CLINICAL PHARMACIST INTERVENTIONS ON MILIARY KOCH’S PATIENT WITH ANTITUBERCULAR THERAPY-INDUCED HEPATOTOXICITY AND PSYCHOSIS: A RARE CASE REPORT

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ABSTRACT

Psychosis and hepatotoxicity are the dangerous side effects of the antitubercular drugs directly observed treatment short course (DOTS) therapy. Hematological spreading of tubercular bacteria in the lungs is also known as miliary tuberculosis. In this case study, a 45-year-old man, weighing 55 kg was brought to the hospital with the chief complaints of vomiting (multiple episodes), fever, pain in abdomen, difficulty in breathing, mucoid cough, and disturbed sleep for the past 1 week. The patient had a known case of smear-positive pulmonary tuberculosis (in the past 1 month), but at that time, patient was not taking regular antitubercular treatment (ATT) medications (DOTS therapy). After 3rd week of irregular antitubercular drug treatment, patient developed with the problems such as vomiting (multiple episodes), fever, pain in abdomen, difficulty in breathing, cough with expectorations, disturbed sleep, and delirium. Pulmonologists had found the provisional and final diagnosis on the bases of subjective and objective observations (Table 1). Although it was started with modified antitubercular drugs therapy, the first ATT medication and tablet pyridoxine, antipsychotic medicines, and modified ATT were added in the therapy. Psychotic in a patient on ATT can be one of the complications of tablet isoniazid. As a clinical pharmacologist, we prevent and minimize drugs-induced complications and adverse drug reactions. Proper patients counseling and patients’ education are important for the better management of patients.

Keywords: Antitubercular drug therapy, Directly observed treatment short course, Psychosis, Miliary tuberculosis, KOCH’S.

INTRODUCTION

Tuberculosis is also known as KOCH’S. It is a granulomatous disease. Hematological spreading of tubercular bacteria in the lungs is also known as miliary tuberculosis. Antitubercular drug therapy is generally used in the tuberculosis, this therapy is also known as directly observed treatment short course (DOTS) therapy [1-3]. Antitubercular drug therapy is mainly responsible for the irreversible/reversible hepatotoxicity, hepatitis, ototoxicity, neuromuscular blockage, neuropathy, ophthalmopathy, thrombocytopenia, and nephrotoxicity. Several antitubercular medications are known to cause neuropsychiatric adverse reactions such as delirium, depression, mania, psychosis, seizure disorder, and hepatotoxic adverse drug reactions (ADRs) such as nausea, vomiting, gastritis, and abdominal pain [4,5]. Psychosis and hepatotoxicity are the known complication of the isoniazid (INH) and other antitubercular drug therapy. Neuropsychiatric ADRs usually appear during the initiation of the treatment or while changing from a previously prescribed regimen [6,7]. Isoniazid is the first-line antitubercular agent for the treatment of tuberculosis. Tuberculosis is the life-threatening public health problem [8]. Although there are many case reports already done previously, INH induced psychosis and hepatotoxicity particularly in tuberculosis (TB) patients in this case, patient’s condition was resolved only after discontinuation of the DOTS therapy and started the modified ATT therapy [9,10].

CASE STUDY

• A case of 45-years-old male, weighing 55 kg was brought to the hospital with chief complaints of vomiting (multiple episodes), fever, pain in abdomen, difficulty in breathing, mucoid cough, disturbed sleep, delirium for the past 1 week with no past and family history of hypertension, diabetes mellitus, thyroid disease, mental disorder, and pulmonary tuberculosis (PTB).

• Patient was an ex-smoker, ex-alcoholic, and preferentially non-vegetarian.

• At the time of general vital study pulse rate (PR)-93 bpm, blood pressure (BP)-120/90 mmHg, oxygen saturation (SpO₂) 94% at the atmospheric air, abdomen examination was soft and non-tender and cardiac sounds S1, S2 positive were noted.

• He had a known case of smear-positive PTB (in the past 1 months), but at that time, patient was not taking regular ATT medications (DOTS therapy).

• After 3rd week of irregular antitubercular drug treatment, patient developed with the problems such as vomiting (multiple episodes), fever, pain in abdomen, difficulty in breathing, cough with expectorations, disturbed sleep, and delirium.

• Pulmonologist had advised the patient for routine laboratory tests such as complete blood counts (CBCs), liver function tests (LFTs), kidney function tests (KFTs), Chest X-ray (CXR), high-resolution computed tomography (HRCT), and magnetic resonance imaging (MRI) brain.

• On the same day, pulmonologist prescribed the following drugs to the patient after examination:

  1. Injection Pantoprazole – 40 mg TDS
  2. Tablet Akurit-4 (3 Tab) OD
  3. Tablet Pyridoxine 40 mg ½ OD
  4. Injection Ondasetron TDS
  5. Injection Piperacillin + Tazobactam 4.5mg TDS, IV
  6. Syrup Mucaine Gel 4 TSSF TDS
  7. Tablet Heptagon OD

• On the 2nd day, BP was recorded as 130/80 mmHg and PR was 92 beats/min. According to the laboratory reports, patient laboratory investigations in the report LFTs, CBCs, CXR, HRCT, and viral marker are show many abnormalities. Chest X-ray was seen the miliary KOCHS. Viral markers for hepatitis, including hepatitis A, B, and C viruses, and human immunodeficiency virus all were negative (Table 1 and Fig. 1).

• Pulmonologist was on hold of previous antitubercular drug therapy. Although it was started with modified antitubercular drugs
Pulmonologist monitored the laboratory investigations in the reports.

Patient was advised to take proper fluid, high protein, and diet with the following:
- Tab. Oflox
- Tab. Benadon

Pulmonologist stopped the tab lorazepam and haloperidol on the patient's S.O. Miliary KOCH'S was non-reactive.

20–40% of LFTs were within the reference value.

4000–11000 BU/mL for ATT was normal, that is, 120/70 mmHg and PR was 86 beats/min with SPO2 concentration 96%. Patient no fresh complaints on day 4.

On 5th day, patient complains loss of appetite, on brief discussion of pulmonologist with a clinical pharmacologist, counseling, along with diet assessment was done of patient.

Patient was advised to take proper fluid, high protein, and diet rich in fibers. Pomegranate juice was advised to be avoided.

Pulmonologist stopped the tab lorazepam and haloperidol on the consultation of neurology doctors. He started Tab Quetiapine 50 mg/day and Tab Risperidone 4 mg/day.

On 6th, 7th, 8th, and 9th days, no fresh complaints were seen, and all vitals and laboratory's reports were normal.

On the basis of subjective and objective observation, pulmonologist had made a final diagnosis of Miliary KOCH'S with ATT-induced hepatotoxicity and psychosis.

After staying 10 days in hospital, the patient condition was improved.

On normalization of patient's conditions, pulmonologist started first-line antitubercular drug therapy containing Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol with continued liver tonics.

Patient discharged with appropriate medication (Table 3) and patient counseling after advising review once in a month with LFTs reports.

DISCUSSION WITH CLINICAL PHARMACOLOGIST INTERVENTIONS

ADRs analysis
On the basis of ADRs analysis on the Naranjo Scale, possible hepatotoxicity and psychosis induced by ATT has found probable and found to be the major ATT-induced ADRs. The case history analysis found the "B" Type of ADRs with H, R, and Z and found to be preventable at a very early stage, and acute phases (Table 4).

ADRs management
ADRs were known as diagnosed at a very early stage of ATT therapy. In general, B Type ADRs are bizarre and need hospitalization if became severe.

![Fig. 1. Chest X-ray and high-resolution computed tomography of chest](https://example.com/fig1.png)

Table 1: Clinically investigational findings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test value (Day-1)</th>
<th>Test value (Last Day)</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFTs</td>
<td>349</td>
<td>66</td>
<td>17–59 IU/L</td>
</tr>
<tr>
<td>SGOT</td>
<td>248</td>
<td>59</td>
<td>9–52 IU/L</td>
</tr>
<tr>
<td>SGPT</td>
<td>175</td>
<td>51</td>
<td>12–43 IU/L</td>
</tr>
<tr>
<td>GGT</td>
<td>1.6</td>
<td>0.8</td>
<td>0.2–1.3 mg/dL</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>1.2</td>
<td>0.2</td>
<td>0.0–0.8 mg/dL</td>
</tr>
<tr>
<td>ALP</td>
<td>233</td>
<td>133</td>
<td>30–126 IU/L</td>
</tr>
<tr>
<td>CBCs</td>
<td>96</td>
<td>72</td>
<td>40–80%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>66</td>
<td>34</td>
<td>20–40%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>18</td>
<td>12</td>
<td>02–10%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>20413</td>
<td>7156</td>
<td>4000–11000 cell/cumm</td>
</tr>
</tbody>
</table>

Viral markers
- Reactive/Non-reactive
  - Hepatitis A: Non-reactive
  - Hepatitis B: Non-reactive
  - Hepatitis C: Non-reactive
  - HIV virus: Non-reactive

Radiological Markers
- Impression's
  - Chest X-ray: s/o Miliary KOCH'S
  - HRCT: Finding a case of suggestive of acute infective airway disease pulmonary KOCH'S.
  - MRI brain: Acute impact and cerebral atrophy.

Table 2: Neurology references

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drugs prescribed (brand name)</th>
<th>Generic name</th>
<th>Dose</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Tab Lanzep</td>
<td>Lorazepam</td>
<td>2 mg</td>
<td>OD</td>
</tr>
<tr>
<td>2.</td>
<td>Inj. Haloperidol</td>
<td>Haloperidol</td>
<td>10 mg</td>
<td>OD</td>
</tr>
<tr>
<td>3.</td>
<td>Tab Benadon</td>
<td>Pyridoxine</td>
<td>20 mg</td>
<td>OD</td>
</tr>
<tr>
<td>4.</td>
<td>Start modified ATT medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tab L-Qn</td>
<td>Levofloxacin</td>
<td>750 mg</td>
<td>OD</td>
</tr>
<tr>
<td></td>
<td>Tab Combutol</td>
<td>Ethambutol</td>
<td>800 mg</td>
<td>OD</td>
</tr>
<tr>
<td></td>
<td>Inj. Streptomycin</td>
<td>Streptomycin</td>
<td>0.75 gm</td>
<td>OD</td>
</tr>
</tbody>
</table>

ATT: Antitubercular treatment

Table 3: Discharge medication

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drugs prescribed (Brand Name)</th>
<th>Generic Name</th>
<th>Dose</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Antitubercular therapy</td>
<td>Tab. Rifampicin</td>
<td>450 mg</td>
<td>OD-BBF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tab. Ethambutol</td>
<td>800 mg</td>
<td>OD-HS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tab. Pyrazinamide</td>
<td>1000 mg</td>
<td>OD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tab. Pyridoxine</td>
<td>20 mg</td>
<td>OD-BBF</td>
</tr>
<tr>
<td>2.</td>
<td>Tab. Benadon</td>
<td>Tab. Olfoxin</td>
<td>500 mg</td>
<td>OD</td>
</tr>
<tr>
<td>3.</td>
<td>Tab. Pentop</td>
<td>Tab. Pantoprazole</td>
<td>40 mg</td>
<td>OD</td>
</tr>
<tr>
<td>4.</td>
<td>Tab. Oflox</td>
<td>Multivitamin</td>
<td>200 ml</td>
<td>TDS-3 TSF</td>
</tr>
<tr>
<td>5.</td>
<td>Syt. R-Qual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Hold isoniazid medications.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
As a health-care team member clinical pharmacologists are need to be made aware of these potentially fatal adverse effects associated with antitubercular therapy through conduction of quality-based seminars, published medical literature, learning programs, conferences, and health-care awareness camps.

The study was done after getting clearance from Hospital Ethical Committee. Informed consent was obtained from all the patients.

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CONFLICTS OF INTEREST

The authors report no conflict of interest that is directly, that is, directly relevant to the content of the case report.

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REFERENCES