

CLINICAL VIGNETTE

Herbal Tea Induced Liver Injury

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An otherwise well 37-year-old female presented to the office with concerns about bloating. She noted that for the past three weeks a progressively worsening sense of fatigue. She was an avid runner and was unable to train for her upcoming half-marathon. She complained of recurrent belching, bloating, along with progressive crampy abdominal pain. Previously, her bowel habits were once to twice daily; she noted she now had hard infrequent stools every other day. Her appetite was significantly reduced and noted a change in her sense of taste. She noted that her urine was bright yellow. There was not weight change noted during this time period.

One month prior the patient had been preparing for a half-marathon and started a Green Tea extract from a reputable tea franchise as a supplement for breakfast. Approximately three weeks into training, she reported the onset of abdominal bloating and stopped the tea. Soon after, she noted a darkening in her urine and yellowing of her eyes. There had been no recent travel and no ill contacts. Her alcohol consumption was limited to one to two beers per week, and she took no other medications over the counter or prescription.

Her examination was notable for diffusely hypoactive bowel sounds without rebound guarding or tenderness. Her scleral grounds were slightly icteric. The rest of her exam was unremarkable.

The patient was started on polyethylene glycol daily, and liver studies were obtained. The presumptive diagnosis of acute icteric hepatitis of unclear etiology. The results of her initial studies were remarkable for abnormal liver functions. Viral Hepatitis Antibodies were added to the specimen and were all negative.

The following day additional studies with a liver ultrasound were obtained. The liver ultrasound was notable for portal triad echogenicity with slightly hypoechoic liver parenchyma. This was nonspecific but potentially indicating acute hepatitis. The gallbladder was contracted and mildly thick-walled, likely exaggerated by decompression. No visible intraluminal stones or biliary ductal dilatation was observed.

Follow-up studies a week later showed increasing liver functions. Autoimmune studies showed a mildly positive anti-smooth muscle antibody, but otherwise normal tests.

The patient began to develop pruritus from her hyperbilirubinemia and so antihistamines were given. She was referred to Hepatology for further evaluation. Due to the historical features of the patient's case, as well as lack of hyper-gammaglobulinemia, it was felt that the most likely diagnosis was Herbal Induce Liver Injury: HILI and so only conservative monitoring was recommended. The patient's labs were followed, and over the course of the next month, her abdominal bloating/pain had subsided. Her liver functions had begun to return to normal.

Herbal Induced Liver Injury - HILI:

The use of herbal and dietary supplements (HDS) in the United States is estimated to be as high as 38%.^{1,2} A large percentage of patients using these complementary herbal therapies do not report them to their physician. In surveys, this is due most often to a perception that physicians don't need to know, don't ask, or that it is beyond the scope of care.³ The incidence of herbal induced hepatotoxicity is not known but have been documented in multiple case reports.⁴

Green tea extract (*Camellia sinensis*) has been reported to cause hepatotoxicity.⁵⁻⁷ The number of reported cases is low; however, there may be a predisposition in women with hepatocellular damage.⁸ It appears to be idiosyncratic. Like many other herbal supplements, Green Tea has been proposed to have anti-inflammatory properties, as well as weight loss and malignancy remedy.⁹ Because it is considered a food supplement, it is not monitored, and there is no uniformity in production or dosing of these products.

In 1994, Congress passed the Dietary Supplement Health and Education Act, in which herbal and dietary food supplements would not be directly regulated by the FDA. According to this act, the product cannot be adulterated or misbranded. Companies producing these products are directly responsible for safety evaluations and labeling of their products.¹⁰ In 2010, there was an attempt to further control which ingredients would be accepted as appropriate food supplements, as well as require companies to provide reports of both serious adverse events and the addition of adverse events. The Dietary Supplement Health and Education Act of 2010 would have "created potential civil liability for retailers that fail to obtain certification from their suppliers or manufacturers that the products they sell have met all upstream regulatory requirements, such as being on the accepted dietary ingredients list" created by the FDA.¹¹ This bill was introduced in 2010 by Congress but was not enacted.

In 2003, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) established the Drug-Induced Liver Injury Network (DILIN). The ultimate goal of this network is to improve the database of information on liver injury events due to both prescription and over-the-counter drugs as well as herbal products.¹² Cases such as the one described above have been submitted to this network.

There is little support in the scientific literature that green tea extracts do improve the quality of health with regular consumption. There is, however, a growing body of medical evidence supporting the possibility that serious side effects can occur. In the case described above, there was a direct correlation with the starting and subsequent holding of this substance and acute liver injury.

Although there is little scientific evidence of the effectiveness of green tea extracts to improve the quality of health of regular users, there is an increasing body of medical literature supporting the concern that they can cause serious side effects. With the increased usage of such products and paucity of control in the regulation of such substances, patients should be encouraged to report the use herbal and dietary supplements and monitored medically if used on a chronic basis.

Tables

Component Latest Ref Rng	6/13/16	6/20/16	6/22/16	6/30/16
Bilirubin, Total 0.1-1.2 mg/dL	6.3 (H)	11.3 (H)	12.3 (H)	10.1 (H)
Alkaline Phosphatase 37-113 U/L	133 (H)	160 (H)	160 (H)	128 (H)
AST (SGOT) 13-47 U/L	466 (H)	842 (H)	817 (H)	406 (H)
ALT (SGPT) 8-64 U/L	950 (H)	1227 (H)	1193 (H)	667 (H)

Component Latest Ref Rng	7/14/2016
Bilirubin, Total 0.1-1.2 mg/dL	3.5 (H)
Alkaline Phosphatase 37-113 U/L	96
AST (SGOT) 13-47 U/L	154 (H)
ALT (SGPT) 8-64 U/L	281 (H)

REFERENCES

- Nahin RL, Barnes PM, Stussman BJ, Bloom B.** Costs of complementary and alternative medicine (CAM) and frequency of visits to CAM practitioners: United States, 2007. *Natl Health Stat Report.* 2009 Jul 30;(18):1-14. PubMed PMID:19771719.
- Barnes PM, Bloom B, Nahin RL.** Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Report.* 2008 Dec 10;(12):1-23. PubMed PMID: 19361005.
- Eisenberg DM, Kessler RC, Van Rompay MI, Kaptchuk TJ, Wilkey SA, Appel S, Davis RB.** Perceptions about complementary therapies relative to conventional therapies among adults who use both: results from a national survey. *Ann Intern Med.* 2001 Sep 4;135(5):344-51. PubMed PMID: 11529698.
- Bunchorntavakul C, Reddy KR.** Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther.* 2013 Jan;37(1):3-17. doi:10.1111/apt.12109. Epub 2012 Nov 5. Review. PubMed PMID: 23121117.
- Molinari M, Watt KD, Kruszyna T, Nelson R, Walsh M, Huang WY, Nashan B, Peltekian K.** Acute liver failure induced by green tea extracts: case report and review of the literature. *Liver Transpl.* 2006 Dec;12(12):1892-5. PubMed PMID:17133573.
- Bonkovsky HL.** Hepatotoxicity associated with supplements containing Chinese green tea (*Camellia sinensis*). *Ann Intern Med.* 2006 Jan 3;144(1):68-71. Erratum in: *Ann Intern Med.* 2006 Mar 7;144(5):380. PubMed PMID: 16389263.
- Javaid A, Bonkovsky HL.** Hepatotoxicity due to extracts of Chinese green tea (*Camellia sinensis*): a growing concern. *J Hepatol.* 2006 Aug;45(2):334-5; author reply 335-6. Epub 2006 Jun 12. PubMed PMID: 16793166.
- Mazzanti G, Di Sotto A, Vitalone A.** Hepatotoxicity of green tea: an update. *Arch Toxicol.* 2015 Aug;89(8):1175-91. doi: 10.1007/s00204-015-1521-x. Epub 2015 May 16. Review. PubMed PMID: 25975988.
- Patel SS, Beer S, Kearney DL, Phillips G, Carter BA.** Green tea extract: a potential cause of acute liver failure. *World J Gastroenterol.* 2013 Aug 21;19(31):5174-7. doi: 10.3748/wjg.v19.i31.5174. PubMed PMID: 23964154; PubMed Central PMCID: PMC3746392.
- <http://www.fda.gov/Food/DietarySupplements/>
- <http://www.sedgwicklaw.com/the-dietary-supplement-safety-act-support-for-proposed-legislation-is-quietly-withdrawn-03-25-2010/>
- Fontana RJ, Watkins PB, Bonkovsky HL, Chalasani N, Davern T, Serrano J, Rochon J; DILIN Study Group.** Drug-Induced Liver Injury Network (DILIN) prospective study: rationale, design and conduct. *Drug Saf.* 2009;32(1):55-68. doi: 10.2165/00002018-200932010-00005. PubMed PMID: 19132805; PubMed Central PMCID: PMC3637941.