



Case Report

Therapeutic-Dose Acetaminophen-Associated Liver Injury Following a Total Dose of 7 Grams Over Five Days: A Case Report

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***Corresponding author:** Asim Rana, Psychiatry, Delaware Psychiatric Center, 103 John Robert Thomas Dr, Exton, Pennsylvania, USA**Citation:** Rana A. (2026). Therapeutic-Dose Acetaminophen-Associated Liver Injury Following a Total Dose of 7 Grams Over Five Days: A Case Report. Ann Case Report. 11: 2653. DOI: 10.29011/2574-7754.102653**Received:** 09 July 2026; **Accepted:** 15 July 2026; **Published:** 17 July 2026**Abstract**

Acetaminophen is considered safe when administered within recommended therapeutic doses. Hepatotoxicity is classically associated with acute overdose; however, rare cases have been reported following therapeutic dosing in susceptible individuals. We describe a patient who developed significant transaminitis after receiving a cumulative acetaminophen dose of only 7 grams over five days. Extensive evaluation excluded other common causes of acute liver injury.

Liver enzymes improved following discontinuation of acetaminophen and supportive management. This case highlights that therapeutic-dose acetaminophen may rarely cause liver injury in predisposed patients and emphasizes the importance of maintaining a broad differential diagnosis when evaluating unexplained elevations in liver function tests.

Introduction

Acetaminophen is one of the most frequently used analgesic and antipyretic medications worldwide. Recommended adult dosing generally should not exceed 3-4 grams daily. Hepatotoxicity typically occurs after ingestion of supratherapeutic doses, resulting in depletion of hepatic glutathione and accumulation of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI). Rarely, liver injury has been described despite therapeutic dosing, particularly among patients with malnutrition, prolonged fasting, chronic alcohol use, critical illness, low body weight, or concomitant medications that increase CYP2E1 activity.

We report a case of significant transaminitis after administration of only 7 grams of acetaminophen over five days.

Case Presentation

A 73-year-old female with a history of chronic lower back pain, hx of HTN who was admitted for a neurosurgical procedure. Hospital medicine was consulted for medication management.

During hospitalization, the patient received scheduled acetaminophen for pain, totaling approximately 7 grams over five days (average daily dose 1.4 grams).

Baseline liver function tests were normal. On hospital day 3 routine laboratory testing demonstrated elevations in hepatic aminotransferases. Aspartate aminotransferase (AST) increased from 70 to 578 U/L, while alanine aminotransferase (ALT) rose from 36 to 467 U/L.

Total bilirubin was 0.6 mg/dL, alkaline phosphatase was 171 U/L, and INR was 1.18. The patient denied excessive acetaminophen use prior to admission. Review of medication administration records confirmed the cumulative inpatient dose. Viral hepatitis testing, including hepatitis A, B, and C serologies, was negative. Autoimmune markers, including antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and antimitochondrial antibody (AMA), were unrevealing. Right upper quadrant ultrasound demonstrated a normal liver and no biliary obstruction. There was no evidence of hypotension or ischemic hepatitis during

hospitalization. Additional potentially hepatotoxic medications were reviewed and considered less likely contributors.

Acetaminophen was discontinued following recognition of worsening liver enzymes. Given concern for possible therapeutic-dose acetaminophen-induced liver injury, the patient was managed with supportive care, and N-acetylcysteine was administered. Serial laboratory testing demonstrated gradual improvement in AST and ALT over the following several days.

The patient remained clinically stable without evidence of acute liver failure and was discharged with outpatient hepatology follow-up [1-4].

Discussion

Acetaminophen-induced hepatotoxicity is among the most common causes of acute liver failure in the United States, but nearly all cases involve overdose or repeated supratherapeutic ingestion. Therapeutic-dose liver injury remains uncommon and is thought to occur primarily in susceptible patients.

Several mechanisms have been proposed. Malnutrition and prolonged fasting reduce hepatic glutathione stores, increasing susceptibility to NAPQI-mediated hepatocyte injury. Chronic alcohol use induces CYP2E1, increasing toxic metabolite production while simultaneously reducing glutathione availability. Critical illness, systemic inflammation, low body weight, and certain medications may further increase risk.

Although causality cannot always be definitively established, our patient's temporal relationship between acetaminophen exposure, exclusion of alternative etiologies, and subsequent improvement following drug discontinuation supports therapeutic-dose acetaminophen-associated liver injury. Application of a structured causality assessment tool such as the Roussel Uclaf Causality Assessment Method (RUCAM) may strengthen this association.

Clinicians should recognize that therapeutic acetaminophen dosing does not entirely eliminate the possibility of hepatotoxicity, particularly in high-risk populations. Early recognition, prompt discontinuation of the medication, and consideration of N-acetylcysteine in selected patients may improve outcomes.

Conclusion

This case illustrates that significant liver enzyme elevation may rarely occur after therapeutic acetaminophen administration, even with a cumulative dose of only 7 grams over five days. Clinicians should maintain awareness of this uncommon presentation, especially in patients with risk factors for impaired acetaminophen metabolism or glutathione depletion. Careful medication review and exclusion of competing etiologies remain essential before attributing liver injury to therapeutic-dose acetaminophen.

Learning Points

- Therapeutic-dose acetaminophen hepatotoxicity is uncommon but well described.
- Predisposing factors include malnutrition, fasting, alcohol use, critical illness, and low body weight.
- Alternative causes of acute liver injury should be systematically excluded.
- Early discontinuation of acetaminophen and consideration of N-acetylcysteine may be appropriate when drug-induced liver injury is suspected.

References

1. Chalasani NP, Maddur HP, Russo MW, Wong RJ, Reddy KR, et al. (2021). ACG Clinical Guideline: Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. *Am J Gastroenterol*. 116: 878-898.
2. Lee WM. Acetaminophen Toxicity: Clinical Practice. *N Engl J Med*.
3. Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, et al. (2005). Acetaminophen-induced acute liver failure. *Hepatology*. 42: 1364-1372.
4. Rumack BH. (2002). Acetaminophen hepatotoxicity: the first 35 years. *J Toxicol Clin Toxicol*. 40: 3-20.