MEROPENEM INDUCED HEPATIC DERANGEMENT: A CASE REPORT

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ABSTRACT

Drug-induced hepato-toxicity is one of the common causes of nosocomial morbidity leading to increased length of hospital stay as well as higher mortality. A variety of drugs may lead to different types of hepatobiliary disorders. Meropenem, is a broad spectrum antibiotic generally prescribed for complicated infection and in intensive unit cases. It is rarely associated with elevation of hepatic enzymes. We report a case of a 56-year-old man who was admitted for complicated diabetic foot and discharging abscess for the past one week. Meropenem was prescribed intravenously for septicemia. However, after 7 days of administration, there was gross elevation of alkaline phosphatase with normal alanine aminotransferase and bilirubin. His INR and hepatobiliary sonograph was repeatedly normal. On discontinuation of Meropenem, there was normalization of alkaline phosphatase and resolution of his symptoms.

Key Words: Hepatotoxicity, Drug induced liver injury, Meropenem

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INTRODUCTION

Drug-induced liver injury accounts for about one-half of the reported cases of acute liver failure that further aggravate all other forms of acute and chronic hepatic diseases[1]. It has been reported that more than 55% of liver injuries are drug-induced[2]. Adverse effects on liver due to drugs may be predictable or unpredictable. The former one is reported with high incidence rate[3]. Meropenem is a broad spectrum antibiotic with an excellent activity against gram positive and gram negative bacteria. It is commonly prescribed in the treatment of sepsis and post-operative cases with complicated infections in majority of tertiary healthcare settings. Few case reports have been published in which elevated levels of liver enzymes have been reported[4,5].

CASE PRESENTATION

A 56-year-old man with poorly controlled type-2 diabetes mellitus (>6 years) was admitted in the Endocrinology Unit of Lady Reading Hospital, a tertiary care, public sector healthcare facility at Peshawar. He presented with left diabetic foot (cellulitis) with underlying abscess formation associated with purulent discharge from the lateral side of foot for last one week. The physical examination of the patient revealed conjunctival pallor with an elevated body temperature (39.3°F), blood pressure 140/100 mmHg and a heart rate 107 bpm. He also had glossitis with oral thrush. Rest of the physical exam. was unremarkable. His past medical history was unremarkable except for bilateral cataract surgery two years ago. The patient's medications included metformin and rosuvastatin in the past and he was recently prescribed sparfloxacin and co-amoxiclav for his foot infection by his GP.

The blood tests performed on admission revealed: hemoglobin: 12.4 g/dl; total leukocyte count: 13.7×103/µl; neutrophil count: 88%; platelet count: 252×103/µl; serum creatinine: 2.55mg/dl; creatinine clearance: 31ml/min; HbA1C: 11.5%; triglycerides: 763mg/dl; HDL cholesterol: 5mg/dl; INR: 1.1, PT: 18 seconds: APTT: 31 seconds; blood urea: 102 mg/dl; total bilirubin: 0.49 mg/dl; ALT: 24 IU/ml; ALP: 175U/l; serum electrolytes levels were normal and viral profile of the patient was negative. Swab for culture and sensitivity from abscess revealed no growth after 48 hours of incubation.

The patient was initiated on intravenous cefoperazone/salbactum and metronidazole for his infection. However, the patient's condition deteriorated in the next 3 days with elevation of his total leucocyte count (15.8 ×103/µl) and raging fever. In view of his clinical condition and laboratory reports, his antibiotic was switched to meropenem (500mg q8h) on 3rd day of admission. Furthermore, heparin (5000IU) TID was administered (prophylactically) subcutaneously along with the meropenem to prevent deep vein thrombosis. One week post administration of initial dose of meropenem, a tremendous increase in alkaline phosphatase levels was noted with relatively milder elevation of total bilirubin and al-

Table 1: Liver enzyme levels during the course of meropenem treatment

Meropenem Day	Total Bilirubin (mg/dl)	ALT Levels (IU/ml)	ALP Levels (U/l)
0	0.49	24	175
1	0.6	32	181
7	2.8	52	953
9	2.97	54	1178
11**	2.74	52	2256
15	1.83	32	1870
19	1.77	34	1575
21	0.34	23	1148
22	0.21	21	836

** Meropenem Stopped

anine transferase. Upon ultrasonic abdominal examination, normal liver with no biliary obstruction/dilatation was revealed. He was clinically unwell at that time with fever and shortness of breath, dehydration, tachycardia and tachypnea suggesting sepsis. Based on certain reported cases in the literature[4,5], meropenem induced cholestasis was suspected in the patient and thus meropenem and metronidazole were discontinued. As the patient was in sepsis, antibiotic was switched over to vancomycin after consultation with the Pharmacy Department, LRH. There was a striking decline of liver enzymes within 48-72 hours of discontinuation of Meropenem; which was noted progressively in the later days. An adverse drug reaction was reported to the Pharmacy Department and the Naranjo algorithm scale indicated a probable relationship (score of 5) between the patient's elevated liver profile and meropenem therapy. The deranged liver enzymes returned to normal levels upon withdrawal of meropenem. The changing patterns of liver enzymes with the course of meropenem therapy are presented in Table 1.

DISCUSSION

The drug induced disorders of liver occur most frequently and may be life threatening in certain conditions. However, the hepatic insult is reversible and it subsides upon cessation of the culprit drug. We had similar observations in our patient in which the enzyme levels got reduced upon discontinuation of meropenem. This drug and its metabolite are mostly excreted via kidney with a clearance of about 70% as intact parent drug molecule over 12 hours of administration[6]. But there is no such pharmacokinetic mechanism being reported in which metabolism of meropenem in liver is revealed and the elevation of liver enzymes in such cases is still questionable.

CONCLUSION

Keeping in view such events, the drug induced hepatic injuries should be kept as a part of differential diagnosis in patients with increased levels of hepatic enzymes. Furthermore, it is important to appreciate that a drug may not present with classical symptoms of overt liver injury. In patients who are critically unwell there should be regular monitoring the liver enzymes.

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