

# The Tale of An Ancient Herb: A Stress Reliever or A Liver Stressor

Minh Tran, MD<sup>2</sup>, Jaison John, MD<sup>2</sup>, Kian Abdul, DO<sup>1</sup>, Joseph Gosnell, MD<sup>3</sup>, Heather Stevenson, MD<sup>3</sup>, Kumar Pallav, MD<sup>2</sup>

<sup>1</sup> Department of Internal Medicine, <sup>2</sup> Division of Gastroenterology and Hepatology

<sup>3</sup> Department of Pathology, The University of Texas Medical Branch at Galveston



## Case Presentation

- A 59-year-old man with a past medical history of hepatitis B and C presented with nausea, vomiting, and RUQ abdominal pain for one day.
- The patient reported 2-week use of an herbal supplement called “Primal Male,” which contained Ashwagandha as the main ingredient.
- His physical exam was remarkable for temperature of 39.7 C and tachycardia (120 bpm).
- Laboratory studies were notable for elevated transaminases (Table 1) and INR level of 1.3.
- CBC, BMP, and creatinine kinase (CK) levels were normal.
- His drug test, alcohol level, and acetaminophen levels were unremarkable. The viral panel showed chronic hepatitis B and C.
- CT abdomen pelvis did not reveal acute abnormality.
- In the following days, he became more encephalopathic with elevating AST, ALT, and INR levels. He also became hypotensive and required fluid and midodrine. N-acetylcysteine treatment was initiated.
- He underwent a transjugular liver biopsy on day 5.
- Biopsy of the liver showed active lymphocytic hepatitis with moderate inflammation (primarily lymphocytes, abundant neutrophils, and occasional eosinophils) around the portal tract.
- He clinically improved on the sixth day with improving mentation and decreasing pain level.
- His vitals were more stable with improvement of his liver enzyme and INR levels.
- Diagnosis was favored to be drug-induced liver injury (DILI) from Ashwagandha use. He was counseled to avoid future use of “Primal Male” and other hepatotoxic products.
- One month later, his liver enzymes were in normal range.

## Images

	Day 1	Day 2	Day 3	Day 4	Day 9	Day 20	Day 26
AST (U/L)	2140	1428	761	722	94	62	41
ALT (U/L)	>2250	>3750	3617	3692	56	56	38
ALK PHOS (U/L)	132	151	147	175	73	73	64
Total bili mg/dL	4.5	4.3	3.5	2.5	1.1	0.7	0.3

Table 1. Trend of liver enzymes during the hospital stay and at follow-up

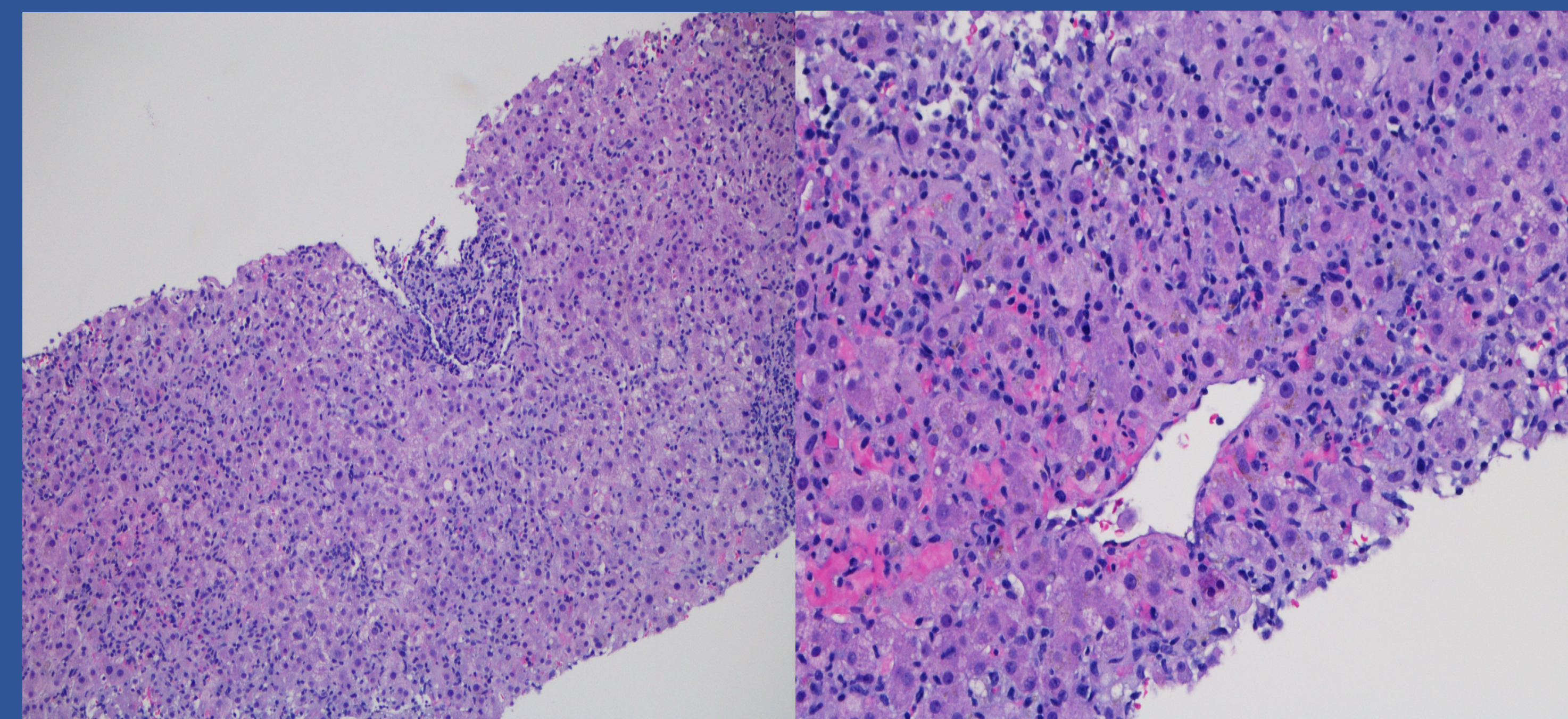


Figure 1. Biopsy of the liver reveals active lymphocytic hepatitis with moderate inflammation (primarily lymphocytes, abundant neutrophils, and occasional eosinophils) around the portal tract

## Discussion

- There are several causes of acute liver injury, including: viral infections, autoimmunity, ischemia, alcohol, and hepatotoxic drugs and substances.
- Drug-induced liver injury (DILI) is a less common form of liver injury but is a leading cause of acute liver failure in the United States.
- According to the Drug Induced Liver Injury Network (DILIN), antimicrobials are recognized as the major cause of DILI, followed by herbal and dietary supplements.
- Ashwagandha is an herbal extract from an evergreen shrub endemic to India and Southeast Asia.
- It is used worldwide for many purposes. In the US, it is commonly used to treat anxiety and stress.
- Ashwagandha-related liver injury is rare, with less than 10 cases reported in the literature.
- Although most cases showed liver enzyme elevation in either cholestatic or mixed pattern, our cases demonstrated a hepatocellular pattern with Ashwagandha-related liver injury.
- Latency period for liver injury is usually from 2 weeks to 10 months.
- It can take up to 3.5 months after medication cessation for the liver enzymes to normalize.

## Reference

1. Chalasani N, Bonkovsky HL, Fontana R, et al. Features and Outcomes of 899 Patients With Drug-Induced Liver Injury: The DILIN Prospective Study. *Gastroenterology*. 2015;148(7):1340-1352.e1347.
2. Björnsson HK, Björnsson ES, Avula B, et al. Ashwagandha-induced liver injury: A case series from Iceland and the US Drug-Induced Liver Injury Network. *Liver Int*. 2020;40(4):825-829.