IJMPR 2023, 7(11), 38-40

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Case Report
SJIF Impact Factor: 5.273

A CASE REPORT ON ATT INDUCED HEPATITIS

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Received on: 17/09/2023
Revised on: 07/10/2023
Accepted on: 27/10/2023

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ABSTRACT

Tuberculosis (TB) is a highly contagious bacterial infection. Although it can occur almost anywhere in the body, the most common site of infection for TB is the lungs. Among the first-line combination therapy medications Isoniazid (INH), Rifampicin (RMP), Pyrazinamide (PZA) and Ethambutol (EMB). INH, RMP, and PZA are hepatotoxic since they are metabolized primarily by the liver. Hepatotoxicity brought on by anti-tuberculosis medications occurs frequently. When jaundice appeared more than 6 weeks after the start of ATT (Anti- Tuberculosis Therapy), death from ATT-induced hepatotoxicity was more likely. Usually, following recovery from ATT-induced hepatitis, anti-tuberculosis medications with a risk of causing hepatitis can be safely reintroduced. Here we report a case of 52-year-old female patient who was admitted in hospital due to ATT induced hepatitis.

KEYWORDS: Hepatitis, ATT, Tuberculosis, Hepatotoxicity.

INTRODUCTION

TB is a potentially fatal infectious illness affecting mostly the lungs caused by Mycobacterium Tuberculosis. When someone coughs or sneezes, tiny droplets of bacteria that causes tuberculosis are released into the air and spread from person to person.[1] Tuberculosis has been proclaimed as a worldwide health emergency as stated by World Health Organization (WHO) nearly one third of world population was postulated to be affected with TB.[2] the bacteria that is responsible for TB infection is spread through the air as it cannot live long on surfaces. When people suffering with lung TB sneeze, cough or spit, they propel these micro-organisms in their immediate surroundings. Upon the inhalation of only a few germs a person can become infected. Tuberculosis can be treated and prevented.[3] According to RNTCP (Revised National Tuberculosis Control Program, DOTS (Directly Observed Therapy) is the mainstay employed for the management of tuberculosis.[4] Currently, the recommended first-line treatment for TB is INH, RMP, PZA, EMB given for 2 months, followed by INH and RMP or EMB for 4 months.

Hepatotoxicity is most occurring serious adverse effect of anti-TB medications and may reduce treatment effectiveness by compromising the treatment regimens. The consequences of this clinical side effect are interrupted regimen, longer duration of therapy, drug resistance, inadequate response to treatment, severe hepatitis in a few cases and considerable morbidity to the patients. Hepatotoxicity caused by ATT affects 2-28 percent of people. An elevated liver enzyme of 5 times the upper limit of normal can be used to confirm ATT-induced hepatitis in the absence of jaundice or other symptoms; in the presence of jaundice or other symptoms. PZA is thought to be the most culprit with the hepatotoxicity rate of 9% followed by INH with 3% and RMP 1%. RMP is less hepatotoxic but it potentiates the toxicity of other drugs like INH. EMB is considered liver friendly. Therefore, when these above mentioned four drugs used in combination during the intensive phase, hepatotoxicity is likely to be higher. The toxicity symptoms noticeable are in the form of nausea, vomiting, yellowish discoloration of eyes. Numerous risk factors contributing to ATT induced toxicity are venerable age, sex, improper use of drugs, liver diseases, viral infection due to Hepatitis B (HBV), Hepatitis C (HCV) and HIV (Human Immunodeficiency Virus), Advanced TB, Asian ethnicity, High intake of alcohol, Elderliness, Associated administration of enzyme-inducers, Drug dependence and Malnutrition status.[5]

Asymptomatic transaminase elevations are common

during anti-tuberculosis treatment, but if hepatotoxicity is not diagnosed in a timely manner and treatment is not stopped, it might be fatal. Drug-induced liver damage (DILI) is an excluded diagnosis. Other causes like acute viral hepatitis, chronic liver disease should be ruled out. Usually, the time of onset to acute injury is within months of initiating a drug. Confirmation of diagnosis is by rechallenge with the offending agent leading to more than twofold serum alanine aminotransferase (ALT) elevation, and discontinuation leading to a fall in ALT.[6] There are no definite recommendations as to whether ATT should be continued or stopped and what should be the schedule for reintroduction of these agents.[7]

CASE PRESENTATION

A 52-year-old female patient with known case of recent pulmonary TB, Type 2 Diabetes Mellitus and Systemic Hypertension presented with complaints generalized tiredness, difficulty in breathing and cough and was admitted on department of Pulmonology. On physical examination the patient was found to be conscious, oriented. On arrival the pulse rate, blood pressure and SPO_2 of the patient was noted as 88 beats/ minute & 130/80 mmHg and 98% respectively. On systemic examination the parameters of cardiovascular system, nervous system and per abdomen are found to be normal.

Her initial laboratory data showed raised Platelet Count (5.09 Lakhs/cumm), RBS (262 mg/dL), ESR (110 mm/hr), CRP (149.3 mg/L), TC (16340 cells/cumm), HbA1C (13.2 %), Total Bilirubin (1.11 mg/dL), Direct Bilirubin (0.46 mg/dL), Indirect Bilirubin (0.65 mg/dL), AST (116 U/L), ALT (109 U/L), ALP (167 U/L) and declined Globulin (3.3g/dL), Albumin (2.2 g/dL). The liver function test showed hyperbilirubinemia, elevated liver enzymes and hypoalbuminemia. Plenty of pus cells are found on urine routine examination.

Patient was admitted and evaluated. Routine investigation was done. Treated with anti-tubercular drugs, IV antibiotics, vitamin supplements and antidiabetics measures. During hospital stay, she had altered liver enzymes. Gastro consultation obtained and Hepatoprotective drugs were started. In spite of all raised liver enzymes. Hence stopped ATT, started second line of ATT drugs. She gradually improved and LFT became normal, Hence the patient is discharged.

Advice on discharge include Tab. INH 300mg, Cap. Rifampicin 450mg, Tab. Ethambutol 800mg once daily for one week, Tab. Livi (Ursodeoxycholic acid)300mg twice daily for 1 week.

DISCUSSION

ATT accounts for roughly 58% of cases of drug-induced liver injury, which is a major contribution. Anti-tubercular drug-induced liver damage is a serious problem; throughout therapy, 2-28% of patients reported having Drug Induced Hepatotoxicity (DIH).[8]

The role of viral hepatitis has been replaced by drug-induced liver disorders, even life-threatening liver failure. Drug-induced liver disorders are only identified once viral hepatitis has been ruled out. In India, drug-induced hepatotoxicity is shown to occur frequently (8–36%). Hepatotoxicity, acute renal injury, gastrointestinal discomfort, rash, a drug fever, and optic neuritis are just a few of the different side reactions that can occur when taking anti-tubercular medications. INH, RMP, PZA and EMB are the first line anti-TB drugs.[9] INH, RMP, PZA are primarily metabolized by the liver, making them the main culprits in cases of drug-induced hepatotoxicity during anti-TB treatment. Geriatric patients, women, undernutrition, alcohol use, a history of liver problems, extra pulmonary TB affecting the abdomen, and infections including HIV and HBV and HBC are other risk factors for anti-TB drug-induced hepatotoxicity. The molecular process and etiology of anti-TB drug-induced hepatotoxicity, however, remain unclear. According to physiology, the liver is a crucial body organ because it is in charge of several xenobiotic metabolisms. It can be challenging to treat underlying tuberculosis once ATT-induced hepatitis has been identified. One of the most significant side effects of ATT is hepatitis since it can force the doctor to change the therapy to medications that are less effective and have more side effects, or it can cause overt fulminant hepatitis, which can be fatal.[10]

In this case, ATT induced hepatotoxicity is treated with Hepatoprotective drug, Ursodeoxycholic acid 300mg twice daily. After stoppage of ATT, second line of ATT drugs was started.

CONCLUSION

A common side effect of newly identified cases of pulmonary tuberculosis is ATT-induced hepatitis. Therefore, all patients who are started on ATT must be monitored for at least the first month. Both the patients and the doctors need to be well-informed on the negative effects of ATT, their early detection, and how to manage them. Although the main therapy option for pulmonary tuberculosis is anti-tubercular medication, one of the unfavorable side effects that might cause treatment stoppage and, ultimately, drug resistance is liver damage. Compared to INH and PZA, RMP is the first-line anti-TB medicine that causes hepatotoxicity the most frequently. As a result, second-line alternatives like levofloxacin are utilized as a replacement to reduce hepatotoxicity.

The clinical pharmacist should advise the patient receiving anti-TB treatment about the danger of hepatotoxicity, screen for susceptibility based on the existence of certain risk factors, and monitor signs and symptoms to determine whether to stop taking the medication. In cases of drug-resistant TB, drug-drug interactions, a patient's sluggish response to treatment, or the presence of multiple underlying disorders, a clinician should additionally do therapeutic drug monitoring (TDM).

In conclusion, most patients who experience ATT-induced hepatotoxicity experience a benign course, but some individuals may experience severe consequences, such as abrupt liver failure, which can be fatal. After recovery from ATT-induced hepatitis, anti-tuberculosis medications that have the potential to cause hepatitis can typically be safely reintroduced.

ACKNOWLEDGEMENT

The authors declare that the contents of this article are their own original unpublished findings and that they did not receive any funding for the writing of this manuscript.

Informed consent

Before taking this case the patient and their families were informed and informed consent was acquired.

Conflicts of interest

The authors have no conflicts of interest to declare.

REFERENCE

1. Nair SS, Rajeev S. An Adverse Drug Reaction: Antitubercular Drug induced Hepatitis: https://doi. org/10.54037/WJPS. 2021.91006. World Journal of Pharmaceutical Sciences, 2021; 1: 31-3.
2. Brewer TF, Heymann SJ. To control and beyond: moving towards eliminating the global tuberculosis threat. J Epidemiol Community Health, 2004; 58(10): 822-5.
3. World Health Organization. Treatment of tuberculosis [guidelines]. Geneva: World Health Organization, 2010; 4.
4. World Health Organization. Treatment of tuberculosis [guidelines]. Geneva: World Health Organization, 2010; 4.
5. Girling DJ. The hepatic toxicity of antituberculosis regimens containing isoniazid, rifampicin and pyrazinamide. Tubercle, 1978; 59(1): 13-32. doi: 10.1016/0041- 3879(77)90022-8, PMID 345572.
6. Tostmann A, Boeree MJ, Aarnoutse RE, de Lange WCM, van der Ven AJ, Dekhuijzen R. Antituberculosis drug-induced hepatotoxicity: concise up-todate review. J Gastroenterol Hepatol, 2008; 23(2): 192-202. doi: 10.1111/j.1440-1746.2007.05207.x, PMID 17995946.
7. Breen RA, Miller RF, Gorsuch T, Smith CJ, Schwenk A, Holmes W, Ballinger J, Swaden L, Johnson MA, Cropley I, Lipman MC. Adverse events and treatment interruption in tuberculosis patients with and without HIV co-infection. Thorax, 2006; 61(9): 791-4. doi: 10.1136/thx.2006.058867, PMID 16844730.
8. Khalili H, Dashti-Khavidaki S, Rasoolinejad M, Rezaie L, Etminani M. Anti-tuberculosis drugs related hepatotoxicity; incidence, risk factors, the pattern of changes in liver enzymes and outcome. Daru, 2009; 17(3).
9. Wondwossen Abera, Waqtola Cheneke, Gemeda Abebe. Incidence of antituberculosis-drug-induced hepatotoxicity and associated risk factors among tuberculosis patients in Dawro Zone, South Ethiopia: A cohort study. Int J Mycobacteriol, 2016; 5(1): 14-20. doi: 10.1016/j.ijmyco.2015.10.002. PMID 26927985.
10. Larrey D. Epidemiology and individual susceptibility to adverse drug reactions affecting the liver. Semin Liver Dis, 2002; 22(2): 145-55. doi: 10.1055/s-2002- 30105, PMID 1201654