

Acute Severe Liver Injury Related to Long-Term *Garcinia cambogia* Intake

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ABSTRACT

Herbal and dietary supplements are frequently used as weight loss supplements. However, they account for 20% of drug-induced liver injury. *Garcinia cambogia*'s (GC) active compound, hydroxycitric acid, can be found among those supplements. We report a 26-year-old woman who had been taking GC for 7 months when she presented with subacute liver failure and ultimately required a liver transplantation. This report highlights the risk of liver injury after long-term use of GC and demonstrates the importance of considering a close and prolonged monitoring of patients in a tertiary liver transplant center.

INTRODUCTION

Herbal and dietary supplements (HDS) are often perceived alternative treatments for obesity.¹ Although HDS might be publicised as safe, they account for 20% of drug-induced liver injury.¹ Found in numerous products available online, *Garcinia cambogia* (GC) has recently grown in popularity. GC is harvested from trees growing in India and Southeast Asia, and its active compound is called hydroxycitric acid (HCA). Several mechanisms of action have been proposed to explain the potential beneficial effects of HCA, but its toxicity mechanisms remain unclear. Most negative reports implicating HCA describe the consumption of multi-ingredient formulations.²

CASE REPORT

We report a 26-year-old woman with morbid obesity (body mass index of 59.8 kg/m²) and occasional social alcohol consumption, with no medical history of liver disease. The patient was admitted directly to the hepatology ward on day 1 with fatigue, nausea, and jaundice. She had been taking 3 different HDS for weight loss for the last 7 months: 1,800 mg of GC (900 mg HCA), 1,275 mg of green tea extract (GTE) with 450 mg of Veldt raisin, and 1,200 mg of coffea arabica daily. She had lost 45 kg in the last few months. All products were stopped 10 days before admission. Initial laboratory results revealed acute hepatitis: aspartate aminotransferase of 1,164 IU/L, alanine aminotransferase of 2,881 IU/L, total bilirubin of 157 µmol/L, and international normalised ratio 1.1 (Figure 1).

Abdominal ultrasound revealed homogenous liver parenchyma, without steatosis nor bile ducts dilatation. Magnetic resonance cholangiography confirmed normal biliary tracts. Transjugular liver biopsy on day 9 showed acute hepatitis changes such as lobular disarray with confluent necrosis and reticulin collapse. Inflammatory infiltrate was mixed and composed predominantly of lymphocytes with some neutrophils, eosinophils, and non-necrotizing granulomas. Very few plasma cells were identified. Evidence of cytologic injury of hepatocytes was seen as well, including ballooning of hepatocytes and apoptotic bodies. Residual viable hepatocytes demonstrated signs of regeneration. No steatosis nor Mallory bodies were noted (Figure 2). All other causes of acute liver failure were excluded: hepatitis A, B, C, E virus, Cytomegalovirus, herpes simplex virus, Epstein-Barr virus, and Varicella zoster virus (serology and nucleic acid testing); autoantibody was negative (antinuclear, antismooth muscle, and antimitochondrial), ceruloplasmin and serum copper were in the ranges. The patient was not known to carry any genetic mutation or biomarker, nor was she tested for it after admission. The patient had not traveled or used intravenous drugs or acetaminophen.

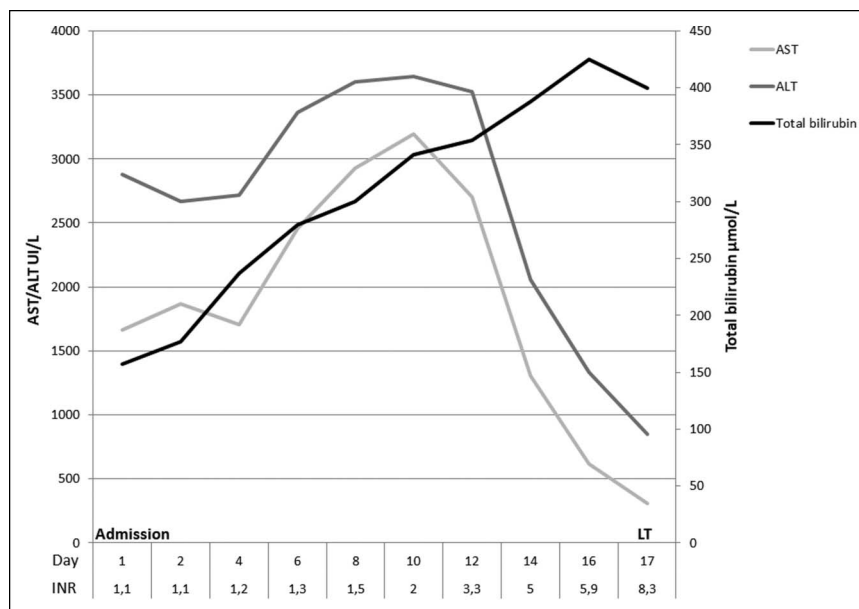


Figure 1. Evolution of laboratory tests from admission to liver transplantation. Liver biopsy on day 9 and 17 (preliver transplantation and explanted liver). ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; LT, liver transplantation.

On day 15, the patient had a sudden onset of grade 2 encephalopathy with elevated ammonia and hypoglycaemia. She was admitted to the intensive care unit and listed emergently for liver transplantation (LT) for fulminant liver failure. Twenty-four hours after listing, she underwent LT. The explanted liver pathology, 9 days after the initial liver biopsy, revealed complete liver necrosis (Figure 3). Her post-transplant course was notable for hepatic artery stenosis, for which she underwent surgical repair on day 5 post-LT. She also suffered from nonthrombotic heparin-induced thrombocytopenia and endoscopic retrograde cholangiopancreatography-treated anastomotic biliary stricture.

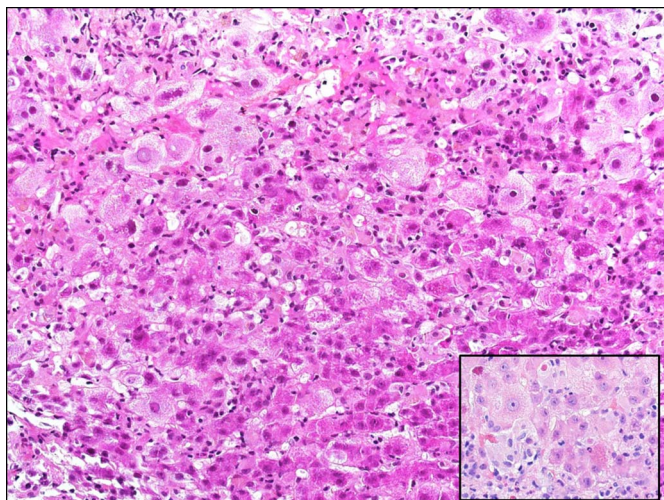


Figure 2. Liver biopsy analysis: Preliver transplantation liver biopsy on day 9 demonstrated both ballooned suffering and regenerating hepatocytes and lymphocytic infiltrates. Image on the right side shows multiple granulomas. There was no steatosis, no Mallory bodies, nor plasma cell inflammation.

She left the hospital 35 days after LT. The patient is now 2 years post-LT. Despite close nutritional follow-up and a trial of liraglutide, she gained 60 pounds since LT. Her liver enzymes remain normal, as all her other routine laboratory tests. The possibility of bariatric surgery is being considered, but the patient is reluctant.

DISCUSSION

Various claims have been made regarding GC, and many physiologic effects have been used to explain its therapeutic benefits. First, HCA use in rats resulted in decreased weight gain and food intake.³ Another study even showed HCA reduced serotonin uptake in mice cortex.⁴ Second, HCA has been found to inhibit adenosine triphosphate-citrate lyase, an enzyme involved in the first step of fatty acid synthesis.⁵ However, the results from human trials have been mixed.⁶ Several studies have been published, evaluating the efficacy and safety of GC and HCA. In a meta-analysis assessing HCA's efficacy as a weight loss supplement for human beings, a small effect favoring HCA over placebo was found, although every study included presented methodological weaknesses and most had significant heterogeneity.⁷

Some reports have come out questioning GC's safety. In a study, no adverse effects were observed at a dose of 2,800 mg/d, which has been suggested as a safe limit.⁸ Spermatogenesis toxicity, serotonin toxicity in combination with an antidepressant, hypomania, pancreatitis, and rhabdomyolysis, and hepatotoxicity have all been reported.^{6,9} Most cases developed hepatotoxicity over a couple weeks to a couple months after initiating the product. Reactions ranged from mild, symptomatic hepatitis to, in a few instances, acute liver failure requiring liver transplant. The daily amount of GC or HCA varied enormously.⁹

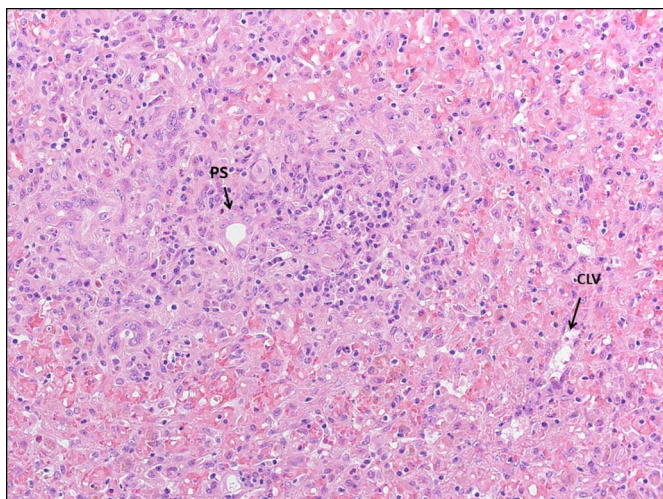


Figure 3. Liver biopsy analysis: Explanted liver on day 17 demonstrated complete necrosis and hepatocyte dropout with reticulin collapse. Hematoxylin and eosin stain, 203 magnification. CLV, central lobular vein; PS, portal space.

To date, only 3 published case reports describe GC-induced liver injury leading to LT.⁹ In 2 of these cases, such as with our patient, the daily dose of GC was approximately 2,000 mg, but with a much shorter exposition time to GC (2.5 weeks and 5 months). The clinical and biological evolution was similar: initial major cytolysis and normal international normalized ratio with acute liver injury developing 20 to 50 days post-admission.^{10,11} In the third case, the patient was taking a combination of GC, GTE, green coffee extract, African mango extract, guarana, and Whey protein. Those supplements were taken for 1 week, approximately 2 months before the clinical presentation. On admission, important cytolysis and international normalized ratio in the normal range were reported. A LT was performed 2 months after hospitalisation.¹² In our case, the patient seemed to stabilise and improve because her cytolysis was trending down, but she ultimately developed fulminant liver failure on day 12 (Figure 1).

The patient was also taking GTE, a known hepatotoxic supplement. However, according to current knowledge, our patient's GTE dosing was considered safe and has not been found to induce liver toxicity.^{12,13} Therefore, GC is probably the substance that lead to liver failure. Using both the Naranjo scale and Roussel Uclaf Causality Assessment Method Causality Assessment Model, a score of 6 was obtained, corresponding to a probable association between GC and liver injury.^{14,15}

Although the patient purchased her HDS in a naturopathy shop, she was never informed on warnings nor possible serious side effects. All these substances are certified by Canada's health authorities. The patient never consulted a primary care physician before GC intake. She undertook this weight loss regimen without being properly evaluated and offered alternative options, such as bariatric surgery.

In this study, we aim to show that GC, a frequently used HDS, can cause liver failure and ultimately lead to LT even after long-term use. It highlights a case of subacute liver failure and demonstrates the importance of considering a close and prolonged monitoring of patients in a tertiary LT centre when GC liver injury is suspected. Patients presenting with acute liver injury should always be questioned on their usage of natural health products and supplements.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. V. Ferreira is the article guarantor.

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Informed consent was obtained for this case report.

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