Rare Initial Presentation of Wilson Disease as Acute Encephalopathy with Recurrent Seizure

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Abstract

Basal ganglia based movement abnormalities are the hallmark of neuropsychiatric presentation of Wilson disease. Seizures are rarely reported in Wilson disease and initial presentation of Wilson disease as seizure is very rare. We report a case of Wilson disease who was admitted with recurrent seizure and treated as a case of Encephalitis ,on subsequent follow up was found to have Wilson disease .This case highlights the importance of considering the diagnosis of Wilson disease in any young patient presenting with otherwise unexplained encephalopathy.

Keywords: Wilson disease; Encephalopathy; Seizure;

Introduction

Wilson disease is an inborn error of copper metabolism caused by a mutation in the ATP7B gene on chromosome 13. The ATP7B protein is involved in the incorporation of copper into ceruloplasmin and the transport of copper into the bile[1]. Neurologic dysfunction is the initial clinical manifestation of Wilson disease in 40% to 60% of patients, with usual appearance at around 20 years of age, while initial hepatic manifestations are seen in approximately 40 to 50 % of patients and have a slightly earlier age of onset[2,3]. Wilson disease with its varied clinical manifestations is a diagnostic challenge. Seizure is uncommon in Wilson disease and its initial presentation as seizure is very rare.

Case report

A 17 year old boy was admitted with recurrent episodes of seizures. One week prior to admission he had low grade fever for two days. He started to have visual hallucinations in the form of seeing things burning at a distance. On the night prior to admission his parents heard a loud cry from his room and found him convulsing. He had six serial seizures. He was

managed as status epilepticus. He was diagnosed as a case of acute encephalopathy with seizures and was evaluated for infectious and autoimmune causes.

His CSF study was normal. CSf viral markers for Herpes simplex 1 and 2 and Varicella zoster was negative. NMDA antibody was negative. He was given a course of acyclovir, methyl prednisolone, followed by oral steroids. He made a gradual recovery in 1 week but remained stubborn and irritable.Upon recovery patient was clinically normal without any neurologic defiicits. MRI brain showed multiple cortical hyperintensities and subcortical white matter hyperintensities (figure 3).Inter ictal EEG showed focal epileptiform discharges from left frontal region.

He was discharged on steroids and sodium valproate as antiepileptic. At 4 month follow up visit to the neurology clinic, an asymmetric tremor of hands and dysarthria was noticed. Initially this was suspected to be post encephalitis sequelae or due to drug effect .He was started on Levodopa and Trihexyphenidyl with which he made mild improvement.

Five months after the first admission, while his steroid was being tapered he was readmitted with recurrent seizures. . He was compliant with anti-epileptic medications.The seizure was characterized by behavioural arrest, head adversion to right side and drooling of saliva lasting for about a minute.

On second admission his parents were again interviewed for any relevant past history. They admitted to a slow decline in his school performance over the past 1 year. His handwriting also worsened (figure 2). There was no relevant family history. He was born out of non consanguinous marriage.

In view of mild parkinsonian symptoms and tremor in a young patient, he was reexamined thoroughly. Slit lamp examination of the eyes showed Kayser-Fleischer (figure 1). Serum ceruloplasmin level was 3 mg/dl (in Wilson disease it is <20mg/dl), 24 hour urine copper was 103 micrograms. (More than 100 mcg is diagnostic of Wilson disease). A follow up MRI brain showed T2 hyperintesities in subcortical white matter, symmetric hyperintensities in caudate, putamen and thalamus (figure 4). His Liver function test showed mild AST elevation, normal coagulation and haemoglobin was 10 gram/dl. Peripheral blood smear was normal. Ultrasound of abdomen showed hyperechoic liver parenchyma and no cirrhosis.

Patient was initially treated with Zinc sulfate and then started on Penicillamine with slow uptitration of dose .He showed improvement in his tremor and parkinsonian symptoms. His antiepileptic drugs were also tapered to minimal dose. Currently he is stable without any new neurologic issues and is compliant with medications.

Discussion

In Wilson disease the major neurological symptoms are extrapyramidal; tremor, dystonia, parkinsonism, dysphagia and dysarthria being the usual manifestation. Chorea, athetosis and myoclonus are rare but can occur[4, 14] .Cerebellar dysfunction develops in approximatey 30%

patients[5]. Initial presentation of acute encephalopathy with seizures in Wilson disease is rare. Only 8% of patients with Wilson's disease have seizures. Out of this 8%, only 20 percent have seizures before the onset of the characteristic clinical features of Wilson disease[6]. It can be simple or complex partial, generalized tonic clonic or secondary generalized or periodic myoclonus. Most common is generalized tonic clonic seizures[6]. Status epilepticus has been reported in few cases[6,7,8].

Prognosis of seizure in Wilson disease is good. Rarely it can be refractory .Seizure outcome is perhaps independent of the type of AEDs used.No specific guidelines as to which antiepileptic to be used is available .MRI imaging characteristics in Wilson disease patients having seizures were similar to those without seizures[6] . The most characteristic abnormalities in Wilson disease are increased signal intensity on T2- weighted images and reduced signal intensity on T1-weighted images in basal ganglia, brainstem and thalamus[9]. The face of the giant panda sign in the midbrain, the face of the miniature panda sign in the pons, and the bright claustrum sign are described, but are present in only few patients and thus, of limited value. White matter signal changes can also be seen in Wilson disease. Presence of subcortical White matter lesion particularly frontal lobe correlated with seizure [6]. Seizure can occur at any stage of Wilson- as first symptom, at initiation of treatment or during treatment or as terminal event. EEG abnormalities include generalized and focal epileptform discharge, diffuse or focal slowing of background activity or periodic high voltage activity[6]. The possible mechanisms postulated for seizure in Wilson are direct toxicity of Copper, pyridoxine deficiency due to penicillamine treatment or metabolic encephalopathy[5,10].

Behavioural and psychiatric symptoms in Wilson disease are common and may precede other symptoms. This may be in the form of declining school performance, impulsiveness or psychotic features. Severe cognitive deterioration are rare and seen only in advanced cases[11].

Serum cerruloplasmin is a readily available screening tool but can be normal in 5 to 15% of patients[3]. Urinary copper levels are typically more than 100mcg/dl in patiens with symptomatic Wilson disease. Free copper (non cerruloplasmin bound) will be elevated in serum. Liver biopsy is a sensitive and accurate test to diagnose Wilson disease[13]. When widely available genetic testing will become the diagnostic test of choice. In patients presenting with either neurologic or psychiatric dysfunction, a combination of Kayser-Fleischer rings, elevated 24-hour urinary copper, and reduced cerruloplasmin essentially confirms the diagnosis of Wilson disease, and liver biopsy is unnecessary.

Our patient presented with behavioural changes and serial seizures.Later he developed parkinsonian features .He had another flurry of seizures and when seizure was controlled he again had parkinsonism picture in forefront. The initial presentation as encephalopathy with seizures, and absence of classic manifestations of Wilson disease early in the course of the illness lead to delay in diagnosis in our case .The parents did notice the slow decline in school performance and deterioration in hand writing but failed to report initially. Though rare reports of Wilson disease presenting initially as seizure are available, initial presentation as

acute encephalitis is very rare. There is one case report of Wilson presenting as acute delirium with automatic writing behaviour [12].

A detailed history and clinical examination in any neurologic or neuropsychiatric presentation is still significant despite advances in imaging and electrophysiology. Wilson disease should be considered in the differential diagnosis in any young patient presenting with otherwise unexplained encephalopathy. Being a treatable disease, screening of Wilson disease should be done in any atypical neurologic presentation.

Conclusion

Delay in diagnosis of Wilson disease can affect the prospects of better outcome. Wilson disease should be considered in the differential diagnosis of any unexplained neurologic or psychiatric dysfunction.

Disclosure

There is no conflict of interest. Informed written consent was taken from patient and his kin.

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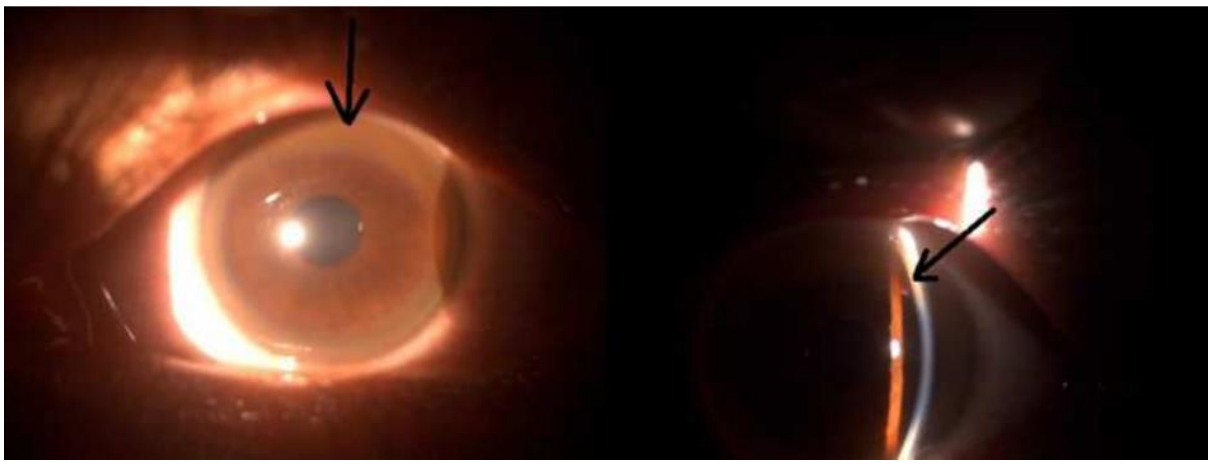
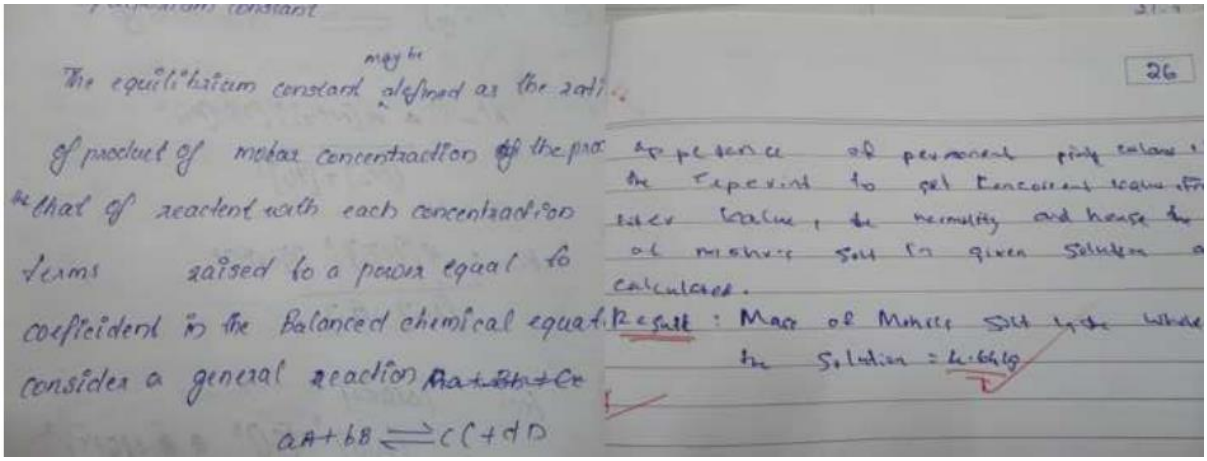


Figure 1



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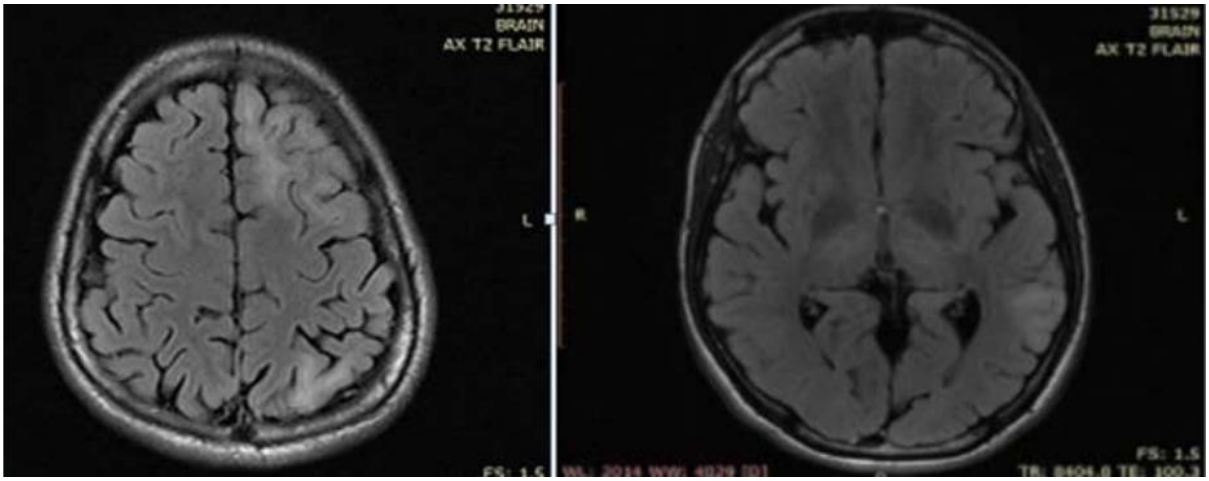

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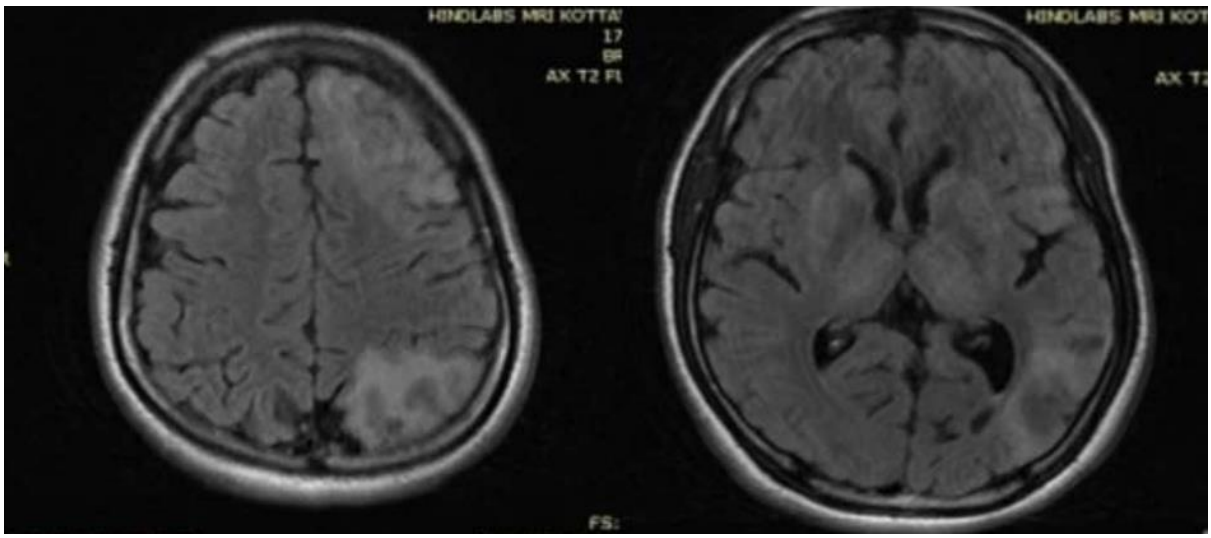

Figure 4