

CASE REPORT

Kombucha-Induced Massive Hepatic Necrosis: A Case Report and a Review of Literature



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Here, we present a case report of a healthy Asian woman with no past medical history presenting with severe acute liver injury associated with ingestion of kombucha. We also discuss the active ingredients in kombucha and the evidence behind its efficacy. This case emphasizes that although herbal teas have been proposed to have numerous health benefits, much is unknown about the amount that can be safely ingested.

Introduction

Kombucha is a black, green, or oolong tea fermented for approximately one week with sugar and a symbiotic culture of bacteria and yeast.¹ Kombucha originated in China in 220 B.C. and has recently become popular in the United States because of the growing trend of consuming herbal and dietary supplements in developed nations and its presumed anti-inflammatory, antihypertensive, and antineoplastic properties.^{1,2} Nevertheless, 2 systematic reviews found no studies showing kombucha-related health benefits.^{3,4} However, kombucha-related adverse events have been described including allergic reactions, mild hepatotoxicity, and lactic acidosis.^{5,6} Here, we present a case report of a healthy Asian woman with no past medical history presenting with severe acute liver injury associated with ingestion of kombucha.

Case Report

A 42-year-old previously healthy Vietnamese female with no significant past medical history was referred to our hospital for elevated liver chemistry test results performed as a part of an investigation of progressive fatigue that had started a few weeks earlier. She had been staying at home for 3 months prior to presentation because of the coronavirus pandemic. During this time, she drank 10–15 ounces of wine and 32 ounces of kombucha tea daily. On physical examination, her vital signs were normal. She was oriented to name, place, and time, and did not show any signs of confusion or encephalopathy. She had conjunctival icterus, while the rest of the physical examination was within

normal limits. Her liver panel was abnormal (Table 1), with a predominately hepatocellular injury pattern. Platelet count was 124 k/uL (reference range, 130–400 k/uL). Serology testing for hepatitis A, B, and C viruses was negative. Antinuclear antibody, antimitochondrial antibody, and antismooth muscle antibody were absent and the serum immunoglobulin G level was within the reference range. Serum acetaminophen, ethanol, and salicylate levels were undetectable. Serum ceruloplasmin level was 13 mg/dL (reference range, 17–54 mg/dL). Testing for SARS-CoV-2 and Ebstein Barr virus was negative and blood cultures showed no growth. Ultrasonography showed a coarse liver echotexture. Kombucha was discontinued and she was started on N-acetylcysteine for suspected drug-induced liver injury. She was transferred to a transplant center on the second day of presentation where N-acetylcysteine was continued, and she also received vitamin K. A liver biopsy showed massive liver necrosis, collapse, and hemorrhage (Figure). After several days, her liver chemistry test results and international normalized ratio improved slightly, and she was discharged after 6 days with outpatient follow-up. Her liver chemistry tests continued to improve with time (Table 1).

Discussion

Kombucha is tea (black, green, or oolong) fermented with sugar and symbiotic culture of bacteria and yeast for 7–10 days. In the United States, kombucha production is categorized as a specialized process and requires producers planning to sell the tea to submit a food safety plan to a regulatory authority. Sales of kombucha in the United States started with a single company in 1995 and have significantly grown since. It has been reported that yearly sales of kombucha in 2013–14 were \$122.7 million. It is the fastest

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Table 1. Liver Chemistry Tests Results

Serum analyte (reference range)	Day 1	Day 2	Day 6	Day 14	Day 60
ALT (0–55 U/L)	634	506	445	232	48
AST (5–34U/L)	581	436	346	198	64
AP (42–98 U/L)	146	111	111	116	100
Bilirubin, total (0.2–1.2 mg/dL)	4.6	3.3	2.8	2.2	1.0
INR (0.9–1.2)	1.8	2.0	1.7	1.3	1.2

ALT, alanine aminotransferase; AP, alkaline phosphatase; AST, aspartate aminotransferase; INR, international normalized ratio.

growing product in the functional beverage market and expected to grow to a \$1.8 billion industry by the end of 2020.⁷ Kombucha tea consumption can produce side effects such as allergic reactions, nausea, vomiting, headache, and even jaundice. Kombucha can also lead to serious adverse events.^{5,6} One patient with HIV developed severe lactic acidosis and renal failure after its consumption.⁵ Another patient developed a cholestatic hepatitis after kombucha consumption.⁶ In 1995, 2 patients from Iowa who consumed excessive amounts of kombucha developed an unexplained illness with lactic acidosis leading to death of one patient.⁸ Per the Food and Drug Administration, reported cases of side effects of kombucha tea consumption are related to preexisting medical conditions, overconsumption, and poor handling of fermented products.⁷ In our patient, overconsumption and concurrent alcohol consumption may have led to extensive liver necrosis. The liver injury in our patient was most likely related to kombucha because of the much higher serum levels of aspartate aminotransferase and alanine aminotransferase than would be expected from alcohol abuse alone. Moreover, the histopathology was not consistent with alcohol liver disease. In extreme cases of

alcohol hepatitis, liver cell necrosis can be diffuse, and the biopsy generally shows prominent ballooned hepatocytes and numerous intrahepatocellular Mallory-Denk bodies. The patient denied acetaminophen use and acetaminophen levels were undetectable on admission. Microscopically, acetaminophen toxicity most commonly demonstrates perivenular (zone 3) confluent necrosis which is often associated with steatosis of the remaining viable hepatocytes.

There is extensive literature on dietary/herbal supplements causing drug-induced liver injury.^{9–22} Although consumption of kombucha has been associated with liver injury ranging from jaundice to hepatitis, a case of extensive liver necrosis on histopathology has not been reported in the literature to our knowledge. However, usnic acid, a component of kombucha tea has been reported to cause hepatic necrosis in humans and experimental mice models.^{10,12–14,16} The mechanism of usnic acid causing liver necrosis was related to oxidative phosphorylation causing apoptosis and lysis of liver cells in animal models.¹³

Our patient was a relatively young, nonobese female with no risk factors for liver disease who developed greater than 95% liver cell necrosis on liver biopsy after excessive intake of kombucha for 3 months. In previously reported cases, patients developed adverse events after consuming kombucha in excessive amount for more than a couple weeks, although an HIV-infected patient developed lactic acidosis within 15 hours of consumption.⁶

Our patient is currently being followed at a transplant center and her liver chemistry tests continue to improve (Table 1). She has stopped consuming both alcohol and kombucha. She has not required liver transplantation. This case emphasizes that although herbal teas have been proposed to have numerous health benefits, much is unknown about the amount that can be safely ingested. Given previously reported adverse effects in addition to our findings, individuals should be cautious while consuming Kombucha and Kombucha-related products.

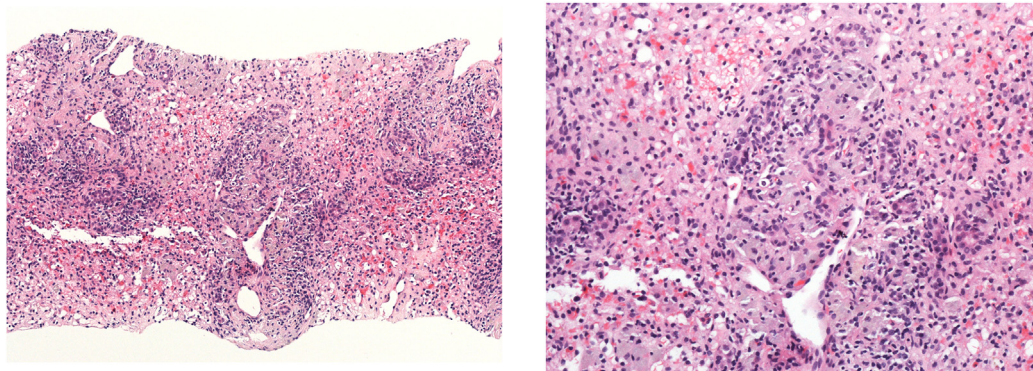


Figure. Microscopically, there is near-complete loss of hepatocytes with lobular collapse resulting in aberrant spacing of portal tracts. Liver cell drop out is accompanied by sinusoidal dilatation, congestion/hemorrhage, and inflammatory cells. Numerous lobular ceroid-laden macrophages are present individually and in aggregates. The closely approximated portal tracts demonstrate ductular proliferation and lymphoplasmacytic infiltrates with occasional eosinophils, rare neutrophils, and scattered ceroid-laden macrophages. Interlobular bile duct injury is present in the form of epithelial disarray (nuclear crowding, abnormal spacing of cholangiocytes) and infiltration by immune cells. Cholestasis is not a prominent feature (H&E, 100× and 200×).

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The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

Data Transparency Statement:

All data generated or analysed during this study are included in this published article (and its supplementary information files).

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