Case Report

Wilson’s Disease Presenting As Status Epilepticus

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Abstract
A patient of Wilson’s disease having neurological as well as psychiatric manifestations who presented with status epilepticus is being reported. The diagnosis was confirmed by biochemical investigations and ‘face of giant panda’ sign was present on MRI brain.

INTRODUCTION

Wilson’s disease is a rare autosomal recessive disease, caused by mutation in ATP7B gene, characterized by failure of copper metabolism leading to copper deposits in liver and brain. The condition usually presents in first or second decade with liver disease and/or neuropsychiatric disease. Seizures occur infrequently, and more commonly movement disorders predominate.

Overall prevalence of seizures in Wilson’s disease is low and there are infrequent reports of seizures as presenting manifestations of Wilson’s disease. Although there are two case reports in which patients developed status epilepticus following institution of d-penicillamine therapy, there are no reports of Wilson’s disease presenting de novo with status epilepticus.

In this article, we are discussing a case that presented to us in status epilepticus and later investigations proved the diagnosis of Wilson’s disease.

CASE REPORT

17 years old boy presented with history of seizures for last 7 days, which were, generalized tonic clonic in nature. For last 2 days he was having multiple seizure episodes without regaining of consciousness in between. Seizures were associated with frothing from mouth, deviation of face towards right side, uprolling of eyeballs and occasional urinary incontinence. Patient was unconscious at presentation and regained consciousness over next 2-3 days after treatment with antiepileptics.

Prior history of behavioral disturbances in the form of disinterest in the surroundings and decreased interaction with friends and relatives with occasional outburst of temper for last 4 months was present. According to parents he had some speech and gait difficulties for last 2 months. There was no history of headache, vomiting, visual disturbances or focal deficits. Past history was unremarkable for liver dysfunction or seizure disorder. None of his siblings had similar illness.

On general examination Kayser-Fleischer rings were present in cornea and his vitals were stable. There was no jaundice or flaps. Abdominal examination did not reveal organomegaly or free fluid.

Neurological examination revealed that the patient was mute, having mask like faces, drooling of saliva and dystonic tongue. Cranial nerve examination including fundi was normal. Motor system examination showed generalized cogwheel rigidity in all 4 limbs including axial musculature, postural tremors of both upper limbs, hyperreflexia, extensor plantars and normal muscle strength. Sensory and cerebellar system examination was unremarkable.

His investigations showed that hemogram, electrolytes, liver and renal function tests were normal. He was subjected to contrast enhanced computed tomographic (CT) scan of brain, which revealed bilateral frontal white matter hypodensities (Fig. 1). So one possibility of late onset leukodystrophy was initially thought of, but owing to predominant extrapyramidal manifestations, which were uncovered after few days, we investigated him for Wilson’s disease. Wilson disease was confirmed on basis of Kayser-Fleischer ring, increased urinary copper (59.83 µgm /24hrs: reference range 25-50 µgm / 24hrs) and low serum ceruloplasmin levels (9.13 mg/dl: reference range 19-57 mg/dl). Cerebrospinal fluid examination showed protein-40mg/dl, sugar-80 mg/dl (corresponding blood sugar-110mg/dl) and cells <5, all lymphocytes. Gram stain and acid fast bacilli stain were negative. Electroencephalographic record was abnormal consistent with a focus in left frontal region. Magnetic Resonance Imaging (MRI) was done which showed low attenuating areas in both thalamus with hyperintensities in bilateral frontal white matter and pallidum on T1 weighted images (Fig. 2). There is increased signal intensity on T2 weighted images in...
bilateral basal ganglia, thalamus, frontal white matter and in midbrain (Fig. 3) Midbrain sections showed bilateral central hypointensities in the region of red nuclei surrounded by hyperintense tegmentum, which did not take up contrast (Fig. 4). This was consistent with classical “face of giant panda” sign described in patients of Wilson’s disease.

Status epilepticus at the time of admission was controlled with intravenous phenytoin and lorazepam. Subsequently he was put on zinc sulphate 150 mg per day along with D- penicillamine 250 mg per day, which was gradually escalated to 500 mg per day and oral phenytoin 300 mg daily. There was no recurrence of seizures and some improvement in neurological status at 3 months follow up.

**DISCUSSION**

As the patient presented with status epilepticus and gait difficulty, and the head CT scan revealed bilateral frontal hypodensities involving the white matter, a possibility of leukodystrophy was initially considered. Encephalitic illness was also considered with herpes simplex and Japanese encephalitis as the likely possibilities. However lack of clinical and seasonal...
correlation, imaging features and normal CSF study refuted them. As the patient regained consciousness, predominant extrapyramidal manifestations led us to consider possibility of Wilson’s disease. This was confirmed by the presence of KF rings, low serum ceruloplasmin levels and an increased urinary copper excretion.

Epileptic seizures are very uncommon as initial manifestations of Wilson’s disease. Dening et al found a seizure prevalence of 6.2% in Wilson’s disease, which is 10 times higher than in general population. Seizures may be focal or generalized tonic clonic in nature. Animal studies have shown that copper deposition in the brain may cause ictus by inhibition of membrane ATPase. Neuronal loss, gliosis and cavitation may also be responsible for focal seizure activity. Hepatic encephalopathy can lead to seizures in these patients. More often seizures have been described after initiation of chelator therapy particularly with d-penicillamine. D-penicillamine can cause lowering of seizure threshold secondary to pyridoxine deficiency or it may lead to increased mobilization and subsequent cortical deposition of copper precipitating seizures. G.J. Brewer in his series of patients inferred that seizures were related directly to brain damage and not due to therapy. Seizures can occur at any stage of the disease but most commonly after beginning treatment.

The two case reports on status epilepticus in Wilson’s disease are different from this case as both developed seizures after initiation of therapy while our patient presented de novo in status. So in the present case seizures were more likely due to direct cerebral copper deposition and he was started on D-penicillamine and zinc therapy, without subsequent seizure recurrence. Due to the presence of subcortical frontal white matter lesions on MRI and the EEG focus in the frontal region, we thought of probable frontal lobe origin of seizures in this case. Hepatic encephalopathy as a cause of seizure was refuted due to absence of jaundice, flaps and normal liver function tests.

The original description of the ‘face of the giant panda’ sign by Hitoshi et al consisted of high signal intensity in the region of tegmentum except for the red nucleus, preservation of signal intensity in substantia nigra and hypointensities in superior colliculus. Our patient had similar findings on MR imaging. Exact pathogenesis of this finding is not known, but it is presumed that the paramagnetic effects of the deposition of the heavy metals such as copper and iron may be responsible.

The present case gives us a lesson that this easily treatable but often forgotten disease should have high index of suspicion while dealing with neurobehavioral abnormalities in a young patient.

REFERENCES


Erratum

This is with reference to our case report "Drug Related Crisis in Myasthenia Gravis" published in JAPI on Page number 820, Vol. 54, October 2006. In the introduction paragraph in the 15th line there is possibly printing (typing) error that reads as “Treatment mainly consists of Acetyl cholinesterase agents”. The line should be read as “Treatment mainly consists of Anticholinesterase agents”.

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