Case report

A CASE OF WILSON'S DISEASE PRESENTING WITH CEREBELLAR ATAXIA

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ABSTRACT

Wilson's disease (WD) is a rare inherited copper metabolism disorder with many clinical symptoms highlighted by hepatic and cerebral features. We present the case of a 17 - year - old female patient with generalized tonic - clonic seizures and cerebellar ataxia who presented to our hospital. The patient was initially diagnosed with encephalitis and epilepsy before being identified with WD based on clinical and laboratory data. The patient had made a significant clinical recovery after six months of follow - up

Keywords: *Wilson's disease, coper, liver, cerebellum .*

I. INTRODUCTION

Wilson's disease (WD) is an extremely rare autosomal recessive copper metabolism disorder caused by mutations in the copper-transporting ATP7B gene [1]. Increased free copper levels in several organs produce harm, with liver and brain injury symptoms, particularly in the basal ganglia and cerebellum, dominating clinical presentations [2]. The main neurologic signs include tremor, dystonia, bradykinesia, chorea, trouble swallowing, difficulty speaking and poor articulation, and excessive salivation [3]. Neuropathy, autonomic system dysfunction, migraines, and seizures are some of the neurologic indications of WD, in addition to mobility abnormalities [3]. Epilepsy is often one of the first signs of WD, appearing years before other neurological problems [4]. Dening et al. revealed the frequency and significance of seizures in WD patients for the first time in 1988 [4]. The authors discovered seizures in 6.2% of 200 patients (in England) in their study, which is ten times higher than the prevalence of seizures in the general population [3]. When compared to hepatic indications, neurologic manifestations of WD appear later in life. They are typically encountered in patients with misdiagnosed hepatic disease, those with asymptomatic hepatic impairment, those who do not comply with de - coppering therapy, and those who do not respond to treatment [5]. Misdiagnosis is common due to the wide range of symptoms.

Here, we present the case of Wilson's disease presenting with generalized tonic-clonic seizures and cerebellar ataxia.

II. CASE REPORT

A 17 - year - old female patient with generalized tonic - clonic seizures, ataxia, intention tremor, and gait and speech disturbances presented to our hospital. During the investigation, it was discovered that she had been suffering from seizure attacks for the previous year. It was accompanied by ataxia, intention tremor, and gait and speech problems in the last nine months. The symptoms had begun subtly and increasingly worsened over time. In the

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previous month, her condition had deteriorated to the point where she could not carry out her regular chores without assistance. During this time, she had been hospitalized for various illnesses, including encephalitis and epilepsy, and had tried a variety of medications with little success.

Her family history revealed nothing notable. The patient appeared alert, cooperative and oriented during a general physical examination. Other than a black ring in the cornea of both eyes, no aberrant findings were found in other systems. Ataxia, intention and resting tremor, dysarthria, tandem gait, dysmetria, and an abnormal finger to finger test were all found on neurologic examination.

Complete blood count, liver function test and renal function test results were all within normal ranges. Antibodies to the hepatitis B surface antigen and the hepatitis C virus were negative. The diagnosis of WD was suspected due to the existence of the dark ring in both eyes; thus further testing was done. Abdominal sonography revealed cholelithiasis and a coarse echotexture of the liver. The presence of a Kayser - Fleischer (KF) ring in both eyes was confirmed using a slit lamp examination. The level of ceruloplasmin in the blood was 0.10 g/L. The left temporal lobe had mesial temporal sclerosis, according to an MRI taken a year before. Due to a budgetary costraint, the patient's guardian was hesitant to undergo a follow - up MRI.

The KF rings on slit - lamp examination, clinical features, and serum ceruloplasmin (0.10 g/L) were utilized to diagnose WD. A patient with a Ferenci score of more than 4 is diagnosed with WD, according to the Ferenci score [7].

Following confirmation of the diagnosis, the following treatment regimen was devised: avoidance of copper - rich foods such as liver, mushrooms, cocoa, chocolate, nuts, and shellfish; penicillamine 250 mg once daily at first, gradually increasing to 1.5 g/day in divided doses; zinc acetate 150 mg daily in three divided doses; pyridoxine 20 mg daily; levetiracetam 500 mg in two divided doses, increased in steps of 250 mg every two weeks according to the patient's response. Six months after treatment, the patient had made significant progress, i.e., she was seizure - free and able to carry out her daily tasks without assistance.

III. DISCUSSION

WD is a rare hereditary copper metabolic illness in which the causal gene, ATP7B, causes malfunction of the ATP7B transporter, which is required for biliary copper excretion and copper incorporation into ceruloplasmin [8]. To date, more than 500 mutations in the ATP7B gene have been discovered. Despite evidence that truncating mutations are associated with earlier onset than missense mutations and that individuals with frameshift mutations are more likely to develop neurologic symptoms, individual gene alterations have not been associated with different WD manifestations. Monozygotic twins with WD who were phenotypically discordant have been described in studies. This finding suggests that, at least in part, environmental and epigenetic variables may have a role in WD [9]. WD generally begins with a clinically quiet period, during which copper buildup in the liver causes subclinical hepatitis, progresses to liver cirrhosis, and neuropsychiatric signs appear [1]. Changes in behavior, a decline in academic performance, or the inability to carry out activities that require great hand - eye coordination can all be seen in the early stages of disease in juvenile patients. In Parkinson's disease, handwriting may deteriorate, resulting in cramped, small handwriting (micrographia). Neurologic signs of WD include tremor, incoordination, excessive salivation, dysarthria, dystonia, and spasticity. Pseudobulbar palsy can cause transfer dysphagia, which can lead to aspiration in extreme situations. Dysautonomia, migraine headaches, and insomnia are all possible symptoms; however, seizures are rare [10]. Epileptic seizures are a rare presenting symptom of WD. They can occur at any stage of the disease and are more common after starting anti-coppering therapy [11, 12]. Patients with neurologic WD who have cortical, subcortical, or cerebellar involvement on MRI are more likely to experience seizures [13]. Seizures of various sorts, such as grand mal, focal,

and absence, may be present [14]. Although there is an increase in focal motor seizures in WD, the types of seizures found in WD patients do not differ significantly from those seen in general population surveys [4]. Involuntary and paroxysmal movements are common in diseases that mimic epilepsy. In such circumstances, detecting the presence or absence of seizures might be difficult [4]. Epilepsy caused by WD appears to have a better prognosis than epilepsy in general [4]. Anticonvulsants appear to have less of an impact on epilepsy prognosis than WD treatment [4]. Treatment for such epilepsy instances is the same as for other types, although Wilson illness requires penicillamine or trientine [14]. The possibility of hepatotoxicity should be considered while choosing antiepileptic drugs for WD patients (as such, treatment with valproate should be avoided) [3, 4]. Cerebellar signs and symptoms are rarely clinically significant and are seldom discovered on their own. Frank limb ataxia is unusual on inspection. Cerebellar symptoms such as overshoot dysmetria of the eyes and extremities or ataxic dysarthria can be detected in addition to limb dysmetria [15]. WD is identified using a series of clinical and biochemical investigations. The hallmark signs of WD are age at onset between 5 and 40 years, visible KF rings, and reduced serum ceruloplasmin [16]. KF rings, a pathognomonic indication induced by copper deposition in Descemet's membrane, can be seen in the eyes, either directly or on slit-lamp examination [17].

WD's initial symptoms are commonly overlooked and misdiagnosed as hepatitis, cirrhosis, splenomegaly, or encephalitis, resulting in treatment delays [18]. It takes an average of two years from the onset of symptoms to the diagnosis. According to Kim et al., the delay in neurologic presentations is longer than in hepatic manifestations (44 vs. 14 months) [18]. A 30 - year delay has also been reported [19]. Prompt diagnosis and treatment can help prevent irreversible organ damage [18]. WD pharmacotherapy focuses on de - coppering with chelators and/or zinc [8]. Because a decreased copper diet cannot address an aberrant copper deposition, drug therapy for WD must be continued for the rest of one's life [11]. Clinical improvement begins 5 - 6 months after starting de - coppering treatment in individuals with neurological symptoms, and most patients eventually show significant improvement [8]. Penicillamine, strangely enough, is reported to worsen neurological symptoms. This could be due to the mobilization of copper from the liver and an increase in unbound copper levels, worsening neurological symptoms. According to certain research, penicillamine therapy causes neurological deterioration in 30 - 75% of patients. Other reports, on the other hand, have refuted this [20]. After receiving penicillamine, our patient's neurologic problems improved.

Because WD is an inherited disease, it is highly advised that WD patients undergo family screening. Screening the first - degree relatives of a proband is recommended by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of Liver (EASL). A proband's first - degree relatives include not just his or her brothers but also his or her children and parents [21]. Our patient had certain uncommon characteristics, including widespread tonic-clonic epilepsy and prominent cerebellar abnormalities. Abdominal sonography revealed asymptomatic liver abnormalities. For a year, she was misdiagnosed with encephalitis and epilepsy. She saw significant changes after six months of WD treatment. This instance emphasizes the need to suspect WD in young patients who arrive with atypical neurological symptoms like seizures or cerebellar impairment. In patients with movement problems, eye examination (direct or by slit lamp) and abdominal sonography (even in the absence of clinical signs of hepatic involvement) can aid in the diagnosis of life - threatening diseases. Similarly, early detection and treatment of WD could help people maintain a healthy lifestyle for the remainder of their lives.

IV. CONCLUSIONS

Wilson's disease (WD) is a rare inherited copper metabolism disorder with many clinical symptoms highlighted by hepatic and cerebral features.It requires clinical understanding of physicians and expensive investigation modalities for prompt recognition and is inaccessible as required, lifelong drugs for treatment.

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