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Acute Liver Failure: An Uncommon Complication of Commonly Used Medication

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The incidence of drug-related acute liver failure is approximately 14 per 100,000 populations. Drug-induced liver injury may take place through a variety of mechanism. Withdrawal of the offending agent may result in complete recovery. Clindamycin is known to cause mild derangement of liver function; however, acute liver injury causing severe derangement of liver function associated with encephalopathy is uncommon.

Keywords: acute liver injury, hepatitis, drug-induced liver injury

INTRODUCTION

The incidence of drug-related acute liver failure is approximately 14 per 100,000 populations.[1] Clindamycin is known to cause mild derangement of liver function; however, acute liver injury causing severe derangement of liver function[2] associated with encephalopathy is uncommon.

CASE

A 73-year-old man was brought to the emergency room with increasing yellowish discoloration of skin for 3 days, abdominal discomfort in the right upper quadrant, and confusion for 1 day. Medical history was significant for diabetes mellitus type 2, peripheral vascular disease, and history of stroke with no residual deficit.

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The patient was in his usual state of health, when he was hospitalized with temperature of 101°F, shortness of breath, and cough. After performing the laboratory work and chest x-ray, right lower lobe aspiration pneumonia was diagnosed and he was started on intravenous clindamycin 600 mg twice daily and was discharged home on oral clindamycin on the third day. Four days after discharge, the patient started to notice yellowish discoloration of the eyes and face, gradually increasing in intensity over the next 2–3 days and ultimately involving the whole body. On further questioning, the patient's family member mentioned some right upper quadrant discomfort with nausea and decreased appetite along with fatigue and increased confusion in the last 24 hours.

His blood pressure on presentation was 98/63 mm Hg, pulse 107 beats/min, respiration 22 breaths/min with oxygen saturation of 94% on room air, and temperature of 99.5°F. On examination, he exhibited grade II encephalopathy and profound jaundice. Abdominal examination was significant for mild tenderness in the right upper quadrant, and chest auscultation revealed rales on right lower lobe. The rest of the examination was unremarkable.

Laboratory work revealed hemoglobin of 12.1 g/dL, white cell count of 11.5 Thou/mm^3, with neutrophils of 80%, platelets 186 Thou/mm^3, urea nitrogen 22 mg/dL, creatinine 0.91, sodium 131 mEq/L, potassium 4.2 mEq/L, chloride 101 mEq/L, bicarbonate 19 mEq/L; liver function test (LFT) showed total bilirubin

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of 6.9 mg/dL with direct bilirubin of 3.43 mg/dL, alanine aminotransferase 1076 IU/L, aspartate aminotransferase 440 IU/L, alkaline phosphatase 203 IU/L, albumin 3.4 g/dL, ammonia 55 μmol/L; international normalized ratio was 2.1, prothrombin time 19.4 seconds, and activated partial thromboplastin time 33.7 seconds. His liver enzymes were normal before this visit. Ultrasound of the liver was reported as normal. Biopsy was not performed due to the elevated international normalized ratio.

Because of confusion and hepatic failure, the patient was admitted to the intensive care unit. The patient was started on intravenous fluids, and clindamycin was held because of possible etiology behind the hepatic injury and it was switched to Zosyn 3.375 g intravenously every 6 hours for broad-spectrum coverage as the patient continued to have rales on examination and infiltrate on his right lower lobe. Lactulose was started to help him with the encephalopathy and elevated ammonia. Patient conditioned worsened, and he developed acute respiratory distress syndrome, for which he was intubated. White cell counts continued to be elevated, in the face of negative sputum and blood culture, perhaps because of initial antibiotic therapy rendering the cultures negative. On the sixth day, his liver function were alanine aminotransferase 437 IU/L, aspartate aminotransferase 205 IU/L, and total bilirubin of 3.6 mg/dL. Hepatitis panel, serum ferritin level, serum cerruloplasmin level, and antibody panel came back as normal. There was no history of alcohol use, Tylenol, or any other medication use that could be contributed to be the cause of hepatic failure. As the patient continued to be dependent on mechanical ventilation and failed multiple weaning trials, support was withdrawn according to his wishes.

DISCUSSION

Drug-induced liver injury may take place through a variety of mechanism.[3] It accounts for up to 10% of all adverse drug reactions.[4] Presentation ranges from just the laboratory derangement to the development of jaundice or even with fulminant hepatic failure.[5,6] The incidence is approximately 14 per 100,000 populations. Withdrawal of the offending agent may result in complete recovery.

Our patient developed signs and symptoms of liver injury due to clindamycin after 5 days of starting the antibiotic for the management of aspiration pneumonia. His liver injury was evident by significant elevation in his LFT, increased international normalized ratio, and raised ammonia level. There was no history of any other known hepatotoxic drug usage or history of alcohol abuse in our patient. In addition to that, normal LFT before starting the clindamycin and improvement in LFTs after the discontinuation of drug supported the diagnosis of acute liver injury due to clindamycin. Ultrasound of liver, viral hepatitis panel, antibody panel for autoimmune hepatitis, and serum level of ferritin and cerruloplasmin were performed to exclude other possible etiology and all came back within normal range.

The probability of spontaneous recovery from the acute liver injury is difficult to be predicted by any single factor alone. The variables, which can help in predicting the outcome in acute liver failure, are the patient's age, degree of encephalopathy,[6] cause of injury, and remaining metabolic capacity of the liver.[7] Our patient was in grade II encephalopathy in which the chances of spontaneous recovery were 65%–70%.[8]

Acute liver failure due to idiosyncratic drug reaction has a poor prognosis with mortality rate of more than 80% without liver transplantation,[1,8] as opposed to the patient who receive liver transplant in whom the 1-year survival rate is more than 80%.[9] However, if patients recover from the acute injury, then the prognosis is favorable.[10] Our patient was not considered for liver transplantation on the basis of the King's College Criteria, which was developed after a cohort study of 588 patients with acute liver failure.[8]

Treatment options in drug-induced liver failure are few. The offending drug should obviously be stopped; however, if either hepatotoxicity is not suspected early or the patient continues to take the offending agent while at home despite the fact of becoming symptomatic, this does not always happen. Once the hepatic failure is clinically apparent, treatment options are either supportive care[6] or transplantation,[8,9] depending on the severity. Whereas the patient in question showed improvement in liver function, he concurrently developed acute respiratory distress syndrome. Patients with liver failure will often die of extrahepatic organ complications rather than liver itself. According to one study in a patient with liver failure, pulmonary and renal complications accounted for approximately of 30% and 30%–50% of the time, respectively.[11] Experimental support options include extracorporeal liver assist devices, which are confined to clinical trials.[12]

CONCLUSIONS

To conclude, our patient developed liver failure after being treated with clindamycin for aspiration pneumonia. Disordered liver enzymes and synthetic function, which improved during his hospital stay after removing the offending agent, would support the diagnosis of clindamycin-induced liver toxicity.

However, more work needs to be done to better understand the pathophysiology of acute liver injury due to clindamycin use.

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