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A New Paradigm of an Old Disease: A Case Report

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Abstract

Anti-tubercular therapy (ATT) induced hepatotoxicity is a major cause of drug induced liver injury[1]. Most of the first line ATT drugs including Isoniazid, Rifampin and Pyrazinamide have proven hepatotoxic potential. The pharmacokinetic profile of these drugs albeit extensive, has failed to adequately explain their hepatotoxicity. Here, we report a case of ATT induced hepatotoxicity in a male, with pulmonary tuberculosis (TB) on ATT since 4 months with a causality score of five (PROBABLE) using Naranjo scale. His laboratory data showed Hyperbilirubinemia with elevation of liver enzymes. He progressively worsened during hospital stay and developed encephalopathy and coagulopathy. Hence, he was evaluated for Living donor liver transplantation (LDLT) which was done within one week of hepatic DE compensation. In patients post LT, a prudent approach would be to continue immunosuppression along with INH prophylaxis. Further investigation into prognostic risk factors and ideal management strategies are warranted.

Keywords : Antitubercular therapy, Living Donor Liver Transplantation, Hepatotoxicity.

INTRODUCTION

Most of the prescribed medication can cause drug induced liver injury because virtually all drugs and foreign substances are mainly metabolized through the liver[2]. Most of the first line ATT drugs including Isoniazid, Rifampin and Pyrazinamide have proven hepatotoxic potential. The pharmacokinetic profile of these drugs albeit extensive, has failed to adequately explain their hepatotoxicity. Liver transplantation is the final remedy to correct liver failure[3]. ATT induced hepatic failure is an uncommon indication for liver transplantation bringing with it a unique conundrum for the transplant team. Post-operative immunosuppression is a risk factor for unsuccessful eradication of tuberculosis and at the same time, liver transplantation is often the only lifesaving remedy in these patients. We report a case of ATT induced hepatotoxicity, which eventually lead to transplantation.

CASE REPORT

A 39 year old male, a case of pulmonary tuberculosis (TB) on ATT since 4 months who presented with complaints of jaundice, anorexia and fatigue. There was no history of vomiting, abdominal pain or altered sensorium. He was conscious, oriented, no distension, with bowel sound heard normally all other system within normal limits. He was admitted with above mentioned complaints. His laboratory data showed Hyperbilirubinemia (12.95mg/dl) with elevation of liver enzymes such as alanine aminotransferase (170.2 iu/l), aspartate aminotransferase (102.7IU/L). On observation he had INR of 7.8 and the ffp transfusion was done. All investigations and management according to the acute liver failure protocol were started .A multiple detected computed tomography (MDCT) abdomen was taken which showed the features of acute hepatitis. He progressively worsened during hospital stay and developed encephalopathy and coagulopathy owing to which he was taken up for an emergency living donor liver transplantation. On seventh day of post -transplant he developed features of acute cellular rejection with rise in transaminase which was managed with pulse methylprednisolone therapy. He showed rapid improvement thereafter and he is currently on t. Tacrolimus 2 mg and t. Mycophenolatemofetil 250mg. Post- transplant, he has been on regular follow up with Isoniazid prophylaxis. He is asymptomatic and sputum negative for tuberculosis. This case of ADR shows a causality score of five (PROBABLE) using Naranjo scale.

DISCUSSION

Previous studies have shown that the prevalence of active Tb infection in transplant recipients is around1.37%.[4]Liver transplant recipients have an 18-fold increase in prevalence of active Tb infection and 4-fold increase in fatality rate when compared with the general population[3]. Among recipients who develop active Tb infection, extra pulmonary involvement is more common (67%), including multi organ disease (27%), short-term mortality is high among these patient (31%) [3].

The incidence of drug induced hepatotoxicity during standard multidrug tuberculosis treatment has been variably reported as between 2% and 28%[4]. Incidence varies between different world regions[6]. Orientals are reported to have the highest rates, especially Indian patient. Active TB is usually treated with multiple drugs .therefore, there are limited data on toxicity rates of anti-tubercular drugs individually[7]. Except isoniazid which has been widely used as prophylactic monotherapy for latent TB infections[6]. Previous reports suggests that about 75 percent of cases of idiosyncratic drug reaction that result in liver transplantation or death were caused by ATT[8].This patient occupies a unique niche among patients with ATT induced hepatitis owing to risk of reactivation of TB under the influence of post-transplant immunosuppression along with high probability of recurrent ATT induced hepatotoxicity in the graft. Management is usually tailored individually owing to lack of published guidelines.

CONCLUSION

ATT induced hepatitis is an uncommon indication for liver transplantation. Liver transplantation for ATT induced liver failure entails a need to carefully balance the risk of rejection post-transplantation with the risk of re-activation of TB. Considering the paucity of data, in these patients post LT, a prudent approach would be to continue immunosuppression along with INH prophylaxis and to keep the patient on a close follow up. Further investigation into prognostic risk factors and ideal management strategies in this subset of patients are warranted.

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