

Cystic Mass on Computed Tomography With Acute Onset Painless Jaundice

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ABSTRACT

Acute onset painless jaundice in the elderly population raises the concern for underlying malignant etiology. We present, we want to alert the clinicians of the significance of thorough medication reconciliation, appropriate interpretation of radiology findings and their clinical implications, and the evolving use of endoscopic ultrasound-guided liver biopsy in patients with abnormal liver function tests. The above-mentioned steps along with eliciting the key detail history pertaining to the recent medication use lead us to the diagnosis of amoxicillin-clavulanate-induced cholestatic liver injury, an uncommon cause of painless jaundice.

INTRODUCTION

The differential for abnormal liver function tests is broad, and a careful medical history is necessary to elucidate the etiology. The main objective of this report is to educate clinicians regarding the full differential of painless jaundice. We hope to demonstrate the importance of integrating radiologic findings with a careful history, especially recent medication use when evaluating jaundice and to recognize amoxicillin-clavulanate as an important cause of cholestatic liver injury.

CASE REPORT

A 71-year-old man was referred for further evaluation of painless jaundice associated with pruritus without any significant weight loss. Laboratory evaluation was notable for total bilirubin 5.8 mg/dL, direct bilirubin 4.3 mg/dL, alanine aminotransferase 51 U/L, aspartate aminotransferase 47 U/L, and alkaline phosphatase 264 U/L. Liver function test from the past 2 months was normal. His cognition and international normalized ratios were also normal. An abdominal and pelvic computed tomography (CT) showed an 11-mm low-density pancreatic body lesion (Figure 1). There was no evidence of biliary or pancreatic duct dilation (Figure 2).

Owing to the acute onset of jaundice, he was then referred for endoscopic ultrasound (EUS) for further evaluation of these CT findings. Before the procedure, on further questioning, the patient reported that he received a course of amoxicillin-clavulanate for a sinus infection about 3 weeks before the onset of his jaundice. EUS showed a normal caliber of the common bile duct and pancreatic duct with no stones or sludge (Figure 3). The lesion seen on the CT scan corresponded to a side branch intraductal papillary mucinous neoplasm in the pancreatic body which was not causing biliary obstruction. Fine-needle aspiration was not performed, given a lack of high-risk stigmata and the small size of the lesion. A EUS-guided liver biopsy was then obtained because examination findings did not support biliary obstruction as a cause of his jaundice.

Liver biopsy revealed areas of cholestasis in a zone 1 distribution and lobular cholestasis with multiple canaliculi demonstrating bile plugs (Figure 4). There was also mild chronic lobular inflammation without significant steatosis. There was no evidence of bile duct injury or proliferation. These histologic changes were consistent with drug-induced liver injury secondary to amoxicillin and clavulanate.¹ The patient was treated with cholestyramine and hydroxyzine for itching and had



Figure 1. Computed tomography showing a small pancreatic body cystic lesion.

a close laboratory follow-up with continued improvement in his liver function tests. His liver panel had normalized by 3 months after the initial presentation.

DISCUSSION

The differential for jaundice is broad. Elevation of unconjugated bilirubin may be caused by overproduction, impaired uptake by the liver, and abnormalities of bilirubin conjugation. On the other hand, the elevation of conjugated bilirubin may be caused by hepatocellular disease, impaired canalicular excretion of bilirubin, or biliary obstruction. The diagnostic evaluation of a patient with jaundice should include a careful medical history, physical examination, and laboratory and often radiological studies. The history should elicit the use of medications (including herbals, supplements, and recreational drugs), use of alcohol, hepatitis risk factors, history of abdominal surgeries, history of inherited disorders (including liver disease and hemolytic diseases), and associated symptoms. Further testing such as imaging in suspected biliary obstruction may include hepatic imaging such as ultrasound and magnetic resonance cholangiopancreatography.

In this case, the patient did not have any evidence of biliary obstruction despite conjugated hyperbilirubinemia. The finding of “cystic mass” in a patient with recent-onset painless jaundice led to the concern of pancreatic malignancy. However,



Figure 2. Computed tomography showing the normal caliber bile duct.

the mass was located in the body of the pancreas, and thus, before performing EUS, a careful medical history including medication use was obtained. No pancreaticobiliary cause of the patient’s jaundice was found on EUS examination, and thus, the decision was made to proceed with EUS-guided liver biopsy, clinching the diagnosis of drug-induced liver injury related to augmentin and clavulanate use.



Figure 3. Endoscopic ultrasound showing the normal caliber bile duct.

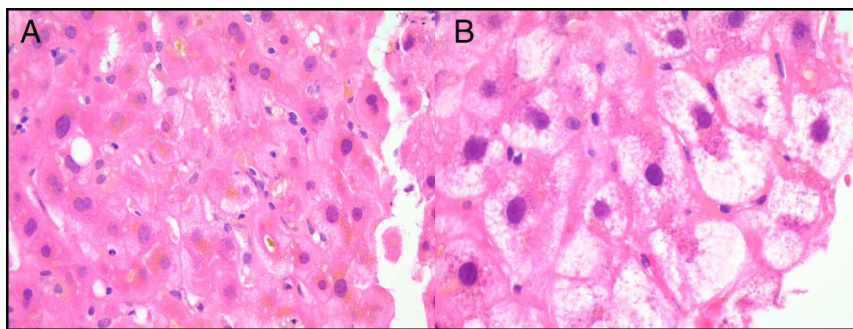


Figure 4. Liver histology showing multiple canaliculi with bile plugs and cholestasis of periportal hepatocytes.

The Roussel Uclaf Causality Assessment Method score is a system that assigns points to clinical, biochemical, serologic, and radiologic features of liver injury to calculate an overall score that reflects the likelihood that the liver injury is due to a specific drug. In this case, the patient's Roussel Uclaf Causality Assessment Method score was 10, indicating a high probability of adverse drug reaction (+2 for onset time, +1 for time from drug withdrawal to onset, +1 for age risk factor, +2 points for greater than 50% improvement within 180 days, +2 for ruling out alternate etiologies, and +2 points for known reaction to drug).²

Per the Drug-Induced Liver Injury Network severity grading system, this would be classified as a grade 2+ moderate injury (increased transaminases and bilirubin greater than 2.5 without coagulopathy and without hospitalization because of liver injury).³ Augmentin and clavulanate is the most common cause of drug-induced liver injury in the United States and Europe.⁴ The onset of liver injury can vary from a few days to up to 8 weeks with an average of 3 weeks after initiation. Associated symptoms may include fatigue, low-grade fever, nausea, abdominal pain, pruritus, and jaundice. The liver injury is typically in a cholestatic pattern but can also be a hepatocellular or mixed pattern. Rechallenge with amoxicillin-clavulanate should be avoided because of the risk of recurrence. On the other hand, amoxicillin alone is generally safe because the clavulanate is typically the likely culprit of liver injury.

The diagnosis of drug-induced liver injury can be challenging and a causality assessment of suspected adverse drug reactions has been proposed to classify injury.⁵ In this case, we would consider the etiology as certain based on several factors. The timing of the liver injury occurred within a plausible time range from the exposure to the medication. Alternative etiologies,

such as biliary obstruction, were ruled out. Liver biopsy was also consistent with this type of drug-induced liver injury. Finally, the liver injury resolved with the withdrawal of the drug.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. P. Chahal is the article guarantor.

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