# Hepatic Steatosis and Acute Liver Injury in Chronic Arsenic Exposure

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## Introduction

Arsenic toxicity may not be apparent on initial presentation given its myriad of effects across many body systems and its rarity in developed countries.

## Case Report

A 29-year-old woman with a past medical history of gastroesophageal reflux disease, irritable bowel syndrome, gastroparesis, post-traumatic stress disorder, obsessive-compulsive disorder, and generalized anxiety disorder presented with abdominal pain, nausea, and vomiting. Her recent medical history included seven months of progressive sensorimotor polyneuropathy, bowel and bladder incontinence, vision decline, skin rash and flaking, poor oral intake with 25% weight loss, and recent hospitalization for stress-induced cardiomyopathy and ventricular tachycardia.

She was found to have coagulopathy (INR 3.33), non-autoimmune hemolytic anemia (Hgb 5.4 g/dL, Hct 16.7%), and elevated transaminases (AST 959 U/L, ALT 274 U/L), alkaline phosphatase (1,691 U/L), gamma-glutamyl transferase (911 U/L), total bilirubin (13.2 mg/dL) and direct bilirubin (11.5 mg/dL), and serum ammonia (207 µmol/L). She developed encephalopathy with rising ammonia requiring scavenger therapy. She underwent diagnostic evaluation for alcohol-related, metabolic, inflammatory, vascular, and toxicity-related causes of liver disease.

Liver biopsy revealed non-cirrhotic portal fibrosis, severe and mostly macrovesicular steatosis, ductular proliferation, canalicular cholestasis, mild parenchymal iron deposition, negative copper stain, and normal quantitative copper analysis. Initial labs revealed high urine orotic acid and low serum citrulline, so empiric treatment for ornithine transcarbamylase deficiency was initially given. Whole exome sequencing was subsequently negative.

Urine and serum heavy metal testing were negative. However, arsenic was highly elevated in hair (25.2 mcg/g, ref <1.0) and nail (6.1 mcg/g, ref <1.0) samples, most consistent with chronic arsenic exposure.

## Pathology

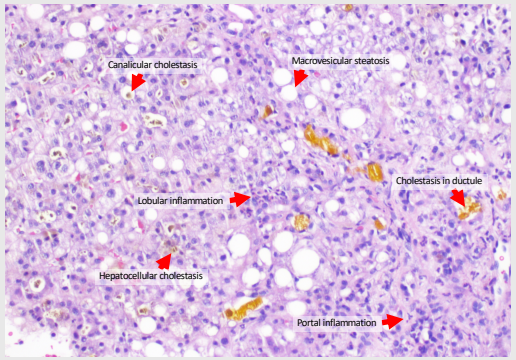


Figure 1. H&E slide of liver biopsy showing canalicular and ductular cholestasis, hepatocellular cholestasis, macrovesicular steatosis, lobular inflammation, and portal inflammation, 200x.

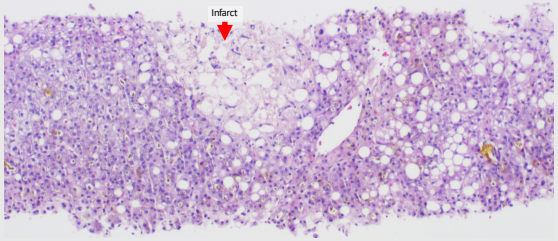


Figure 2. H&E slide of liver biopsy demonstrating a portion of infarct, 100x.

***We thank Dr. Won Jae Huh (Department of Pathology, Yale School of Medicine) for contributing these images.***

## Discussion

We present a case of hepatic steatosis and acute liver injury in chronic arsenic exposure. Research in mice and zebrafish has demonstrated an association between arsenic toxicity and hepatic steatosis.[1] Chronic arsenic exposure in humans has been linked to elevated liver chemistries, non-cirrhotic portal fibrosis, and increased risk of non-alcoholic fatty liver disease.[1,2] In this patient, arsenic exposure may explain the hepatic steatosis, either directly or indirectly via rapid weight loss. Arsenic toxicity also explains the hepatic injury and portal fibrosis, encephalopathy, polyneuropathy, hair loss, skin changes, ventricular arrhythmia, and anemia.

## Conclusion

Recognizing metal toxicity as a potential cause of liver injury was crucial, as arsenic testing dramatically altered our course of management and patient care. Identification of appropriate sampling material for arsenic testing in suspected chronic exposure was an important diagnostic step, given the shorter half-life of arsenic in serum and urine compared to hair and nails.[3] Managing symptomatic acute arsenic poisoning can include chelation, whole-bowel irrigation depending on radiopaque visualization, administration of activated charcoal with airway protection, nasogastric suction, fluid administration, and decontamination of skin and hair by soap and water. On the other hand, treatment of chronic arsenic toxicity focuses on identification and removal of the exposure source, decontamination, and supportive management.[4] Our patient's condition improved with hospitalization for supportive care.

## References

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