THE POTENTIAL RELATIONSHIP BETWEEN PIMOZIDE AND CHOLESTATIC HEPATITIS

Salih Saygin Eker, Cengiz Akkaya, Asli Sarandol, Canan Yusufoglu, Selcuk Kirli

ABSTRACT

We describe a 40 year-old woman who was diagnosed as a case of Major Depressive Disorder with Psychotic Features. Patient’s physical examination and laboratory tests revealed no abnormalities at the time of admission. Just after two days of addition of pimozide to the ongoing therapy, jaundice and elevated liver enzymes were detected which may indicate a drug induced hepatitis. Serologic tests, hepatobiliary ultrasonography and pelvic MRI were performed and no abnormality was detected. Patient was diagnosed with drug induced cholestatic hepatitis by gastroenterology department. Following discontinuation of all drugs, liver enzymes were gradually normalized and jaundice resolved.

Key words: Pimozide, Hepatotoxicity, Antipsychotics, Adverse event.

INTRODUCTION

Neuropsychiatric drugs have been reported to account for 16% of drug induced hepatotoxicity. Both typical and atypical antipsychotics have been associated with cholestatic liver disease.

Though antipsychotics are associated with hepatitis, cholestatic type of hepatotoxicity is not reported with pimozide so far. Though it is hard to clarify by which drug hepatotoxicity caused abrupt presentation of hepatitis, but occurring just after two days of pimozide initiation may indicate a pimozide associated cholestatic hepatitis in this case.

Since drug induced liver disease may have life threatening consequences in some cases, early diagnosis and identification of the drug in such cases will prevent even fatal outcomes. The possibility of pimozide-induced cholestatic hepatotoxicity presented here may help clinicians in this regard.

CASE HISTORY

A 40 year-old woman was diagnosed with “Major Depressive Disorder, Single Episode, Severe With Psychotic Features (296.24)” brief name of diagnostic criteria and reference according to the criteria of Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition, Text Revision 2. Patient’s physical examination and laboratory findings were normal at the time of admission at the Psychiatry Department of Uludag University Medical Faculty. Since she refused to take oral medication, haloperidol 15 mg/day and chlorpromazine 75 mg/day were given intramuscular the day she was hospitalized. At the fourth day of her hospitalization the doses were reduced to haloperidol 10 mg/day and chlorpromazine 50 mg/day. Venlafaxine 150 mg/day was also started due to her depressive symptoms. At the eighth day of her admission haloperidol and chlorpromazine were discontinued and risperidone 3 mg/day was combined with venlafaxine. At the twenty-first day of hospitalization, risperidone was discontinued due to galactorrhea. Therefore risperidone was replaced with pimozide 2 mg/day. Two days after pimozide initiation, patient suffered from pruritis, yellow scleras and jaundice. Due to clinical presentation and laboratory findings, all medications were discontinued.

Laboratory findings including leukocyte and platelet count, hemoglobin level, prothrombin time and electrolytes were normal. Physical examination was normal except for observed jaundice. She was referred to gastroenterology department the same day and she was initially diagnosed with toxic hepatitis. We were advised to give patient liver protective diet and hydration. Progress of transaminases is summarized in Table 1.

Results of serologic tests for hepatitis A, B, and C viruses, HIV, antimitochondrial and antinuclear antibod-

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ies were negative. Hepatobiliary ultrasonography and pelvic MRI were performed and no abnormality was detected. Jaundice began to resolve at the third week of hepatitis. The patient was regularly monitored by gastroenterology department and they concluded that the patient had a drug induced cholestatic hepatitis.

Personal medical history of the patient revealed no previous liver disease or any infectious disease that may be harmful to liver, no alcohol or substance use, no previous psychotropic medication or psychiatric disorder. Patient was discharged on sertraline 50 mg/day medication on the fifty-first day of her hospitalization with partial remission. Patient gave documented informed consent for the publication of her data.

**DISCUSSION**

The diagnosis of drug induced liver disease is determined by elevation of ALT, AST, ALP and GGT or clinical signs such as hepatitis and jaundice. Following the addition of pimozide to the ongoing therapy, detected serum liver enzyme elevations and jaundice confirms hepatotoxicity in this case.

Haloperidol, risperidone and chlorpromazine were associated with cholestatic hepatitis. Though it is hard to clarify by which drug hepatotoxicity is caused, one may presume chlorpromazine or risperidone are usual suspects for the hepatotoxicity. However, in this case, chlorpromazine and risperidone had been stopped and the patient was on pimozide and abrupt presentation of hepatitis two days after pimozide initiation made us think of a pimozide induced cholestatic hepatitis or a drug-drug interaction.

Though there are several reports that have been published involving cholestatic hepatitis associated with several antipsychotics but to the best of our knowledge, cholestatic type of drug induced hepatotoxicity was not reported with pimozide so far.

**CONCLUSION**

Early diagnosis of drug induced liver disease and identification of the drug may prevent more severe even fatal outcomes. Sufficient knowledge of literature with reported cases may help clinicians to clarify the causes of drug induced liver diseases. Therefore, the possibility of pimozide-induced cholestatic hepatotoxicity presented here may help clinicians in this regard.

**REFERENCES**


<table>
<thead>
<tr>
<th>Table 1</th>
<th>Progress of liver function test results following pimozide initiation</th>
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<tbody>
<tr>
<td></td>
<td>AST (10-40 UI/L)</td>
</tr>
<tr>
<td>2 days after pimozide initiation</td>
<td>155</td>
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<tr>
<td>3 days after pimozide initiation</td>
<td>151</td>
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<tr>
<td>6 days after pimozide initiation</td>
<td>200</td>
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<tr>
<td>8 days after pimozide initiation</td>
<td>153</td>
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<tr>
<td>13 days after pimozide initiation</td>
<td>39</td>
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<tr>
<td>17 days after pimozide initiation</td>
<td>21</td>
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<tr>
<td>27 days after pimozide initiation</td>
<td>26</td>
</tr>
</tbody>
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AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TB: Total bilirubin; ALP: Alkaline phosphatase. Normal range of transaminases are given in parenthesis.