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Case Report

DRUG-INDUCED HEPATOTOXICITY OF ANTI-TUBERCULAR DRUGS THERAPY: A CASE REPORT

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ABSTRACT

According to WHO, one third of the population is affected by TB and 1 in 4 adult male deaths is attributed to TB. The first line anti-TB drugs are potentially hepatotoxic. The incidence rate of anti-TB drugs induced hepatotoxicity has found to be 2% to 28% in India. A case of 62 years old man, weighing 49 kg was brought to hospital with chief complains of coughing, loss of appetite vomiting, melaena, fever, gastritis since 3 days. He had a history of pulmonary koch's 15 days back and was taking regular first line anti-tubercular drug therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol). After 15 days of anti-tubercular drug treatment, patient was found to develop hepatotoxicity with the findings of elevated total bilirubin and liver enzymes level. Patient was also the known case of diabetes-mellitus past 10 years. He was already taking the regular anti-diabetic medications. Patient was on hold of previous anti-tubercular drugs therapy. Although it was started modified anti-tubercular drugs (Streptomycin, Levofloxacin, Ethambutol) therapy along with liver tonics. Upon normalization of patient conditions, physician started first line anti-tubercular drug therapy containing Rifampicin, Isoniazid, Pyrazinamide and Ethambutol with continued liver tonics. Routine monitoring of liver enzymes, total bilirubin and blood sugar level were followed up till discharge. Clinicians need to be made aware of these potentially fatal adverse effects associated with anti-tubercular therapy via conduction of quality based seminars, conferences, published medical literature and learning programmes.

KEYWORDS: *Anti-tubercular drugs, adverse effects, hepatotoxicity, liver enzymes.*

INTRODUCTION

According to WHO, one third of the population is affected by tuberculosis (TB) and 1 in 4 adult male deaths is attributed to TB [1]. Anti-TB drugs have the ability to kill *Mycobacterium tuberculosis* effectively and also known to induce various adverse effects, including liver injury, skin reactions, gastrointestinal and neurological disorders. Anti-tuberculosis drug induced liver injury is one of the most important and serious adverse effects, which results in a low treatment success rate. Hepatitis is one of the most commonly seen adverse effect in tubercular suffered patient due to anti-tubercular drug therapy [2, 3].

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The liver has a central role in drug metabolism, detoxification, and is consequently vulnerable to injury. The liver, referred to as the "metabolic factory" of the body, is central to the metabolism of virtually every foreign substance including anti-tuberculosis drugs. Drug-induced Liver Injury (DILI) is a problem of increasing significance, but has been a long-standing concern in the treatment of tuberculosis infection in India and much of the developing countries. Drug-induced liver injury is a common, but often unrecognized cause of liver damage that continues to fascinate and challenge the clinician [4, 5].

From first line anti-TB drugs, isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) causes hepatotoxicity such as transaminasitis and fulminant hepatic failure [6-8]. The incidence rate of anti-TB induced hepatotoxicity was found to be 2% to 28% based on hepatotoxicity diagnosis criteria [9].

The risk factors for anti-TB induced hepatotoxicity includes high alcohol intake, older age, pre-existing chronic liver disease, chronic viral infection due to hepatitis B (HBV) and hepatitis C viruses (HCV), human immunodeficiency virus (HIV) infection, advanced TB, asian ethnicity, concomitant administration of enzyme-inducers, inappropriate use of drugs and poor nutritional status [10-13].

CASE REPORT

A case of 62 years old man, weighing 49 kg was brought to hospital with chief complains of vomiting, melaena, fever, coughing, loss of appetite, gastritis since 3 days. Patient was ex-smoker, ex-alcoholic and non-vegetarian. He had a history of smear positive tuberculosis and was taking regular first line anti-tubercular drug therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol). After 15 days of anti-tubercular drug treatment, patient was found to develop hepatotoxicity with the findings of elevated total bilirubin and liver enzymes level. Patient was also the known case of diabetes-mellitus since 10 years. He was already taking the regular anti-diabetic medications.

At the time of presentation, general physical examination PR- 103/min, BP-110/70 mmHg, oxygen saturation 94% at the room air, abdomen soft and tender, cardiac S1, S2 positive was noted. Chest X-ray was non-homogenous opacity with air bronchospasm noted in right lobe suggestive of consolidation. Therefore, a diagnosis of recently smear positive pulmonary TB was made, and the need for adequate prophylactic treatment to reduce the risk of active TB was explained to the patient. According to the laboratory report patient liver function test (LFT) count was not in the normal limits. However, the prothrombin time (PT) was prolonged and the levels of liver enzymes were extremely elevated, with an aspartate aminotransferase (AST) level of 412IU/L, alanine aminotransferase (ALT) level of 368IU/L, alkaline phosphatase (ALP) level of 195IU/L, glutamyl transpeptidase level of 235IU/L, total bilirubin level of 2.7mg/dl, direct bilirubin 1.8 mg/dl and the RBS level is elevated (Table-1). Viral markers for hepatitis, including hepatitis A, B and C viruses, and human immunodeficiency virus (HIV) all were negative. A provisional diagnosis of anti-tubercular drug induced hepatitis was made. So, previous anti-tubercular drugs therapy were stopped and modified anti-tubercular therapy regimen was started i.e. Streptomycin 750mg, Levofloxacin 750mg, Ethambutol 800mg and liver tonic. The patient was thus finally diagnosed with first line anti-tubercular drugs therapy (ATT) induced hepatotoxicity. Although AST and ALT levels began to improve, PT and total bilirubin values continued to deteriorate. Continuous monitoring of laboratory data especially LFT was required. Upon normalization of patient conditions, physician started first line anti-tubercular drug therapy containing Rifampicin, Isoniazid, Pyrazinamide and Ethambutol with continued liver tonics. Routine monitoring of liver enzymes, total bilirubin and blood sugar level were followed up till discharge.

Table No. 1: Laboratory Data Upon Admission

S.No.	Parameter	Test value (Day-1)	Test value (Last Day)	Normal Value
1.	AST/ SGOT	412	68	17-59 IU/L
2.	ALT/ SGPT	368	75	9-52 IU/L
3.	GGT	235	86	12-43 IU/L
4.	Total Bilirubin	2.7	1.3	0.2-1.3 mg/dl
5.	Direct Bilirubin	1.8	0.8	0.0-0.8 mg/dl
6.	ALP	195	86	38-126 IU/L
7.	PT	15	13	9.5-13.5 sec

CONCLUSION

Anti-TB drugs induced hepatotoxicity is a serious problem and it was reported that 2-32% of TB patients experience drug induced hepatotoxicity (DIH) during the course of the treatment. The incidence rate of drug induced hepatotoxicity in india 8-36%. In this case, after 15 days of anti-tubercular drugs treatment, patient was found to develop hepatotoxicity with the findings of elevated total bilirubin and liver enzymes level. At the time of discharge, patient was consulted regarding the medications and course of the treatment. As a suggestive measure for future incidences, clinicians need to be made more aware of such potentially fatal adverse effects associated with anti-tubercular therapy via conduction of quality based seminars, conferences, published medical literature and learning programmes.

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