Gut and Gastroenterology

CASE REPORT

Amlodipine Induced Cholestasis: A Case Report

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Abstract

Amlodipine, a dihydropyridine calcium channel blocker, is used in treatments for hypertension and angina pectoris. Hepatotoxicity due to calcium channel blockers is very rare. We report a case of an 84-year-old man who developed cholestatic liver injury and pruritus following initiation of treatment with amlodipine for hypertension. The patient underwent workup regarding obstructive causes for liver injury which was negative. Following negative obstructive work-up the medication list was examined. The pruritus and all hepatic biochemical abnormalities completely resolved after withdrawal of the drug. The mechanism of amlodipine hepatotoxicity is not known, but is likely due to formation of a toxic intermediate in its metabolism. Similar to previously reported cases, the pathogenic mechanism of amlodipine-associated liver injury in our patient was, most probably, idiosyncratic.

Introduction

Drug induced liver injury (DILI) is common, and can be devastating. Fifty-two per cent of cases of acute liver failure are reported to be due to DILI, with the majority resulting from acetaminophen ingestion [1]. Other commonly implicated medications include antibiotics, such as fluoroquinolones and amoxicillin-clavulonic acid, and anti-epileptic medications [2]. DILI may present as a dose-dependent process or may be idiosyncratic, and presentation can vary from subclinical to fulminant liver failure [3]. Hepatotoxicity from calcium channel blockers has been rarely reported. Previous cases have involved presentation of idiosyncratic acute liver injury that is typically mild and reversible but can be severe [4, 5]. Hypersensitivity and metabolic injury appear to be involved as opposed to blockade of the calcium channel [4]. The injury induced by calcium channel blockers does not appear to be a class effect [5]. Amlodipine is a second generation calcium channel blocker used in treatments for hypertension and angina pectoris [5]. We report a case of DILI resulting from the use of amlodipine with resolution of both symptoms and laboratory abnormalities promptly following cessation of the drug.

Case Report

An 84-year old male was referred by his primary care provider to general surgery for evaluation of jaundice of approximately four weeks duration. He denied abdominal pain, nausea or vomiting and fevers, but did note intense pruritus. Past medical history was significant for hypertension, benign prostatic hypertrophy and a prior hernia repair. The patient denied known liver disease or a family history of liver disease, and there was no history of alcohol use or abuse. Medications included acetaminophen as needed, oxybutynin 5 mg oral tablet daily, and amlodipine 5 mg daily. Examination was remarkable for jaundice only. The abdomen was soft and non-tender with no palpable mass. Ultrasound demonstrated no dilation of the intrahepatic or extrahepatic ducts, with the common bile duct diameter of 4.5 mm. At referral the total bilirubin was 22.6 mg/dL, alkaline phosphatase 496 U/L, AST 76 U/L and ALT 71 U/L (Figure). Serum amylase was 395 U/L with a lipase of 634 U/L. The tumor marker Ca 19-9 was low at 27 U/ml, as was the carcinoembryonic antigen at 2.3ng/ml, Gastroenterology was asked to perform an ERCP which revealed no evidence of biliary obstruction. A review of the record revealed that the patient had been started on amlodipine just prior to becoming jaundiced. Prior to this his liver enzymes were normal. Amlodipine was held and over the next few weeks the jaundice cleared, itching stopped and, after approximately three months, his liver enzymes had essentially normalized (Figure). Additionally, his serum lipase also returned to normal 12 weeks after the drug was discontinued. The patient was not re-challenged with amlodipine.

Discussion

Amlodipine is a dihydropyridine calcium channel blocker commonly prescribed in the treatment of coronary artery disease and hypertension that is generally well tolerated. During clinical trials, researchers noted increase of edema, dizziness, and flushing in a dose-dependent manner [6, 7]. Drug induced liver injury due to amlodipine is rare, however. In fact, hepatotoxicity due to calcium channel blockers as a group is clinically uncommon [4, 8]. Chalasani et al. [9]

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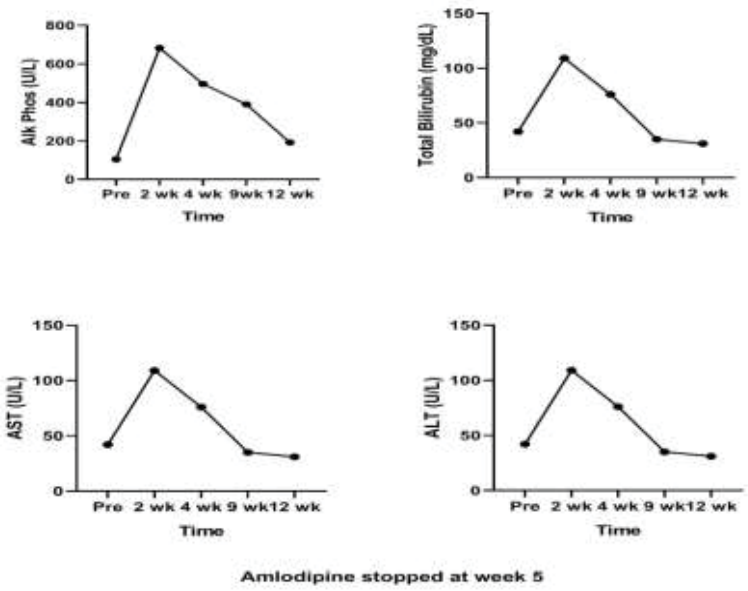

Figure 1: Graphical representation of the course of liver enzymes and total bilirubin from before initiation of amlodipine therapy (Pre) to discontinuation at week 5 and subsequent normalization.

found one patient of 899 in the Unites States Drug Induced Liver Injury Network in whom amlodipine was possibly implicated as the offensive agent. A handful of case reports are available that report DILI associated with amlodipine use, with both a hepatocellular and mixed pattern of injury reported [10-14]. Basile et al. [10] described an individual who developed cholestasis on nifedipine, another dihydropyridine calcium channel blocker. After this resolved the patient was placed on amlodipine and cholestasis re-developed promptly. Amlodipine has not been reported to cause fulminant liver failure. We report a cholestatic response to amlodipine exposure which meets previously proposed criteria (alkaline phosphatase elevation of at least twice the upper limit of normal with an ALT-to-alkaline phosphatase ratio of <2) [13]. Discontinuation of amlodipine was followed by resolution of jaundice and pruritis, and rapid normalization of liver enzymes. This individual also developed asymptomatic elevation of his pancreatic enzymes which resolved with discontinuation of the drug. Drug-induced pancreatitis is uncommonly the result of amlodipine exposure [15].

Acknowledgement

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Conflicts of interest

None

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