A CASE REPORT ON ATT INDUCED DYSTONIA WITH HEPATITIS

G. Sarah Marlyn*, Neelam Injeti, Safura Tasneem and Ayesha Sami Uddin

Department of Pharm D, CMR College of Pharmacy, Kandlakoya (V), Secunderabad, 501401, Telangana state, India.

ABSTRACT
Anti-tuberculosis therapy is a goal standard therapy for active TB. The regimen involves Isoniazid, Rifampicin, Ethambutol, Pyrazinamide and Streptomycin. These drugs are given generally in multi-drug combination therapy depending on the requirement of the patient and the severity. These drugs have been associated with a variety of adverse effects ranging from mild to severe. Ototoxicity and Hepatotoxicity are common. Hepatitis and neuropathy leading to involuntary muscle movement (dystonia) has also been noted which is the drug induced condition in this patient.

KEYWORDS: Anti tuberculosis therapy, Involuntary muscle contractions, Myopathy, Neupathy, Hepatotoxicity.

INTRODUCTION
It is a chronic disease caused by the bacillus Mycobacterium tuberculosis and spreads from person to person through air. TB usually affects the lungs but it can also affect other parts of the body, such as brain, intestines, kidneys, or the spine. Symptoms of TB depend on where in the body the TB bacteria are growing.\textsuperscript{[1]} There are multi drug regimens available for the treatment of tuberculosis. The number of drugs and the combinations depend on the severity and the type of TB involved (Active TB or Latent TB).\textsuperscript{[2]} The first line drugs for TB include Isoniazid (H/Inh), Rifampicin (R/Rif), Pyrazinamide (Z/Pza) and Ethambutol (E/Emb). Patients with TB are required to take treatment consisting of a two month intensive phase for two months (Inh+Rif+Pza+Emb) and a continuation phase for the next four months (Inh+Rif).\textsuperscript{[3]} Some of the common adverse drug reactions associated with the anti-tuberculosis therapy include hepatitis, peripheral neuropathy, hematological disorders, exanthema, myopathy, rhabdomyolysis, neuritis and myocarditis.\textsuperscript{[4]} Once an ADR develops it
can cause significant morbidity and mortality and by causing withdrawal of the first line treatment, and ultimately preventing adherence to the second line therapy as a result.[5]

Dystonia refers to the intermittent muscle contractions that causes involuntary movements of the limbs.[6] The mechanism in which ATT drugs are responsible for causing neuropathy is unsure. It is likely that isonicotinic acid hydrazide interferes with vitamin B6 (pyridoxine) metabolism, leading to deficiency in biological active B6 by inhibition of pyridoxine-dependent enzyme systems.[7] INH is generally known to be one of the major causes of hepatotoxicity in the treatment of TB, and is metabolized to hepatotoxic intermediates mainly by N-acetyltransferase (NAT). Polymorphic NAT acetylator status with DIH have been published and have indicated that slow acetylators are a risk factor for anti-TB DIH and that patients are prone to developing more severe hepatotoxicity than with rapid acetylators.[8]

Monitoring and confirming the culprit drug(s) can therefore lead to proper steps to implement in order to eradicate the bacilli as well as ensure that there are no complications associated with the involuntary muscle spasms tissue or liver functioning.[9]

Safe systems for treating patients, patient and staff education, appropriate selection of patients for treatment, careful regimen selection, and monitoring help minimize risks. The ability to adapt to a changing medical landscape will be crucial to continued safe and effective treatment for TB.[10]

**Case Presentation**

A 38 year old female, known case of HTN (since 10 years) and DM (since 10 years) was admitted in the General Medicine Department of a tertiary care hospital with chief complaints of altered sensorium (since 10 days) and abdominal pain and abdominal distension (since 10 days). She has a history of fever (since 5 days), vomitings (3 episodes) and not passing stools (since 3 days). On examination, patient was conscious/coherent, BP-110/80mmHg, PR-110/min, P/A-soft, distended+, CVS- S1S2+, R/S-BAE+, CNS-neck stiffness+.

**Past medication History**: She was suspected with TB abdomen and ATT(Anti-Tuberculosis Therapy) was started for her. She later developed loss of limb function, vomitings and involuntary movement of hands and limbs.

**Laboratory Investigations**: Revealed increase in serum creatinine levels- 3.9mg/dL (0.7-1.2mg/dL). Her MRI report was normal. Her CSF analysis reveals lymphocytes-100%,
Glucose-69mg/dL(45-80mg/dL), protein-45mg/dL (15-45mg/dL). Her Ascitic fluid analysis shows lymphocyte count at 3,200 leukocytes/µL(<500leukocytes/µL) and ADA levels at 72.45 IU/L(<26IU/L). Her CT scan of abdomen reveals ascites and fatty liver with hepatomegaly.

Provisional Diagnosis: ?Meningitis ?TB abdomen
Confirmeral Diagnosis: K/C/O TB abdomen on ATT with HTN and DM

**Treatment:** She was started with the following medications

<table>
<thead>
<tr>
<th>S. NO</th>
<th>BRAND NAME</th>
<th>GENERIC NAME</th>
<th>DOSE</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inj. Monocof</td>
<td>Ceftriaxone</td>
<td>2gm</td>
<td>1-0-0</td>
</tr>
<tr>
<td>2</td>
<td>Inj. Pantop</td>
<td>Pantoprazole</td>
<td>40mg</td>
<td>1-0-0</td>
</tr>
<tr>
<td>3</td>
<td>Inj. ZofeR</td>
<td>Ondansetron</td>
<td>4mg</td>
<td>SOS</td>
</tr>
<tr>
<td>4</td>
<td>IVF NS</td>
<td>Normal Saline</td>
<td>1 pint</td>
<td>1-0-1</td>
</tr>
<tr>
<td>5</td>
<td>Inj. H. insulin</td>
<td>Human Insulin</td>
<td>4U</td>
<td>1-0-1</td>
</tr>
<tr>
<td>6</td>
<td>Inj. Rantac</td>
<td>Ranitidine Hydrochloride</td>
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<td>1-0-1</td>
</tr>
<tr>
<td>7</td>
<td>T. Tenelife</td>
<td>Teneligliptin</td>
<td>250/500</td>
<td>1-0-1</td>
</tr>
<tr>
<td>8</td>
<td>T. MetXL</td>
<td>Metoprolol</td>
<td>12.5mg</td>
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<td>T. Telmisafe</td>
<td>Telmisartan</td>
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<tr>
<td>10</td>
<td>Syp. Lactulose</td>
<td>Lactulose</td>
<td>10ml</td>
<td>1-1-1</td>
</tr>
</tbody>
</table>

**DISCUSSION**

ATT is a goal standard therapy for patients with active Tuberculosis and is recommended for usage till complete eradication of the disease. Here ATT is attributed to the following conditions:

1. ATT drugs can lead to neuropathic changes and in turn cause dystonia and myopathy by altering the mitochondrial network. In animal studies, axonal swelling is observed and in vitro, at least in rat retinal ganglion cells, there is mitochondrial damage, which may occur as a result of glutamate mediated excitotoxic pathway. In human fibroblasts, the drug ethambutol can produce a mitochondrial coupling defect, decreased mitochondrial membrane potential and fragmentation of the mitochondrial network. Mitochondrial injury could be a putative mechanism for myopathy.\(^{[11]}\)

2. Fatty liver due to ATT has an adverse effect on liver metabolism. The pathogenesis is suggested to be an 8 fold increase in serum transaminase levels, especially with the combination therapy. Isoniazid alone has the capacity to cause hepatotoxicity by altering live enzymatic action.\(^{[12]}\)
CONCLUSION

ATT leading to involuntary muscle contractions may be attributed to neuropathic changes for the most part. Hepatitis due to ATT is a serious physiological condition which may progress to cause further metabolic impairment. To recognize the offending agent (in the multi-drug regimen of ATT) is anticipated for immediate withdrawal and future recurrence of the condition. In this patient, appropriate dosage tapering in proportion to the severity of objective data observed and LFT monitoring is highly recommended.

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REFERENCES

