ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

Severe Liver and Renal Injury From Tribulus Terrestris

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ABSTRACT

Tribulus terrestris is a shrub that is found worldwide. Although it has been linked to severe jaundice and death in grazing animals, there are only a few case reports of hepatotoxicity in humans. We describe a case of a 46-year-old man who took tribulus supplements daily for 2 months. He developed severe jaundice prompting hospital admission. His total bilirubin peaked at 48 mg/dL, with concomitant renal dysfunction (creatinine of 7.1). His liver biopsy showed features consistent with drug-induced liver injury. He was initiated on a trial of plasmapheresis and underwent 3 sessions with a subsequent decrease in bilirubin with each session. He had appropriate renal recovery and was discharged home and on follow-up, continues to do well with most recent bilirubin of 1.1 mg/dL.

KEYWORDS: drug-induced liver injury; plasmapheresis; liver failure; testosterone supplement

INTRODUCTION

Tribulus terrestris is a common weed found in North and South America, Asia, Africa, and Australia. The active ingredients of *T. terrestris* are steroidal molecules: dioscine, diosgenin, and protodioscin.[1] Tribulus extracts are readily available and found in multiple dietary supplements used for enhancing athletic performance and sexual performance.

Tribulus has been linked to liver injury and death in animals in a phenomenon described as "geeldikkop" or tribulosis.[2] Animals grazing on different tribulus species can develop marked photosensitivity and icterus, followed by severe jaundice and death. Histology of the liver from sheep dying after feeding on this plant has shown crystals in bile ducts and renal tubules.[1] There are only a few case reports in current literature regarding tribulus toxicity in humans. We describe a case of liver and renal toxicity after ingestion of tribulus supplements.

CASE REPORT

A 46-year-old man presented to the emergency department (ER) with complaints of jaundice, fatigue, and 20 lb weight loss before presentation. He had a history of bipolar disorder for which he was on long-term lamotrigine. He had no history of liver disease and denied any alcohol use or illicit drug use. He was a healthcare worker and lived an active lifestyle including frequent strength training. The patient endorsed using tribulus supplements for 2 months before admission, which he purchased online. He had reportedly stopped these supplements 3 weeks before his presentation.

Blood work obtained in the emergency department noted a total bilirubin of 8.4 mg/dL, aspartate aminotransferase 180 U/L, alanine aminotransferase 636 U/L, and alkaline phosphatase 112 U/L. He underwent a contrasted abdominal computed tomography, which noted a non-cirrhotic liver and normal biliary tree and was incidentally found to have sub-cm hepatic hemangiomas. He was administered intravenous fluids in the ER and discharged home with instructions to follow-up with his primary care physician.

Days later, he re-presented to the ER with complaints of worsening fatigue. Repeat blood work noted a total bilirubin level of 14 mg/dL. Further hepatobiliary imaging (magnetic resonance imaging and magnetic resonance cholangiopancreatography) was unrevealing, and the liver parenchyma was noted to be unremarkable. He was advised to stop lamotrigine as a suspected cause of his elevated bilirubin and again discharged home from the emergency department.

ACG Case Rep J 2024;11:e01267. doi:10.14309/crj.0000000000001267. Published online: February 7, 2024

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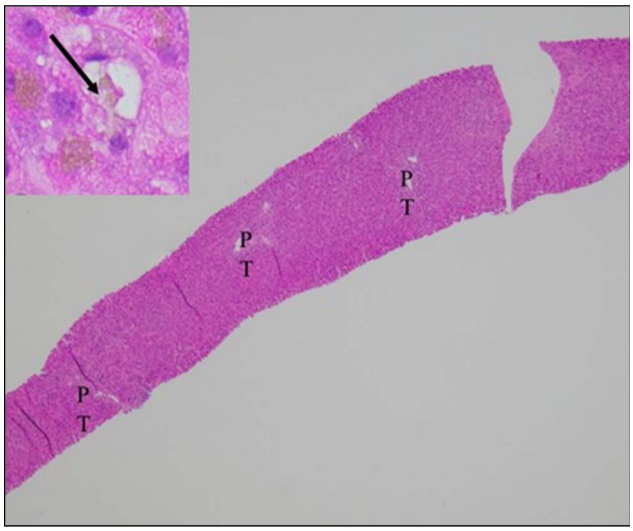

Figure 1. Liver biopsy with marked cholestasis with labeled portal triads.

At follow-up with his primary care physician later that week, he underwent workup for infectious hepatitis and autoimmune diseases (hepatitis A, hepatitis B, hepatitis C, antinuclear antibody, anti-smooth muscle antibody, anti-mitochondrial antibody, immunoglobulin levels, ceruloplasmin, and alpha-1 antitrypsin), all of which were unremarkable. He was initiated on ursodiol 900 mg daily for his cholestatic liver injury, and an outpatient liver biopsy was scheduled. However, owing to worsening jaundice and pruritus, he presented to the ER a few days later. He was found to have a total bilirubin of 40 mg/dL and creatinine (Cr) of 2.6 mg/dL and subsequently admitted to the hospital.

He was deemed to have acute severe liver injury and had no features of liver failure (normal international normalized ratio [INR] and no encephalopathy). He underwent a thorough workup for his elevated liver function tests including infectious hepatitis and autoimmune serologies, which were unremarkable. A liver biopsy was subsequently performed, and this noted severe cholestasis and minimal inflammation with no ductopenia or fibrosis, consistent with drug-induced liver injury.

His bilirubin and Cr continued to worsen during his hospital stay, with a peak in total bilirubin of 48 mg/dL and Cr of 7.1 mg/dL. The etiology of his renal dysfunction was thought to be bile cast nephropathy in the setting of his elevated bilirubin, and he was initiated on hemodialysis.

Owing to his worsening liver function, the patient underwent expedited transplant evaluation and was listed for a liver transplant, but made inactive with the decision to trial plasmapheresis. The patient underwent 3 sessions of plasmapheresis, with a subsequent decrease in bilirubin after each session (total bilirubin decreased from 41 to 11.6 mg/dL after 3 sessions of plasmapheresis). His bilirubin continued to decrease, and he was also liberated from hemodialysis because of return of renal function with a decrease in Cr. The patient was subsequently discharged from hospital after a 3-week hospital stay.

On most recent outpatient follow-up, 2 months after hospital admission, he was noted to have a bilirubin of 1.1 mg/dL and Cr of 1.3 mg/dL (Figures 1 and 2).

DISCUSSION

Our case is the one of few reported cases in the literature regarding liver and kidney toxicity from tribulus. In addition, it highlights the usage of plasmapheresis for acute severe liver injury and exploiting plasmapheresis for its ability to lead to rapid decline in serum bilirubin allowing for both liver and renal recovery.

One of the other few reported cases in the literature describes a 30-year-old man who developed nausea and poor appetite

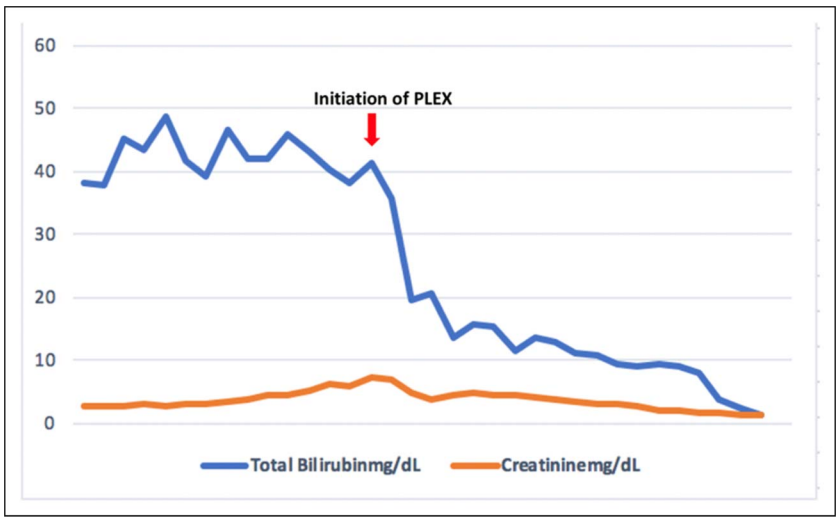

Figure 2. Trend of bilirubin and creatinine during hospital stay and follow-up. PLEX, plasma exchange.

after taking tribulus tablets as part of his muscle building program. His total bilirubin peaked at 39 mg/dL, with a Cr of 3.1 mL/dL. His liver biopsy showed bland cholestasis. After 6 weeks of stopping tribulus, his bilirubin downtrended to 4.4 mg/dL with a Cr of 1.2 mg/dL.[1]

The above-described case is similar to ours, in that there is a clear correlation between ingestion of tribulus supplements and development of liver and renal injury. However, in our case, even after discontinuation of tribulus for >2 months, severe liver and renal injury persisted, which only improved after plasmapheresis was performed. Larsen et al[3] investigated the therapeutic effect of plasmapheresis in acute liver failure and showed a higher survival in patients treated with plasmapheresis. However, the role of plasmapheresis for acute liver injury in the absence of liver failure is unclear, but may be beneficial to support liver recovery by decreasing serum bilirubin. A systematic review analyzed the efficacy of plasmapheresis of 19 patients with drug-induced liver injury, noting outcomes of laboratory parameters and clinical signs and symptoms of liver function (aspartate aminotransferase, alanine aminotransferase, bilirubin, INR; <20% reduction in serum bilirubin from baseline after 3 sessions of plasmapheresis or reduction in serum bilirubin by < 5 mg and INR <1.5). The review reported positive outcomes of plasmapheresis in all included patients.[4]

In conclusion, while tribulus supplements are readily available online and in stores claiming to help with sexual dysfunction, muscle building, and hypertension, these supplements present an increased risk of severe liver and renal dysfunction, and their use should be discouraged in the absence of proven clinical benefit. Our case highlights the importance of a thorough evaluation for elevated liver function tests with a detailed history of supplements that patient's may consume that can be beneficial in revealing the etiology of their liver injury.

DISCLOSURES

Author contributions: N. Mohy-ud-din: drafting the case report. N. Jonassaint: critical review and is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received September 3, 2023; Accepted December 22, 2023

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