ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

Drug-Induced Liver Injury After Soy Protein Supplement Use

Ajish Pillai, MD, and Manish Thapar, MD

Division of Gastroenterology and Hepatology, Drexel University College of Medicine, Philadelphia, PA

Abstract

Drug-induced liver injury (DILI) is an important and often elusive cause of iatrogenic hepatic injury which complicates its recognition and treatment. We describe a rare case of severe liver injury in a previously healthy individual associated with a commonly used and reportedly safe soy protein powder supplement. Discontinuation of the supplements and initiation of ursodeoxycholic acid provided symptomatic relief, decreased pruritus, and resulted in a resolution of hepatic panel labs.

Introduction

Drug-induced liver injury (DILI) is an important and often elusive cause of iatrogenic hepatic injury, and may present with a broad array of histologic signatures, further complicating its recognition and treatment. Establishing a diagnosis of DILI requires a careful exclusion of other etiologies and an awareness of the hepatotoxicity profile of suspected agents. DILI is the leading cause of drug withdrawal from the United States market, both before and after approval.[1] With an increasingly large market for dietary supplements, the demand for herbal remedies and health food supplements has soared, with up to 53% of the population using such products in 2006, up from 42% of the population in 1994.[2] Case reports have described cholestatic liver injury associated with whey protein and creatine supplement use.[3]

Case Report

A 48-year-old man without significant past medical history developed jaundice and fatigue after experiencing dark urine and indigestion for a few weeks. He had recently begun dieting, exercising, and taking 20 mg of soy protein supplement (EAS Sports Nutrition, Abbott, Columbus, OH) per day in his diet. Two months after initiating these changes, he noticed urine and stool color changes, right upper quadrant tenderness, and jaundice.

The patient had no family history of liver disease or colorectal cancer. His only medication was a vitamin C supplement; otherwise, he denied other daily medications or weight loss medications/aids, including acetaminophen. There was no significant history of alcohol use, IV drug use, tattoos, or blood transfusions. There was no history of recent travel or sick contacts. On examination, he appeared well, with a body mass index (BMI) of 30 kg/m^2. On admission, he was afebrile, icteric, with a benign abdomen with no organomegaly, and had no asterixes or evidence of encephalopathy.

Initial laboratory results showed AST 1737 IU/mL, ALT 1939 IU/mL, total bilirubin 10.2 mg/dL (peaked to 16.4), direct bilirubin 7.3 mg/dL, and normal amylase, lipase, albumin, platelet count, white blood cell count, and INR. Work-up for autoimmune hepatitis, viral hepatitis, Wilson's disease, and alpha-1 antitrypsin deficiency was negative. He had a ferritin 7790 mcg/mL with an iron saturation 81% and a hemochromatosis gene analysis noted heterozygous for C282Y. Liver biopsy demonstrated subacute hepatitis with submassive collapse of portal

ACG Case Rep J 2015;2(3):178-180. doi:10.14309/crj.2015.47. Published online: April 10, 2015.

Correspondence: Ajish Pillai, 219 North Broad Street, 5th Floor, Philadelphia, PA 19107 (ajish.pillai@drexelmed.edu).

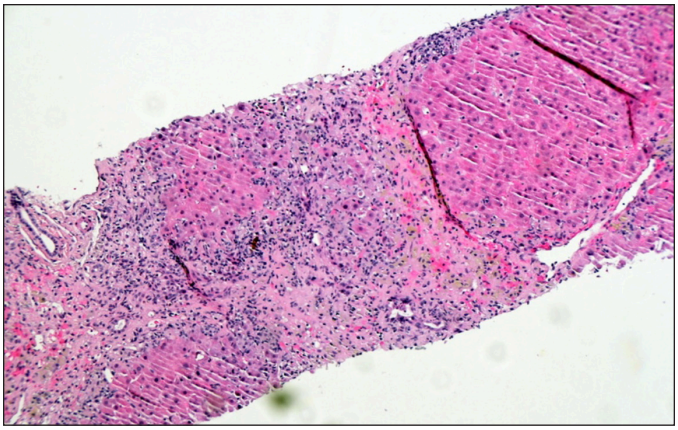

Figure 1. Low-power view of liver biopsy showing collapse of parenchyma from portal area into lobule.

tracts and lobules, with absence of viral cytopathic changes (Figure 1). Inflammatory activity was evident, particularly in zone 3, with lymphocyte and neutrophils predominant and a paucity of plasma cells (Figure 2). There was necrosis of ~30% of the hepatic parenchyma (Figure 3). Additional bile duct proliferation was evident, but no regenerative nodules or bridging fibrosis was described. Iron stain showed hyperfocal Kupffer cells with mild iron staining on liver tissue. Hepatic iron index score was less than 1.9, suggesting against underlying hemochromatosis. Abdominal and pelvic CT showed no hepatic masses or biliary ductal dilatation with a normal spleen and pancreas. Abdominal ultrasound showed the common bile duct at 4 mm.

Ursodiol 300 mg 3 times per day was started for pruritus, jaundice, and mildly elevated cholestatic liver function. However, he developed clinical ascites and leg edema a month later. He required a 4.5 L paracentesis, and fluid studies showed low protein (1.9 mg/dL) and high serum-ascites albumin gradient (>1.1) ascites. He was started on furosemide 40 mg per day, spironolactone 100 mg per day, and had a dramatic improvement with a 30-pound weight loss.

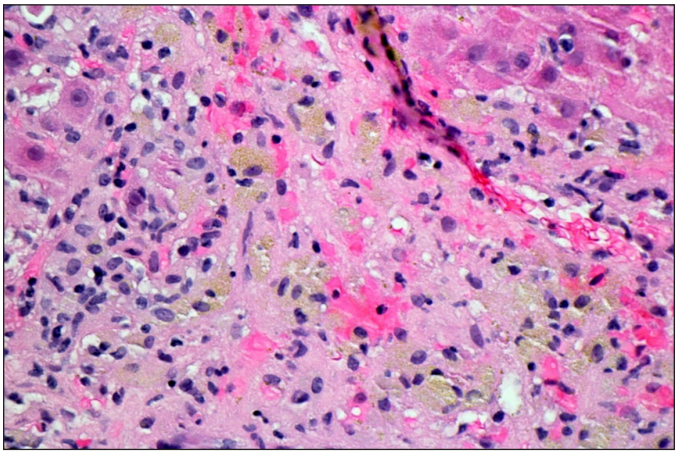

Figure 2. Liver biopsy showing collapsed area with pigmented histiocytes and scattered lymphocytes.

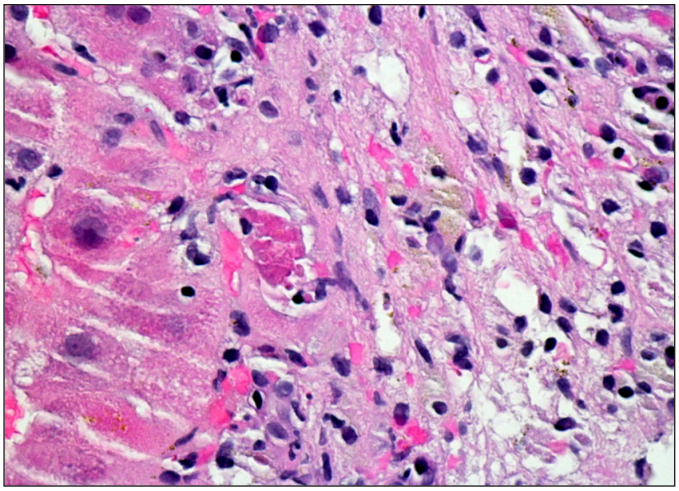

Figure 3. Liver biopsy showing a rare necrotic hepatocyte rimmed by lymphocytes.

Follow-up lab tests 105 days after drug discontinuation showed improving liver function tests with AST 86 IU/mL, ALT 66 IU/mL, alkaline phosphatase 110 IU/mL, total bilirubin 2.7 mg/dL, and albumin 3.7 g/dL. His bilirubin and INR have since returned to normal, yet his transaminases remain persistently elevated. Since discontinuing usage of soy protein powder supplements, the patient has reported increased energy and is off all diuretics. Follow-up lab tests 150 days after drug discontinuation showed AST 56 IU/mL, ALT 55 IU/mL, alkaline phosphatase 113 IU/mL, total bilirubin 0.8 mg/dL, and albumin 4.5 g/dL.

Discussion

Our case is unique in that DILI occurred in a low-risk patient who presented with jaundice without other etiologies. This is a rare case in which hepatotoxicity is due to soy protein powder supplement use. The Roussel Uclaf Causality Assessment Method (RUCAM) is a core system that includes means of assigning points for clinical, biochemical, serologic, and radiologic features of liver injury, which gives an overall assessment score reflecting the likelihood that hepatic injury is due to a specific medication. RUCAM is now widely used in assessing causality of drug-induced liver injury, both in the published literature and in support of regulatory decisions regarding medications implicated in causing hepatic injury.[4] Our patient's RUCAM score was 10, supporting the conclusion that the liver injury was likely related to the supplement use. Health care professionals should be aware of the potential for liver injury associated with soy protein supplement use and should be vigilant in identifying patients who would benefit from education and discontinuation on supplement use.

Disclosures

Author contributions: A. Pillai wrote the manuscript and is the article guarantor. M. Thapar edited the manuscript.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received: October 23, 2014; Accepted: February 17, 2015

References

1. United States Department of Health and Human Services Food and Drug Administration. Guidance for industry: Drug-induced liver injury: Premarketing clinical evaluation. http://www.fda.gov/downloads/Drugs/.../Guidances/UCM174090.pdf. Published July 2009. Accessed October 23, 2014.
2. Gahche J, Bailey R, Burt V, et al. *Dietary Supplement Use Among US Adults Has Increased Since NHANES III (1988-1994)*. Hyattsville, MD: National Center for Health Statistics; 2011. NCHS Data Brief No 61.
3. Whitt KN, Ward SC, Deniz K, et al. Cholestatic liver injury associated with whey protein and creatine supplements. *Semin Liver Dis*. 2008;28(2):226–31.
4. Danan G, Benichou C. Causality assessment of adverse reactions to drugs-I. A novel method based on the conclusions of international consensus meeting: Application to drug-induced liver injuries. *J Clin Epidemiol*. 1993;46(11):1323–30.