JPPS 2008; 5(2): 120-121 CASE REPORT

THE POTENTIAL RELATIONSHIP BETWEEN PIMOZIDE AND CHOLESTATIC HEPATITIS

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# 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 dis- continuation 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 hepatotoxicity1. Both typical and atypical antipsychotics have been associ- ated with cholestatic liver disease.

Though antipsychotics are associated with hepa- titis, 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 hepa- titis, but occurring just after two days of pimozide initia- tion may indicate a pimozide associated cholestatic hepa- titis in this case.

Since drug induced liver disease may have life threatening consequences in some cases, early diag- nosis 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.

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# CASE HISTORY

A 40 year-old woman was diagnosed with “Major Depressive Disorder, Single Episode, Severe With Psy- chotic Features (296.24)” brief name of diagnostic crite- ria and reference according to the criteria of Diagnostic and Statistic Manual of Mental Disorders, Fourth Edi- tion, Text Revision 2. Patient’s physical examination and laboratory findings were normal at the time of admission at the Psychiatry Department of Uludag University Medi- cal 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 hospitaliza- tion, 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 clini- cal presentation and laboratory findings, all medications were discontinued.

Laboratory findings including leukocyte and plate- let count, hemoglobin level, prothrombin time and elec- trolytes were normal. Physical examination was normal except for observed jaundice. She was referred to gas- troenterology 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-

Table 1

Progress of liver function test results following pimozide initiation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **AST**  **(10-40 UI/L)** | **ALT**  **(20-50 UI/L)** | **TB**  **(0.2-1.1 g/dL)** | **ALP**  **(37-147 UI/L)** |
| 2 days after pimozide initiation | 155 | 322 | 5.82 | 297 |
| 3 days after pimozide initiation | 151 | 320 | 6.69 | – |
| 6 days after pimozide initiation | 200 | 383 | 6.87 | 312 |
| 8 days after pimozide initiation | 153 | 370 | 4.05 | – |
| 13 days after pimozide initiation | 39 | 138 | 2.14 | – |
| 17 days after pimozide initiation | 21 | 61 | 1.5 | 183 |
| 27 days after pimozide initiation | 26 | 22 | 1.68 | 94 |

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TB: Total bilirubin; ALP: Alkaline phosphatase. Normal range of transaminases are given in parenthesis

ies were negative. Hepatobiliary ultrasonography and pelvic MRI were performed and no abnormality was de- tected. Jaundice began to resolve at the third week of hepatitis. The patient was regularly monitored by gas- troenterology 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 disor- der. 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 de- termined by elevation of ALT, AST, ALP and GGT or clini- cal signs such as hepatitis and jaundice 3. Following the addition of pimozide to the ongoing therapy, detected serum liver enzyme elevations and jaundice confirms hepatotoxicity in this case.

Haloperidol4, risperidone5 and chlorpromazine6 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 presenta- tion 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 pre- sented here may help clinicians in this regard.

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