Hepatotoxicity Associated with the Use of White Flood, a Nutritional Supplement

by Stanley Martin Cohen, Elizabeth Heywood, Anjana Pillai, Joseph Ahn

Complementary and alternative medical (CAM) therapies are used by a large percentage of the US population. These agents are poorly regulated. Several of these agents have been associated with hepatotoxicity. We present the first case report of cholestatic hepatitis attributed to the use of White Flood, an herbal muscle-building supplement. A patient using this agent presented with significant cholestatic hepatitis. A full serologic and imaging evaluation failed to reveal any other likely sources. His liver tests normalized with removal of the suspected offending agent. Evidence to support White Flood as the causative agent include a correct temporal relationship, lack of other likely etiology after extensive evaluation, and resolution of symptoms after withdrawal of this agent. Clinicians should be aware that this supplement may have the potential to induce cholestatic hepatitis.

INTRODUCTION

Complementary and alternative medical (CAM) therapies include a variety of herbal and dietary supplements. The use of CAM therapy has been reported by a large percentage of the US population in a variety of survey studies. The use of herbal and dietary supplements has increased by 50% between 1997-2002. These agents are poorly regulated by drug administrations worldwide.

The US Congress defined the term “dietary supplement” in the Dietary Supplement Health and Education Act of 1994. Under this act, such supplements are categorized as food, rather than drugs. As such, the FDA must show that a supplement is unsafe before action may be taken. This is in contrast to drugs and medications which must be proven safe and effective before they are eligible for marketing.

The exact incidence of herbal-induced hepatotoxicity is unknown. Many patients do not report the use of these agents to their health-care providers. The United States Drug-Induced Liver Injury Network (DILIN) found that approximately 10% of drug-induced liver injury (DILI) could be attributed to the use of herbal and dietary supplements.8

Several herbal products have been implicated as causes of DILI. Recently, there have been reports of hepatotoxicity resulting from the use of herbal products for weight loss and muscle building, including Hydroxycut and Herbalife.9-16 These cases prompted the FDA in May of 2009 to release a warning recommending that consumers stop using Hydroxycut-containing products.17

White Flood™ (Controlled Labs, New Rochelle, New York) is an herbal muscle-building supplement which is touted as a pre-workout nitric oxide energy-enhancing drink.18 The product contains a variety of ingredients including calcium silicate, potassium gluconate, folic acid, selenium, citrulline, ornithine, carnitine tartrate, Carno-Syn ® beta-alanine, L-tyrosine, beet root, gamma-aminobutyric acid (GABA), glucuronolactone, caffeine, cocoa bean, Evodia rutaecarpa (a Chinese herbal agent), L-norvaline, sugar cane, vinpocetine (from the Vinca plant), zeaxanthin,
cryptoxanthin, lutein, Huperzia Serrata (used in Chinese herbal medications), malic acid, natural and artificial watermelon flavor, acesulfame potassium, and sucralose.

No previous reports of hepatotoxicity have been reported with the use of White Flood or its component ingredients. We report the first case of cholestatic hepatitis attributed to this muscle-building supplement.

Case Report

A 23 year old Caucasian male was referred to our liver center for evaluation of elevated bilirubin and jaundice. In February 2011, he began taking White Flood as an oral muscle building supplement when he began a weight-lifting program. He denied using any injection supplements or anabolic steroids. Between February 2011 and April 2011, he was able to gain approximately 20 pounds with significant increase in his muscle size, strength, and tone. In early May 2011, he began to notice dark urine, dysgeusia and anorexia. He stopped using the White Flood at that point. Within approximately one week, he noticed the onset of jaundice and pruritus. He had minimal relief with Benadryl and sought medical attention. He was placed on cholestyramine for symptomatic relief by his primary care physician, but due to progressively increasing bilirubin levels, he was referred to our institution.

The patient denied any prior history of hepatitis, liver disease or jaundice. There was no known family history of liver disease. The patient denied any GI bleeding, or confusion. Except for the White Flood, he had taken no other supplements, herbal agents, prescription medications, or illicit drugs prior to the onset of his symptoms. He denied any travel, toxic exposures, or ill contacts. Social history revealed no tobacco, alcohol, IV drug use, tattoos, or transfusions. Except for the jaundice and pruritus, his review of systems was unremarkable. Physical examination revealed grossly icteric sclera, but was otherwise normal. There was no hepatosplenomegaly, stigmata of chronic liver disease or asterixis.

Upon presentation, his CBC, electrolytes, INR and TSH were normal. His other pertinent chemistry trends are outlined in Table 1. Serologic evaluation was performed and revealed anti-nuclear antibody (ANA) negative, smooth muscle antibody (SMA) at 1:20, ceruloplasmin 47.9, anti-mitochondrial antibody (AMA) negative, hepatitis A IgM negative, hepatitis B surface antigen negative, hepatitis B core IgM negative, hepatitis C antibody negative and hepatitis C RNA negative.

An ultrasound revealed a normal examination except for a contracted gallbladder. The clinical impression was that the patient had developed an acute supplement-induced hepatitis due to the White Flood. Despite his rising bilirubin, he showed no evidence of impending liver failure. The decision was made to avoid liver biopsy, continue symptomatic treatment with the cholestyramine and follow serial labs. The patient was instructed to avoid the use of any medication or supplements except as prescribed by us.

Within 2 weeks of seeing us, he began to feel better (continued on page 48)

Discussion

The use of complementary and alternative medical and herbal dietary supplements has been growing in popularity over the last several years. This is likely due to the cost and adverse effects of prescription medications, as well as a perception that herbal remedies are safer and have no adverse effects. In fact, many case reports and case series are available demonstrating hepatotoxicity from a wide variety of herbal supplements. We present another case report of such an adverse event associated with the use of a new energy enhancing supplement used to promote muscle growth.

White Flood is marketed as an energy-enhancing drink which is touted to enhance the natural effects of weight lifting. The product contains a variety of ingredients including vitamins, minerals, and herbs.

To our knowledge, this is the first reported case of hepatotoxicity associated with the use of White Flood. Review of the published literature did not reveal any previous case reports of hepatotoxicity from this agent. In addition, none of the individual ingredients have previously been specifically implicated as causes of hepatotoxicity.

The exact mechanism of hepatotoxicity from this supplement is unclear. However, as noted above, there are multiple ingredients in this agent. It is possible that one of the ingredients or several of the ingredients interacting together could have contributed to the hepatotoxicity.

As with any case report of a suspected liver injury from a supplement, there can be no unequivocal, definitive guarantee that White Flood was the causative agent. However, given the lack of prior liver disease, no other potential medications or supplements, a reasonable temporal relationship of liver damage after the ingestion, negative viral, autoimmune, and metabolic serologies, and the resolution of symptoms after removal of the suspected offending agent, the etiology of his cholestatic hepatitis seems extremely likely to be the White Flood. Given a lack of evidence supporting that the patient was developing frank liver failure (i.e. normal INR and mental status), the decision was made to avoid a liver biopsy. Because there is no pathognomonic liver biopsy of drug-induced hepatotoxicity, the biopsy would only have provided supporting evidence of DILI rather than an absolute diagnosis anyway. Although it would be the gold standard to prove causation, a rechallenge with White Flood would not be ethical or safe.

Clinicians should be made aware of the possibility that White Flood, a supplement used to promote muscle and weight increase, may have the potential to induce cholestatic hepatitis. An increased effort to educate clinicians and patients about the potential risk of herbal-associated hepatotoxicity is warranted. Clinicians should continue to question patients with unexplained hepatitis or jaundice about the use of medications as well as herbal supplements.

References

17. Available at URL:http://www.fda.gov/ForConsumers/Consumer Updates/ucm152152.htm
18. Available at URL:http://www.whiteflood.com