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Case Report

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ANTI-TUBERCULAR DRUGS INDUCED HEPATITIS: A CASE REPORT

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ABSTRACT

Anti-TB drugs have shown that they are able to contain and kill *Mycobacterium tuberculosis* effectively, they are known to induce various adverse effects, including liver injury, skin reactions, gastrointestinal and neurological disorders. Anti-tuberculosis drug induced liver injury (ATLI) is one of the most important and serious adverse effects, which results in a low treatment success rate. Hepatitis adverse effect seen in tubercular suffered patient due to anti tubercular drug therapy. We report 22 year old male with tubercular right pleural effusion, on anti-Tb dugs.

KEYWORDS: Tuberculosis, ATT, Hepatitis, rifampicin.

INTRODUCTION

Drug-induced liver injury is a common, but often unrecognized cause of liver damage that continues to fascinate and challenge clinician. The liver, referred to as the "metabolic factory" of the body, is central to the metabolism of virtually every foreign substance including antituberculosis drugs.[1] Isoniazid, rifampicin and pyrazinamide are essentialcomponents of thedirectly observed treatment, short-course (DOTS) strategy for control of tuberculosis endorsed by theWorld Health Organization (WHO)[2,3] and all the three drugs have been observedto have hepatotoxic potential. drug-induced hepatotoxicity (DIH) is an important and commonly encountered adverse effect with anti-tuberculosis treatment.[4-6]

MECHANISMS OF DRUG-INDUCED HEPATOTOXICTY

Several types of drug-induced liver damagehave been described. These include, (i) idiosyncratic damage;(ii) dose-dependent toxicity; (iii) induction ofhepatic enzymes; (iv) drug-induced acute hepatitis; and (v) allergic reactions; among others.[1-3,5]

Antituberculosis drugs and hepatotoxicity

The pathogenesis of DIH caused by isoniazidis not well-understood.[6] Altered profile of antioxidant enzymes with increased lipid peroxidation indicated that isoniazid and rifampicin-induced hepatotoxicity appeared to be mediated through oxidativestress.[7] Compared with isoniazid, DIH caused by rifampicin occurs earlier and produces a patchy cellular abnormality with marked periportal inflammation. Rifampicin-induced hepatitis has been postulated to occur as a part of systemic allergic reaction and due to unconjugated hyperbilirubinaemia as a result of competition with bilirubin for uptake at hepatocyte plasma membrane.[8]

Factors Implicated in The Development of Antituberculosis Treatment-Induced Hepatotoxicity:

Advanced age, female sex, alcoholism, underlying liver disease, acetylator phenotype, N-acetyltransferase (NAT) activity, glutathione S-transferase activity, hepatitis B and C virus,human immunodeficiency virus (HIV) infection, extensive disease, malnutrition, have also been observed to be risk factors for the development of DIH (Table 1).[9-11]

Table 1: Risk factors for the development of antituberculosis treatment-induced hepatotoxicity.

Advanced age
Female sex
Moderately/far advanced/extensive disease
Hypoalbuminaemia, malnutrition
Alcoholism
Underlying liver disease
Hepatitis B virus infection
Hepatitis C virus infection HIV infection
Acetylator phenotype N-acetyltransferase (NAT) activity
Glutathione S-transferase activity

Data from references 6.9-11

CASE REPORT

A 22yr old male, chronic alcoholic, Gutka chewer was brought to tertiary care hospital in semi-conscious condition with complaints of seizures 4 episodes, fever on & off, and cough with expectoration since 1 month,

abdominal pain since 1week, neck stiffness and altered behavior on day before admission to the hospital.

History of herbal medication intake for jaundice 3months back. Known case of B/L pleural effusion with extra pulmonary Koch on category –II, Seizures disorder since 5 months. On general and physical examination urine was found to be red in colour as using ATT. Meningeal sign +ve, kernigs & Brudzinski +ve. A provisional diagnosis of anti-tubercular drug induced hepatitis was made. so, ATT were stopped and SLE regimen was started i.e. Streptomycin 750mg, IM, OD; Levofloxacin 750mg, OD; Ethambutol 800mg,OD.

Routine investigations showed normal count in blood picture report and normal differential count, Renal function test and liver function test[serum Albumin-2.0(3.5 to 5m/dl); serum total bilirubin-1.9(0.1 to 1.0mg/dl). serology report was found to be –ve.

The diagnosis made was TB meningitis with Rt. focal seizures on basis of CT scan of brain (motion artifacts +ve, subtle hypo density noted in right capsule ganglionic and left occipital suggestive of ?infarcts).

The drugs prescribed on day 1st.
Inj. Monocef 1gm BD.
Inj. Pan 40mg OD.
Inj. Optineuron 1amp OD.
Inj. Eption 100mg TID.
Inj. Streptomycin 750mg OD.
Tab. Levofloxacin 750mg OD.
Tab. Ethambutol 800mg OD.
Tab. Udiliv 300mg OD.
Inj. Decadron 8mg OD.

This treatment was continued for 4days. on day 5th patient was advised category –I ATT. Day 6th inj. Albumin 20% 100ml OD was added and patient was recommended high protein diet. This same treatment was continued for 7 days i.e. till day 13th.

DISCUSSION

Anti-Tb drugs induced hepatotoxicity is a serious problem and it was reported that 2-32% of TB patients experience drug related hepatotoxicity (DIH) during the course of the treatment. The incidence rate of drug induced hepatotoxicity in india 8-36%. In this case, the patient is chronic alcoholic and consumed large amounts of alcohol which may leads to changes liver conditions – fatty liver, hepatitis and cirrhosis. Upon discharge, patient was counselled regarding the medications and course of the treatment.

CONCLUSION

On admission, our first hypothesis was that the patient had suffered a drug –induced hepatitis. Patient developed hepatotoxicity and severe alcohol induced hepatitis following the administration of 1st line anti –Tb drugs, Which were administered for the treatment. Pulmonary koch's. Following the withdrawl of alcohol, standard treatment and standard care, we were able to achieve a favorable outcome. Clinicians need to be made aware of these potentially fatal adverse effects associated with anti –Tb drugs.

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