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WILSON'S DISEASE PRESENTING AS STATUS EPILEPTICUS: A CASE REPORT

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ABSTRACT

Wilson's disease (WD) is a rare disorder of copper metabolism, caused by a mutation in the ATPB7 gene, resulting in a defect in copper elimination leading to its accumulation in various organs, with the liver being the most common. Here, we describe a case of a 19-year-old boy who presented with a history of hallucinations and status epilepticus. Initial investigations were normal, but due to a rising trend in alanine transaminase (ALT), a slit lamp examination was performed, revealing Kayser-Fleischer (KF) rings in the eyes. The patient was diagnosed with WD due to the presence of these KF rings and increased urinary copper excretion. Wilson's disease should be suspected in cases where the first manifestation of symptoms is neurological without evidence of prior such symptoms and no evidence of other neurological disorders.

KEYWORDS: Wilson's disease, Status epilepticus, Keyser-Fleischer ring

INTRODUCTION

Wilson's disease (WD) is a rare disorder of copper metabolism that is inherited as an autosomal recessive disorder. The disease affects about 30 individuals per million population.[1] It is caused by a mutation in the ATP7B gene, which encodes a transmembrane copper-transporting protein on chromosome 13.[2-4] This mutation impairs the copper elimination pathway, preventing the incorporation of copper into apoceruloplasmin and its excretion into bile, resulting in WD.[3] Excess copper is initially bound to metallothionein until saturation, leading to dense lysosomal copper deposits and hepatocyte injury.[3] The defective ATP7B protein causes pathological accumulation of copper in the brain, liver, cornea, kidney, and other organs. WD patients present with various complex clinical symptoms, including both neurological and non-neurological manifestations, with hepatic involvement being common.[1] The liver is typically the first organ affected in WD, resulting in liver cirrhosis, abdominal pain, jaundice, splenomegaly, and upper gastrointestinal bleeding.[2,3] Increased free copper levels in the blood reach the brain, depositing particularly in the basal ganglia near the lenticular nucleus, followed by the cerebellum in the brainstem.[4] Clinical manifestations vary widely and may include abnormal movements such as tremors, dystonia, bradykinesia, and chorea, along with dysphagia, dysarthria, poor articulation, and hypersalivation.[5] Other neurological signs of WD are rare and include neuropathy, autonomic system dysfunction, headaches, and epilepsy.[5]

CASE PRESENTATION

A 19-year-old boy, a student, was brought in the ER of Pakistan Air Force Hospital, Islamabad with a history of hallucinations and abnormal behaviour for one week, followed by fever and generalized tonic-clonic seizures. There were three episodes of seizures in one day, each lasting for 1-2 minutes and occurring 10-15 minutes apart (status epilepticus). He did not regain consciousness between the seizures. There was no history of fever, drug intoxication, or family history of epilepsy.

His presenting GCS was E3M5V2 (10/15), pupils were dilated but reactive to light, and there was an extensor plantar response bilaterally. He was afebrile and vitally stable with a heart rate of 90 beats per minute, a respiratory rate of 18 beats per minute, and a BP of 120/80 mmHg.

Status epilepticus management protocol was activated, and antiepileptics were administered to control the seizures. He responded well, and his GCS improved to E4M6V5 (15/15), with plantar response becoming flexor (downgoing). There were no signs of meningeal irritation. All four limbs had normal tone and movement. There was no optic disc edema on fundoscopic examination. Systemic examination was also inconclusive.

Initial investigations were normal, including hemogram, serum electrolytes, blood sugar, and creatinine levels. Liver function tests revealed elevated ALT at 50 U/L. Workup for hepatitis B and C, and herpes simplex virus PCR were normal. His EEG showed generaliz mild

slowing of the background rhythm, with no epileptic discharges. An ultrasound (USG) of the abdomen was unremarkable. An MRI brain with contrast was normal. Cerebrospinal fluid (CSF) analysis showed WBC 03/cmm3, protein 40 mg/dl (<45), glucose 64.2 mg/dl (40-70), with BSR 100 mg/dL. CSF gram staining and AFB staining were negative, and no growth was obtained on culture. HSV PCR was negative. The autoimmune profile for autoimmune encephalitis was normal. Due to the rising trend in ALT (210 to 340 U/L), a slit lamp examination for Kayser-Fleischer (KF) rings was repeated and found to be positive (Figure 1). Serum copper (Cu+2) was normal, but 24-hour urinary copper excretion was >100 μg/day. The Leipzig score was calculated to be 6 (Table 1).

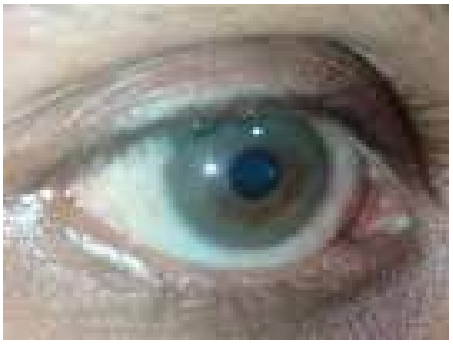

Figure 1: Keyser-Fleischer ring

Table 1: LEIPZIG SCORING SYSTEM FOR WILSON'S DISEASE

TYPICAL CLINICAL SYMPTOMS AND SIGNS		OTHER TESTS	
KF RINGS		LIVER COPPER	
PRESENT	2	5x ULN (>4 micromol/g)	2
ABSENT	0	0.8-4 micromol/g	1
		NORMAL (<0.8 micromol/g)	-1
		RHODANINE-POSITIVE GRANULES	1
NEUROLOGICAL SYMPTOMS		URINARY COPPER (IN THE ABSENCE OF ACUTE	
SEVERE	2	HEPATITIS)	
MILD	1	NORMAL	0
ABSENT	0	1-2x ULN	1
		>2x ULN	2
		NORMAL, BUR 5x ULN AFTER D-PENICILLAMINE	2
COOMBS-NEGATIVE HEMOLYTIC ANEMIA		MUTATION ANALYSIS	
PRRSENT	1	ON BOTH CHROMOSOME DETECTED	4
ABSENT	0	ON 1 CHROMOSOME DETECTED	1
		NO MUTATION DETECTED	0
SERUM CERULOPLASMIN			
NORMAL (>0.2 g/L)	0		
O.1-0.2 g/L	1		
<0.1 g/L	2		
TOTAL SCORE		EVALUATION	
4 OR MORE		DIAGNOSIS ESTABLISHED	
3		DIAGNOSIS POSSIBLE, MORE TEST NEEDED	
2 OR LESS		DIAGNOSIS VERY UNLIKELY	

He was initially treated with antibacterial and antiviral (empirical) medications and antiepileptics. After the diagnosis of WD, he was treated with D-penicillamine 250 mg three times a day along with zinc. His symptoms improved, and treatment was continued. The patient showed improvement after two months of therapy.

DISCUSSION

Status epilepticus in WD is a very rare presentation, occurring in about 6-7% of cases.[3] In this case, the boy presented with status epilepticus. Seizures were controlled with initial antiepileptic treatment. Due to worsening liver function tests, he was evaluated further for acute hepatitis and encephalitis, but results were normal. The diagnosis of WD was made based on the presence of KF rings, high 24-hour urinary copper, and low serum ceruloplasmin levels along with clinical symptoms. He had no past history of psychosis, fits, or family history of neuropsychiatric disorders. Eye signs are one of the main extrahepatic clinical manifestations of the disease.[6] They occur due to the accumulation of copper, appearing as a granular layer of golden to green color near the limbus of the cornea, known as Kayser-Fleischer rings.[2,7]

Epilepsy is one of the earliest symptoms of WD, appearing earlier than other neurological symptoms.[8] Seizures are more prevalent in WD compared to the general population. A study in England states that the frequency of seizures is 10 times more prevalent in WD patients compared to the general population, though neurological manifestations of WD are more commonly seen in older patients.[5] In this case, neurological symptoms started with hallucinations and abnormal behaviour, eventually leading to seizures. Cases of status epilepticus are less commonly reported in WD.[9] The first case of WD presenting with status epilepticus was reported in 2005 in India.[9] Several mechanisms for epilepsy in WD include copper deposits in the cerebral cortex inhibiting membrane ATPase, resulting in increased neuronal activity.[10] Histological findings in WD include loss of neuronal tissue, gliosis, laminar necrosis, spongy degeneration, and cavitation of the cerebral cortex, leading to increased neuronal discharge.[9] Moreover, penicillamine, used in WD treatment, is responsible for pyridoxine deficiency, which may further aggravate seizures.[9]

Seizures in WD are generally generalized, less frequently partial, and can occur at any stage of the disease. It is hypothesized that seizures may be due to lesions of white matter tracts in the cortex, overtreatment in WD, and treatment-induced copper deficiency; however, this needs further confirmation.[11,12] In this case, an MRI brain with contrast was normal.

CONCLUSION

Status epilepticus could be an atypical presentation of WD, often remaining undiagnosed and misinterpreted as another systemic disease. They are usually misdiagnosed as acute hepatitis, cirrhosis, or encephalitis, resulting in delays in the diagnosis of WD.[13] It is important to consider WD when a patient's first presentation is of psychiatric nature without a previous history of psychosis, especially when presenting with other clues such as a history of jaundice, as delays result in increased morbidity and mortality.[14] The earlier the diagnosis is made, the better the outcome, especially if treatment is started before the development of irreversible symptoms.

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All the authors have approved the final version of the article and agree to be accountable for all aspects of the work.