Case Report

Wilson’s Disease Presenting with Hypokalemia, Hypoparathyroidism and Renal Failure

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Abstract  
Wilson’s disease (WD) is not as rare as once believed, and has a wide range of presentations with equally wide range of age of onset. Sometimes the primary presentation might be unusual and may require a thorough investigation to avoid a misdiagnosis. Our case presented with uncontrolled seizures, severe hypokalemia, renal failure, and hypoparathyroidism. After being diagnosed as WD and treated for the same patient made a remarkable recovery.

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. It is widely acknowledged that the disease is not as rare as once believed. Diagnostic errors are well recognized, and delays in diagnosis and initiation of treatment are common even in patients with a positive family history. The prevalence in Asian countries other than India varied between 33 and 68/100 000. There are no community-based incidence and prevalence studies of WD in India. Most of the studies were hospital-based. 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. Few patients present with renal impairment as the initial symptom, which might lead to a misdiagnosis. Recurrent hypokalemia with muscle weakness may be an initial manifestation of Wilson’s disease. Parathyroid insufficiency may be associated with WD due to deposition of copper in the parathyroid glands. Renal involvement occurs in the form of renal tubular defects (renal tubular acidosis type 1 and 2 and/or Fanconi’s syndrome) and hypercalciuria, nephrolithiasis with renal insufficiency.

In this article, we are discussing a case that presented to us with uncontrolled seizures, hypokalemia, renal dysfunction and hypoparathyroidism, later investigations proved the diagnosis of Wilson’s disease.

Case Presentation

An 18 year old, youngest sibling of a Muslim couple, born of non-consanguous marriage, presented with history of poorly controlled seizures (age of onset 14 years and on second line antiepileptic drugs). General examination revealed a tall stature, marfanoid features, and sunflower cataract in left eye, multiple maculo-papular rashes over body, oral candidiasis, gum hypertrophy, pallor without icterus. Systemic examination revealed quadriparesis with lack of neck holding, diminished motor reflexes and intact sensory system. Investigations revealed quadriparesis with lack of neck holding, diminished motor reflexes and intact sensory system. Investigations revealed renal failure with hematurna and no significant proteinuria; severe hypokalemia, hypocalcaemia, hyponatremia and normal serum phosphorus level; reduced S. PTH level, undetectable amount of Vitamin-D and normal serum ceruloplasmin level, raised urinary copper, liver function tests showed SGOT >SGPT (3:1) (Table 1). CT scan brain showed bilateral symmetrical confluent calcification in dentate nuclei, basal ganglia, thalami, cortical and subcortical white matter of high parietal region and centrum semi-ovale (Figure 1). Slit lamp examination revealed a Kayer-Fleischer ring.

With the preliminary picture of hypocalcaemia, bilateral basal ganglia calcification, seizures, hypoparathyroidism, severe persistent intractable hypokalaeimia, hypocalcaemia, mild metabolic acidosis, renal failure, altered liver enzymes, raised urinary copper and a K-F ring, a working diagnosis of WD was established. Pedigree chart failed to determine parental linkage. Patient’s Prognostic Index of Nazar was 4, indicating medical management.

Patient’s quadriparesis improved completely after potassium correction. Seizures were controlled after parenteral calcium supplementation along with oral cholecalciferol. On presentation he was taking combination of antiepiletics (Levetiracetam, Zonisamide and Carbamazepine) which were subsequently tapered and the patient was discharged on the carbamazepine alone. Patient was having no hepatic decompensation and no residual neuropsychiatric manifestations after electrolyte and nutrient supplementation; thereby tetrathiomolybdate was not considered and zinc acetate (25mg/dose 3 times a day) was started. On follow up patient maintains a serum potassium level of about 3.5 mEq/dl and serum calcium of 8 mEq/dl in subsequent 3 visits with oral supplements. Serum creatinine is 1.8 on last follow up. There were no further seizures and he is asymptomatic till date but azotemia persists. He was recently successfully operated for his sunflower cataract and has resumed his routine work.

Discussion

Except for the various well known and well documented neuropsychiatric manifestations of WD, involvements of other organs are also known. This young patient had a variety of baffling presentations ranging from severe hypokalemia induced quadriparesis to poorly controlled seizures. In the emergency ward, the initial differentials were that hypocalcaemia may be due to anti-epileptics and hypokalemia secondary to renal tubular acidosis. Further findings of hypoparathyroidism, deranged liver enzymes in the presence of raised urinary excretion of copper and K-F ring prompted us to consider this as an unusual presentation of WD. There has been a case report of an 11 year old girl presented with respiratory distress secondary to severe intractable hypokalemia in WD. Various other case reports suggest multisystem involvement along with hypoparathyroidism secondary to direct copper deposit in the glands. Renal tubular acidosis, a disorder of bicarbonate handling by the proximal tubules leads to nephrocalcinosis; weakening of the bone (due to calcium and phosphate loss) and occasionally aminoaciduria can be precipitated in WD, which has been reported by Carpenter TO et al. Since the patient had
not received any prior therapy, his manifestations were directly attributable to the WD itself.\textsuperscript{5,6}

The case is presented for its uniqueness in having all the various systemic manifestations of WD together like hypokalemia, hypocalcaemia, seizures, renal insufficiency and hypoparathyroidism (WD should be excluded from patients with unexplained renal impairment, while those with WD should take examinations of the kidney to identify renal impairment).\textsuperscript{2}

WD is perhaps more common than reported from India. There is a need for epidemiological studies and also multicentric genetic study in view of high degree of consanguinity in certain parts of India, particularly in south India. A nationwide registry may improve awareness among medical communities and lead to early diagnosis and prompt treatment. Once diagnosis is established the patient and the caregiver need to be educated regarding compliance and long-term follow-up. Governments, both central and state, should see that the drugs are made available at subsidized prices as WD is a potentially curable disease.

\textbf{Acknowledgement}

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\begin{table}[ht]
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\caption{Important Laboratory Investigations}
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Laboratory test & 09-05-10 & 17/05/2010 & \\
& (On admission) & & \\
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Haemoglobin (13 − 17 g/dl) & 11.3 & 10.4 & \\
S. Creatinine (0.6 − 1.4 mg/dl) & 2.61 & 2.29 & \\
S. Sodium (136 − 145 mEq/L) & 123 & 138 & \\
S. Potassium (3.8 − 5.2 mEq/L) & 1.6 & 3.32 & \\
Ionised Calcium(1.13-1.32 mEq/L) & 0.55 & - & \\
Total S.Calcium(8.6-10.2 mg/dl) & 3.2 & 5.78 & \\
S. Magnesium (1.32-2.14 mg/dl) & 1.42 & 1.75 & \\
S. Phosphorus (2.7-4.5 mg/dl) & 3.09 & 3.15 & \\
S.PTH(12-56 pg/ml) & - & 9.14 & \\
S.Vitamin D 3 (30-80 ng/ml) & - & <4 & \\
S. Alkaline Phosphatase (40 – 129 IU/L) & 73 & - & \\
ALT (0 – 40 IU/L) /AST (0 – 40 IU/L) & 99/275 & 36/37 & \\
24 Urinary Copper(up to 100 mcg/24 hours) & - & 185 & \\
S.Ceruloplasmin (20-35 mg/dl) & - & 25 & \\
S. Bilirubin (T/D/I) mg/dl & 0.43/0.16/0.27 & - & \\
PT with INr & 21.9/1.89 & - & \\
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\textbf{References}