ANTI TUBERCULAR THERAPY INDUCED LIVER INJURY: A CASE REPORT

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ABSTRACT:

Introduction: Drug induced liver injury (DILI) is caused by several drugs. In our case report the patient presented with the relapse of TB and laboratory data shows elevated liver enzymes which might be due to anti-tubercular drugs, as the main adverse effect of ATT is hepatotoxicity which is majorly reported in 2-28% of patients. **Case presentation:** This was a relapse case of TB where the patient discontinued the treatment causing relapse of TB. Initially the patient was given with combination of all first line anti tubercular agents and the liver enzymes started raising above the normal levels indicating liver injury so, isoniazid, rifampicin and pyrazinamide were stopped which are majorly hepatotoxic. Ethambutol and streptomycin were given and the liver enzyme levels were normalized. **Conclusion:** The risk of affecting TB is greater in adults and persons who are immunocompromised. If left untreated, it leads to further complications like hemoptysis, septic shock, extra pulmonary TB, malignancy, chronic pulmonary aspergillosis. Timely detection and temporary withdrawal of offending agent can completely cure ATT induced liver injury.BCG vaccine helps in prevention of TB.

Keywords: anti-tubercular therapy, hepatotoxicity, tuberculosis, aspergillosis, malignancy, hemoptysis.

INTRODUCTION: Tuberculosis which is an infectious disease that usually affects lungs is said to be the second biggest cause of death globally. According to WHO around 9 million people a year get affected with TB. This is one among the top three causes of death in women of age 15-44 years. Early warning signs of TB include feeling sick or week, loss of appetite, weight loss, chills, fever, cough with sputum etc.[1] The most common diagnostic tests for TB are a montaux test and AFB. The standard length of time of TB antibiotics is 6months. TB drugs can be toxic to liver.[2] Hepatotoxicity with first line drugs is a major complication of anti-tubercular drugs. Of the first line anti-tubercular drugs Isoniazid, Rifampicin and pyrazinamide are all hepatotoxic when used together.[3] Drug-induced injury to hepatocytes leads to cholestasis which in turn causes accumulation of bile acids and excretory products leading to liver injury.[4] Different recommendations were made for monitoring the LFT's in patients on anti tubercular therapy; all the expert recommendations include cessation of treatment of ATT.[5] Of all the first line anti tubercular drugs, isoniazid and rifampicin are the major hepatotoxins whereas rifampicin is a powerful enzyme inducer, which may enhance the hepatotoxicity of isoniazid. Ethambutol and streptomycin do not have any hepatotoxic potential.[8] So in case of DILI stopping the offending agents can prevent from further complication.

Case report:

A 42 years old male patient was admitted to the hospital with chief complaints of fever, cough with sputum, shortness of breath, vomiting, loose motions and loss of appetite since 15 days. Past medical history of the patient shows that he was a TB patient on irregular antitubercular treatment. He was presently admitted to the hospital with relapse of TB. His family history shows that his father died of jaundice. Social history includes he was occasionally alcoholic and consumes mixed diet. Laboratory investigations demonstrated

the following: temperature 99.9^{0}F, blood pressure 90/70mmHg, ESR 46mm 1st hour. Liver function tests demonstrated: total bilirubin 3.9mg/dl (on 1st day), 2.2mg/dl (on 3rd day), direct bilirubin: 2.8mg/dl (on 1st day), 1.5mg/dl (on 3rd day). SGOT 336 U/L (on day 1), 146 U/L (on day 3). SGPT 623U/L (on day 1), 349U/L (on day 3). Potassium levels include 2.6Eq/L (on day 1), 2.5 Eq/L (on day 3) which showed hypokalemia. Sputum for AFB was positive. X-ray of chest demonstrated right upper and mid-zone consolidation. The patient was prescribed with forecox (isoniazid 150mg+ rifampicin 225mg + ethambutol 400mg + pyrazinamide 750mg), streptomycin 750mg intramuscular once daily, syrup Benadryl 10ml thrice daily, nebulizers ipratropium bromide+ levosalbutamol and budesonide thrice daily. Injection ondansetron was given to control vomiting tablet pyridoxine 40mg was given orally once a day. Based on the LFT investigations isoniazid, rifampicin and pyrazinamide were stopped and tablet levofloxacin 750mg once daily, tablet ursodeoxycolic acid 300mg twice daily, tablet ethambutol 800mg once daily was given. IV fluids: DNS 2 pints, RL 2 pints with 2 ampoules of Potassium Chloride and NS 1 pint were added on day 2. On day 5 Gene Xpert MTB with rifampicin resistance, qualita was performed which demonstrated medium presence of mycobacterium tuberculosis and rifampicin resistance was not detected.

Discussion:

Tuberculosis is one the most common infectious diseases in the world. The first line treatment which is currently prescribed for TB is isoniazid (INH), rifampicin (RMP), ethambutol (EMB) and pyrazinamide (PZA). Hepatotoxicity is one of the most frequent and the serious adverse effect of these medications. Quadruple therapy consists of INH, RMP, EMB, PZA in which INH, RMP and PZA are mainly metabolized by the liver, frequently causing hepatotoxicity.[7] The reported incidence of hepatotoxicity in controlled trails of anti TB drugs that included INH, RMP and PZA ranged from 0.6%-3%.[6] Initially the patient was on treatment with the combination of all first line anti tubercular drugs. In the present case as the liver enzymes were raised isoniazid, pyrazinamide and rifampicin were stopped and ethambutol alone with streptomycin was given, as isoniazid and pyrazinamide are hepatotoxins while rifampicin is an enzyme inducer which increases the hepatotoxic effect of isoniazide.[8] Tab. Ursodeoxycholic acid 300mg twice daily, Tab. Levofloxacin 750mg once daily was given to treat hepatic injury and treatment for symptomatic relief has been given.

As the patient presented with main symptoms of vomitings, loose motions and fever since 15days, initially he has been treated with Tab. Acetaminophen 650mg, Tab. Pantoprazole 40mg and advised for laboratory investigations. Based on the laboratory findings the patient was advised to stop forecox (isoniazid 150mg+ rifampicin 225mg + ethambutol 400mg + pyrazinamide 750mg) immediately and ethambutol in combination with streptomycin was prescribed and the symptomatic treatment was given. The patient has been recovered, the laboratory investigations of liver enzymes were found to be normal, then he was discharged and advised for review with LFT's after 10 days.

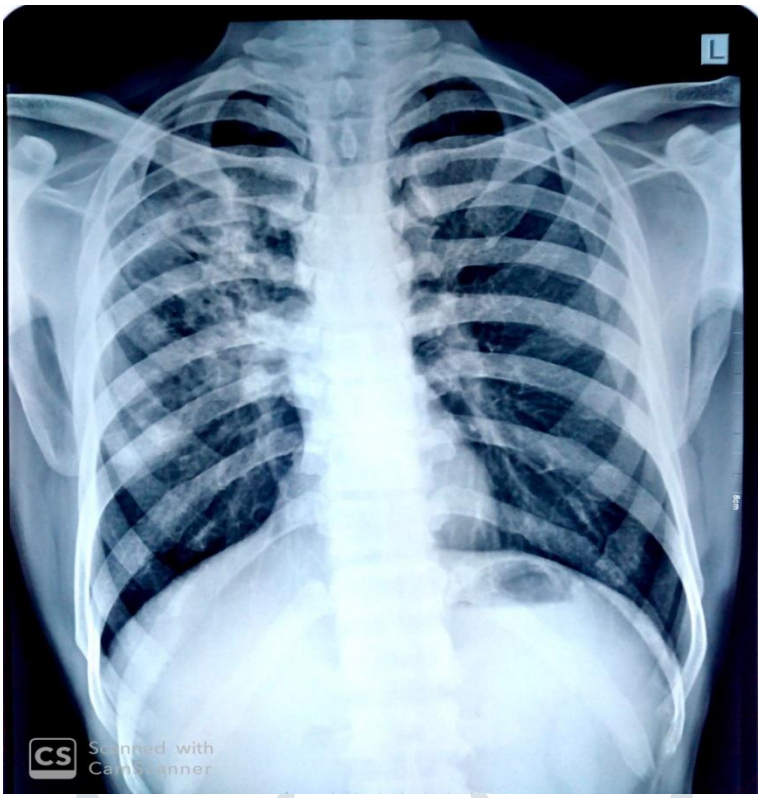

Figure 1 Chest X-ray demonstrating right upper and mid zone consolidation

CONCLUSION: TB is found to be the most common infectious disease, now-a-days immediate and effective treatment is required. If not treated it may lead to further complications like hemoptysis, septic shock, extra pulmonary TB, malignancy, chronic pulmonary aspergillosis. As hepatotoxicity is the common side effect of ATT, LFT's are to be monitored regularly and in cases of abnormal LFT's immediate cessation of first line ATT is advised and ethambutol in combination with second line agents for TB is recommended.

ABBREVATIONS:

DILI: Drug Induced Liver Injury

ATT: Anti-Tubercular Therapy

TB: Tuberculosis

BCG: Bacillus Calmette-Guerin

WHO: World Health Organization

AFB: Acid- Fast Bacilli

ESR: Erythrocyte Sedimentation Rate

SGOT: Serum Glutamate Oxalate Transaminase

SGPT: Serum Glutamate Pyruvate Transaminase

IV: Intravenous

DNS: Dextrose Normal Saline

RL: Ringer Lactate

MTB: Mycobacterium Tuberculosis

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