Detection of Undiagnosed Wilson’s Disease after Hepatitis A Virus Infection

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Abstract

Introduction: Some reports have considered hepatitis A as a possible factor in the development of acute decompensation in patients with Wilson’s disease. Here we report the case of a delayed diagnosis of Wilson’s disease in the end of the third decade of life in a patient infected with hepatitis A.

Case report: The patient was a 26 year old woman with complaints of nausea and vomiting, anorexia, ichter, fever and epigastric pain since a week before admission. She had not any history of previous disease in herself and her families. Considering an increase in liver enzymes, serum bilirubin levels, serum IgM HAV antibody positivity and symptoms suggestive of hepatitis A associated with autoimmune hepatitis considered and patient was treated and then discharged.

The patient returned two weeks later and symptoms such as ichter, fatigue and edema of the lower extremities were still present. Wilson’s disease is suspected, laboratory testing and ophthalmologic examination was performed and diagnosis was confirmed. The patient was treated with D-penicillamin, pyridoxine, and zinc sulfate. On re-examination, the patient’s symptoms largely resolved and in the following experiments response to treatment was appropriate.

Conclusion: Hepatitis A can be considered as a factor for acute decompensation in undiagnosed patients with Wilson’s disease.

Keyword: Wilson’s disease; Hepatitis A; Copper; Coruloplasmine

Introduction

Wilson disease is an autosomal recessive disorder of copper metabolism in the liver and causes degenerative changes in various organs such as the brain, liver and other organ involvement such as Kayser–Fleischer ring in eyes [1,2]. The relative prevalence of this disorder is one in one hundred thousand to one in five hundred thousand at live births [3,4]. In this disease, copper accumulates, as the result of mutation of ATP7B gene located on chromosome 13, and causes damage to the liver and other organs, such as brain and kidneys [2,5].

Wilson’s disease can have several manifestations. Classic findings include liver disease, kidney disease, and nerve problems. Liver involvement may be includes asymptomatic hepatomegaly (with or without splenomegaly), sub-acute or chronic hepatitis or fulminant hepatic failure. Due to hepatic dysfunction patients may be at risk for delay in puberty or coagulopathy. Arthritis and glandular disorders are unusual manifestations in these patients [5].

Changes in the basal ganglia that are seen on MRI are diagnostic for the disease [6]. Neurological and psychological symptoms appear much later in life [4].

Early diagnose of this disease, prevents the damaging effects of the accumulation of copper in various organs and also provides possibility of screening of disorder in the patient’s family [7]. More than 80% of patients with early signs of the disease will develop in the first three decades of their life, but even disease has also been reported in later decades of life [2]. Iran is among the countries where hepatitis A infection is endemic and high prevalence rate in 6 months to 1.9 year children have been reported (61.5%) [8]. Increases in incidence has been reported with age between 85 to 99% in different part of the country [9]. Some reports have been considered hepatitis A infection as a possible factor in the development of acute decompensation in unknown patients with Wilson’s disease [10]. Here we report the case of a delayed diagnosis of Wilson’s disease in the end of the third decade of life in a patient infected with hepatitis A.

Case Report

The patient was a 26 year old woman with complaints of nausea and vomiting, anorexia, ichter, fever and epigastric pain since a week before admission. She had not any history of previous disease in herself and her families. She had a history of medicinal use of Senna for constipation since 12 years ago. In physical examination she was ichteric, had mild epigastric tenderness and 38˚C fever which fever resolved after 48 hours. There was not any sign of encephalopathy. Increase in liver enzymes, serum bilirubin levels, and serum IgM HAV antibody positivity was seen in primary laboratory test. Initial laboratory tests are presented in Table 1 and 2.

Abdominal ultrasound was performed on the patient’s liver, gallbladder and spleen was normal. Bone marrow aspiration was performed in the patient and showed erythroid hyperplasia. Results of the patient’s laboratory tests in the second and seventh day after admission and diagnosis was confirmed. The patient was treated with D-penicillamin, pyridoxine, and zinc sulfate. On re-examination, the patient’s symptoms largely resolved and in the following experiments response to treatment was appropriate.

Conclusions

Hepatitis A can be considered as a factor for acute decompensation in undiagnosed patients with Wilson’s disease.

Table 1: Laboratory data of patient in admission.

<table>
<thead>
<tr>
<th>Fractions</th>
<th>%</th>
<th>% Normal</th>
<th>grid/l</th>
<th>(grid/l) Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>51.0</td>
<td>54-66</td>
<td>2.7</td>
<td>3.2-5.3</td>
</tr>
<tr>
<td>Alpha_{a1}</td>
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<td>1.4-2.8</td>
<td>0.1</td>
<td>0.1-0.2</td>
</tr>
<tr>
<td>Alpha_{a2}</td>
<td>5.7</td>
<td>9.1-13.8</td>
<td>0.3</td>
<td>0.6-1.1</td>
</tr>
<tr>
<td>Beta</td>
<td>11.2</td>
<td>8.7-14.4</td>
<td>0.6</td>
<td>0.5-1.2</td>
</tr>
<tr>
<td>Gamma</td>
<td>29.4</td>
<td>10.6-19.2</td>
<td>1.5</td>
<td>0.6-1.5</td>
</tr>
</tbody>
</table>

Table 2: Patient’s Serum Protein electrophoresis.

Table 3: Laboratory data of patient in second admission.

Table 4: Laboratory data of patient in second admission.

Table 5: Trend of laboratory findings of patient in two week after second admission.

and third weeks after admission is shown in Table 3 which did not show any much change.

Core needle liver biopsy was performed in patient that results are as follows; swollen and pale changes with accumulation of numerous inflammatory cells in parenchyma, infavor of postnecrotic collapse and early fibrosis of viral hepatitis. Due to the decrease in serum bilirubin levels, improve in the general situation and the lack of signs and symptoms of hepatic encephalopathy and no increase in the PT and INR during admission patient was discharged with a hepatits A plus autoimmune hepatitis diagnosis. 10 mg/day prednisone was administered and advised for came back after 2 weeks after doing laboratory tests for follow up.

The patient returned two weeks later and symptoms such as icter, fatigue and edema of the lower extremities were still present. She was icteric and had +2 lower extremities edema. Results of the patient’s laboratory tests in follow up evaluation are shown in Table 4. Due to clinical sign and laboratory findings Wilson’s disease is suspected and laboratory test were requested and the results were as follow: serum coruloplasmine was 13 mg/dl, serum copper level and unbounded serum copper level were 170 mcigr/dl (normal value) and 129.5 mcigr/dl (normal value) respectively and finally copper level in 24 hour urine was 476 mcigr (normal value). To confirm the diagnosis of Wilson’s disease ophthalmologic examination was performed and typical Kayser–Fleischer ring in eyes was confirmed. The patient was treated with D-penicillamin, pyridoxine, and zinc sulfate. Trend of patient’s laboratory tests in follow up evaluation are shown in Table 5.

On re-examination, the patient’s symptoms largely resolved and in the following experiments one month after treatment the response to treatment were appropriate. The last patient’s laboratory results is showed in Table 6.

Discussion

We report a case of delayed diagnosis of Wilson’s disease in a 26-year-old woman after Super infection with hepatitis A. In this disease, copper accumulates, as the result of mutation of ATP7B gene located on chromosome 13, and causes damage to the liver and other organs, such as brain and kidneys [2,5].

The natural balance of the copper in the body is done through biliary excretion of copper by the liver Lysozymes. Most copper is excreted in the bile as a non-absorbable. Impairment in biliary excretion of copper in Wilson’s disease causes liver damage. Gradual accumulation of copper in the liver exceeds the capacity of the liver and by leaving it leads damage in the other organs, especially in the brain and kidneys [2,6].

Histological changes in liver tissue are not specific for Wilson. The earliest microscopic findings are abnormal deposition of glycogen and fat, varying degrees of fibrosis, nucleic vaculization, active hepatitis and cirrhosis may be outdated. Nodular cirrhosis is the most common abnormality. Liver involvement may be in the form of acute hepatitis, fulminant hepatitis, chronic active hepatitis or cirrhosis with portal hypertension [11]. Non-specific symptoms may cause diagnostic confusion with other chronic and acute liver diseases such as viral and autoimmune hepatitis [12]. Pathologic findings in our patient largely were consistent with viral and autoimmune hepatitis.

Sometimes the symptoms in patients even in one family depending on various factors, and different range in severity may occur [7]. Mak et al. [7] reported a case of Wilson’s disease which diagnosed after 18 years in one boy which had a confirmed symptomatic Wilson’s disease in his sibling which had not been diagnosed despite screening in previous years and he was given the diagnosis after genetic evaluation after 18 years. While obvious symptoms of the disease did not occur in this patient unlike his sister. Accordingly, authors said only rely on the biochemical screening, particularly among families with Wilson disease is not correct and recommends made genetics screening in these cases.

Czlonkowska et al. [1] reports two Wilson’s cases in 30 and 33 years old women who were presented with HELLP syndrome in pregnancy and Wilson disease confirmed in them in postpartum period.

Table 1: Laboratory data of patient in admission.

Table 2: Patient’s Serum Protein electrophoresis.

Table 3: Laboratory data trend of patient in one month after admission.

Table 4: Laboratory data of patient in second admission.

Table 5: Trend of laboratory findings of patient in two week after second admission.

Table 6: Last patient’s Laboratory data one month after Wilson’s disease treatment.
Researchers listed the factors such as ApoE, MURR1 and copper content of the diet as effective factors on delay in Wilson’s disease sign and symptoms presentation [7,13,14]. In our patient, this can also be considered. Hepatitis A and E infection in patients with chronic liver disease has been reported as a cause for decompensation of the underlying liver diseases and increased mortality in these patients and accordingly hepatitis A vaccination is recommended in these patients [10,15,16]. Sallie, et al. [16] reported a six year old girl with fulminant hepatic failure resulting from hepatitis E and coexistent Wilson’s disease. In addition, chronic liver disease may exacerbate by drugs, the addition of sepsis, gastrointestinal bleeding, hepatic and portal vein thrombosis and hepatocellular carcinoma [15].

Our patient also presented with signs of liver failure without history of liver disease and the reason for this were determined super infection of hepatitis A on Wilson’s disease after performing diagnostic tests. Due to the nonspecific nature of the symptoms of Wilson’s disease which is well seen in our patient, the diagnosis may be delayed and often be with a sign of liver failure [17] or other diagnosis being considered for the patients.

Gao and colleagues [12] in their study were evaluated the clinical picture and diagnosis conditions such as mis-diagnosis in 128 Wilson’s cases. Based on their results, 55 patients (42.9%) of patients initially diagnosed with other diseases and the most common cause for mis-diagnosis in Wilson’s cases, including hepatitis A and chronic hepatitis.

In general, it seems hepatitis A super infection in Wilson’s disease cases that have not been diagnosed nor have not severe symptoms may worsen the symptoms of this disease. Hepatitis A can be considered as a factor for acute decompensation in undiagnosed patients with Wilson’s disease. Therefore, considering the diagnosis of Wilson’s disease in patients with similar signs like our patient and screening biochemical tests in them to evaluate Wilson disease are recommended.

References