Case Report

Wilson disease: early screening for better living

Maha Lakshmi Jagatha*, Arulkumaran Arunagirinathan, Bondada Hemanth Kumar

Department of Pediatrics, Sri Manakula Vinayagar Medical College and Hospital, Kalitheerthalkuppam, Puducherry, India

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*Correspondence:
Dr. Maha Lakshmi Jagatha,
E-mail: mahaparvesh23@gmail.com

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ABSTRACT

Autosomal recessive diseases are more common among consanguineous marriages noted particularly in southern parts of India. There is a gradual increase in the genome wide homogenecity with the increasing levels of consanguinity. Here we are reporting a case series of such an autosomal recessive condition, namely Wilson Disease (WD), where three children were affected with the disease, who were born out of consanguineous marriages. The first case presented with neuropsychiatric manifestations, the second case and third cases were diagnosed through screening of family members leading to earlier identification of the disease. In these cases consanguinity has been emphasised as the major predisposing factor leading to their manifestations. This case series highlights the importance of screening the other family members of the index case. Conditions such as Wilson disease have an excellent prognosis if pharmacotherapy is initiated appropriately.

Keywords: Consanguinity, Screening, Wilson disease

INTRODUCTION

Wilson Disease (WD), also known as hepatolenticular degeneration is an autosomal recessive disorder caused by the mutations in ATP7B gene which leads to impaired cellular copper transport resulting in excessive accumulation of copper in several organs, most notably the liver, brain and cornea.1 Clinical presentation of WD ranges from silent carrier to liver failure and irreversible brain damage, leading to death.

CASE REPORT

Case 1

The 11-year-old developmentally normal female child, born to a third-degree consanguineous couple brought with history of gait disturbances for 6 months in the form of swaying on both sides which was gradually progressive in nature. Child also had history of drooling of saliva, slurring of speech and decreased scholastic performance. Her hand writing deteriorated over the past few months and she was noticed to have emotional lability by her parents. There is no history of involuntary movements, seizures, weakness of limbs and paresthesias. No history suggestive of cranial nerve involvement or visual disturbances. She had a past history of jaundice on two occasions for which native treatment was taken. She never had any history of hematemesis. On examination, child was alert, conscious and oriented. Except for dysarthria, rest of the CNS examination was normal. Child had hepatosplenomegaly on abdominal examination.

Slit lamp examination showed bilateral KF rings. USG abdomen showed coarse liver (with surface irregularities
and altered echoes) and splenomegaly. USG Doppler showed Portal Vein (PV) diameter of 10mm at porta-hepatis. UGI endoscopy showed grade II esophageal varices. On further evaluation (Table 1) the child was diagnosed to have NEURO WILSON DISEASE and started on D-Penicillamine and pyridoxine following which her symptoms improved.

### Table 1: Laboratory investigations.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case No 1</th>
<th>Case No 2</th>
<th>Case No 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. ceruloplasmin</td>
<td>&lt;3mg/dl</td>
<td>4.44mg/dl</td>
<td>19.92mg/dl</td>
</tr>
<tr>
<td>24hr urinary copper excretion</td>
<td>217mcg/24hrs</td>
<td>109mcg/24hrs</td>
<td>181.73/24hrs</td>
</tr>
<tr>
<td>KF ring</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>53/43</td>
<td>348/401</td>
<td>32/22</td>
</tr>
<tr>
<td>Alkaline phosphate</td>
<td>429/90</td>
<td>747</td>
<td>284</td>
</tr>
<tr>
<td>GGT</td>
<td>90</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>PT/INR</td>
<td>60/5.5</td>
<td>20.1/1.57</td>
<td>Initial-14/1.03; Later-60/5.5</td>
</tr>
<tr>
<td>T. bilirubin/direct bilirubin</td>
<td>0.16/0.1</td>
<td>0.73/0.22</td>
<td>0.68/0.32</td>
</tr>
<tr>
<td>Nazer’s index</td>
<td>4</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

**Case 2**

The 8-year-old developmentally normal female child, younger sibling of case no 1 was screened for WD during which she was found to have mild fatty liver and splenomegaly with a PV diameter of 9mm without collaterals. UGI endoscopy was done which was found to be normal. Based on the rest of the investigations (table no 1), child diagnosed to have Asymptomatic Wilson disease for which she was started on D-Penicillamine and Pyridoxine.

**Case 3**

The 11-year-old developmentally normal male child, paternal cousin of case no. 1, born to a second degree consanguineous marriage was also screened for WD and found to have low serum ceruloplasmin, for which child was started on zinc therapy prophylactically. 6months later, he developed symptoms in the form of upper gastrointestinal bleed following which he was started on D-Penicillamine and pyridoxine.

**DISCUSSION**

While the worldwide prevalence of Wilson Disease (WD) is 1 in 30,000, the carrier frequency is as high as 1 in 90 persons. The mortality and morbidity has been reduced in the past few decades due to the increased awareness, recognition and aggressive management.

A classic case of WD in pediatrics usually presents with hepatic involvement which may be missed or it may not be the only initial symptom. By 10 years of age, 83% will present with hepatic manifestations and 17% with neuropsychiatric manifestations; between 10 and 18 years, 52% present with hepatic and 48% with neuropsychiatric symptoms. After the age of 18 years, 75% patients present with neuropsychiatric features and 25% patients develop liver disease. The variability in the age of onset of WD probably reflects differences in mutations and penetrance, extragenic factors, and environmental influences including diet.

Hepatic presentation varies from subclinical stage where elevated transaminases may be an incidental finding to acute fulminant liver disease. Most of the patients present initially with jaundice (50%) as seen in our case no 1, which was not investigated further due to low index of suspicion which indicates the importance of screening. In an analysis of 100 cases from Bangladesh, 69% patients presented only with hepatic manifestations, 6% only with neurological features and 14% manifested with both hepatic and neurological disease. The age of onset of hepatic WD was between 5 to 10 years and that of neurological was after 10 years.

Among neurological manifestations, dystonia, dysarthria and cognitive decline are the most common manifestations. In particular, WD should be considered in children with liver abnormalities with uncertain etiology, especially in those presenting with liver disease accompanied by neurologic and psychiatric symptoms. A study by Ala A et al reported that WD can present as late as eighth decade of life which highlights the wide range of phenotypical expression for the disease.

Our study included three large families which spanned three generations that included 19 members and three consanguineous marriages were noticed among them. Out of these, three children were diagnosed to have WD. Extensive pedigree was obtained for all the families (Figure 1). This indicates inbreeding as one of the important factors that contribute to the prevalence of the disease. The result of this is limited genetic heterogeneity among them as they would share common genetic factors.
*Case no 1 (Index case) and Case no 2 are siblings. **Case no 3 is a paternal cousin of case no 1 and 2.


