of Wilson's disease was considered and an ophthalmology referral revealed the presence of K-F (Kayser-Fleischer) ring by a slit lamp examination. The patient was further investigated for serum ceruloplasmin, 24 hour urinary copper and urine ceruloplasmin levels. Although serum ceruloplasmin and urinary ceruloplasmin levels were within normal limits, the 24 hour urinary copper was 85.41 µg, which was 1.7 times the upper limit of the normal range (Normal reference range: 3–50 µg per day/24 hours of urine sample). On the basis of Leipzig criteria (Table 1) (score = 4), a diagnosis of Wilson's disease was made. The patient was started on an oral dose of elemental zinc 50 mg per day and observed for a period of 2 weeks. At the end of two weeks the MSAS score decreased to 13, and the BPRS score was 32. During this period of two weeks, tablet pro-

methazine 25 to 50 mg daily was used for sedation and the patient was kept free of antipsychotic. Subsequently, the opinion of a neurologist was sought from higher centre when it was decided that there was no need to consider a chelating agent and the patient can be continued on 50 mg of elemental zinc daily. Currently, the patient is free of any behavioral disturbance and there is no movement disorder. The patient is on regular monthly follow up with the treating team.

Discussion

The threshold for clinical suspicion of Wilson's disease should be high in patients presenting with the first episode of unspecified psychosis and/or movement disorder, and they should be investigated accordingly. Although brain magnetic resonance imaging findings are abnormal[6] in patients with a neurologic variant of Wilson's disease, our patient had a normal brain MRI study. The current treatment guidelines for Wilson's disease recommend copper chelation therapy for up to 5 years, followed by maintenance therapy with zinc when they are clinically well, with stable hepatic function and normal serum and urinary copper levels.[7] Zinc is typically reserved for maintenance treatment, but it has been used as first-line therapy for asymptomatic or pre-symptomatic patients.[8] However, in our patient, as there was no evidence of copper deposition in the brain and the 24-hour urinary copper was less than twice the upper limit of normal, it was clinically decided to use zinc as the first line of management. Zinc also has a lower propensity to cause neurologic deterioration compared to chelating agents; however, lifelong medical supervision (in the form of monitoring of liver function tests and copper level estimation for the next five years after the initial diagnosis and subsequently depending on the individual case) is of utmost importance in the management of such patients.[9]

Conflict of Interest

The authors declare no conflict of interest with regard to this manuscript

References

1. Sean Cleymaet, Katsuko Nagayoshi, Edward Gettings & Justin Faden (2019): A review and update on the diagnosis and treatment of neuropsychiatric Wilson disease, Expert Review of Neurotherapeutics, DOI: 10.1080/14737175.2019.1645009
2. Merle U, Schaefer M, Ferenci P, et al. Clinical presentation, diagnosis and long-term outcome of Wilson's disease: a cohort study. Gut. 2007; 56:115– 120.
3. Członkowska A, Litwin T, Dzieżyc K, et al. Characteristics of a newly diagnosed Polish cohort of patients with neurological manifestations of Wilson disease evaluated with the Unified Wilson's Disease Rating Scale. BMC Neurol. 2018; 18:34.
4. Hedera P. Wilson's disease: A master of disguise. Parkinsonism Relat. Disord. 2019.
5. Carta M, Mura G, Sorbello O, et al. Quality of Life and Psychiatric Symptoms in Wilson's Disease: the Relevance of Bipolar Disorders. Clin. Pract. Epidemiol. Ment. Health. 2012; 8:102–109.
6. Sinha S, Taly AB, Ravishankar S, et al. Wilson's disease: cranial MRI observations and clinical correlation. Neuroradiology. 2006; 48:613–621.
7. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: An update. Hepatology. 2008; 47:2089–2111.
8. Brewer GJ, Dick RD, Johnson VD, et al. Treatment of Wilson's disease with zinc: XV long-term follow-up studies. J. Lab. Clin. Med. 1998; 132:264– 278.
9. Linn FHH, Houwen RHJ, van Hattum J, et al. Long-term exclusive zinc monotherapy in symptomatic Wilson disease: Experience in 17 patients. Hepatology. 2009;50:1442–1452