A Case of Low-Dose Ceftriaxone-Induced Liver Injury in an Adult

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ABSTRACT

Introduction: Ceftriaxone is a commonly used third-generation cephalosporin; however, rare cases of drug-induced liver injury have been reported. Atypical hepatic responses in adults at standard doses warrant clinical attention.

Case Presentation: A 48-year-old woman with a history of nephrolithiasis, cholecystectomy, and Roux-en-Y gastric bypass presented with abdominal pain. After receiving a 1-g dose of ceftriaxone, she developed significant liver enzyme elevation aspartate aminotransferase 725 U/L, alanine aminotransferase 455 U/L, and alkaline phosphatase 319 U/L). Evaluation for viral and autoimmune causes was negative. A chart review revealed prior similar episodes linked to ceftriaxone use.

Discussion: Ceftriaxone-induced hepatitis is more frequently reported in pediatric populations and typically associated with higher doses. Adult cases with such marked liver function test elevations are rarely documented.

Conclusions: This case highlights an unusual adult presentation of ceftriaxone-induced hepatitis. Clinicians should consider ceftriaxone as a potential cause of liver injury, even at standard doses, particularly in patients with a history of adverse reactions.

INTRODUCTION

Drug-induced liver injury (DILI) is a significant adverse reaction to antibiotic therapy, accounting for more than 50% of acute liver failure cases.[1] DILI is a complex diagnostic challenge because it mimics various hepatic disorders. Among antibiotics, ceftriaxone—a third-generation cephalosporin—is favored for its efficacy against a broad range of bacterial infections. Although ceftriaxone is generally well tolerated, it has been linked to liver toxicity, ranging from mild, transient enzyme elevations to severe hepatocellular injury and acute liver failure.[2]

Ceftriaxone is excreted in both the urine and bile, with hepatic excretion playing a significant role in its metabolism. The drug's hepatic processing involves the biliary system, where alterations can lead to cholestasis and biliary sludge, factors implicated in hepatic injury.[3] Moreover, ceftriaxone's high plasma protein binding and its ability to displace bilirubin from albumin may exacerbate liver stress, particularly in patients predisposed to bilirubin accumulation.[4]

The pathophysiology of ceftriaxone-induced DILI is complex and not fully understood but is thought to involve direct hepatocyte toxicity and immune-mediated mechanisms.[5] Given that DILI is often idiosyncratic and not dose-related, it poses significant diagnostic challenges. Ceftriaxone-induced liver injury may present as an asymptomatic elevation in liver enzymes; severe cases can manifest with jaundice, coagulopathy, and hepatic encephalopathy. Diagnosis relies on excluding other causes of hepatic dysfunction through a detailed drug history, serologic testing, imaging, and, in some cases, liver biopsy.[6]

This report discusses the case of a 48-year-old female with a history of recurrent urological issues and multiple abdominal surgeries who exhibited significant liver enzyme elevations following ceftriaxone administration.

CASE PRESENTATION

A 48-year-old woman with a history of recurrent nephrolithiasis requiring stent placement and stone extraction, status post-cholecystectomy and Roux-en-Y gastric bypass, presented to the emer-

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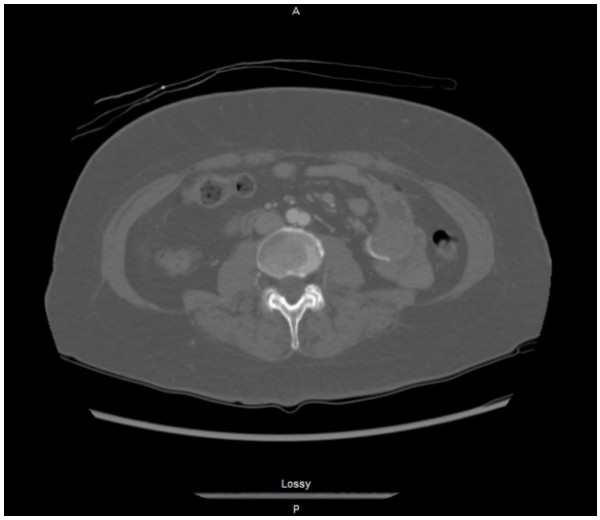
Table. Liver Function Test Trends Over Hospitalization

Laboratory Test	Day 1	Day 2	Day 3	Day 8	Reference Range
Aspartate aminotransferase (U/L)	725	537	187	53	10–40
Alanine aminotransferase (U/L)	455	671	436	123	7–56
Alkaline phosphatase (U/L)	319	343	287	165	44–147

Figure. Axial Contrast-enhanced Computed Tomography of the Abdomen on the Day of Admission Demonstrating a Short Segment Intussusception at the Jejunojejunal Anastomosis



gency department (ED) with abdominal pain. Initial computed tomography (CT) showed focal intussusception at the jejunojejunal anastomosis without associated small bowel obstruction. A follow-up CT scan showed resolution of the intussusception without intervention, confirming its transient nature. Given her symptoms, urinalysis was ordered on admission; results revealed nitrites and bacteria, prompting administration of 1 g of ceftriaxone.

On the same day, liver function tests (LFTs) showed aspartate aminotransferase (AST) 725 U/L, alanine aminotransferase (ALT) 455 U/L, and alkaline phosphatase (ALP) 319 U/L. Because of these elevations and a 2-day history of right upper quadrant and right lower quadrant pain radiating to the back, along with subjective fevers and chills, an extensive chronic liver disease workup was initiated. Results were unremarkable for alpha-1 antitrypsin, mitochondrial antibody IgG, ceruloplasmin, antinuclear antibody (ANA), hepatitis B core antibody, hepatitis B core antibody (IgG and IgM), hepatitis B surface antibody, hepatitis E antibody IgG, and hepatitis C antibody. Magnetic resonance cholangiopancreatography (MRCP) reported no focal liver lesions, normal liver size, patent hepatic and portal veins, and no biliary duct dilation. Infectious, autoimmune, and structural hepatic disorders were effectively ruled out, strengthening the case for ceftriaxone-induced liver injury as the most plausible diagnosis.

A chart review revealed multiple hospitalizations since 2019. Each visit involved ceftriaxone administration (1 g or 2 g) due to recurrent urinary tract infections (UTIs) or pyelonephritis, followed by transiently elevated liver enzymes that normalized within weeks after ceftriaxone cessation. Given the pattern and lack of alternative explanations, ceftriaxone was implicated as the likely cause. The patient's LFTs improved over 48 hours, and she was discharged with outpatient follow-up (Figure).

The transient nature of the intussusception, in the absence of bowel obstruction or ischemia, suggested it was an incidental finding. Subsequent imaging confirmed resolution without intervention, supporting an alternative etiology for the patient's presentation. Serial LFTs during hospitalization are summarized in the Table, demonstrating a progressive decline in hepatic enzymes following cessation of ceftriaxone. AST levels decreased from 725 U/L on admission to 53 U/L by day 8, while ALT declined from a peak of 671 U/L on day 2 to 123 U/L by day 8. ALP also trended downward, decreasing from 343 U/L on day 2 to 165 U/L by day 8. The decline in transaminases without additional therapeutic intervention supports ceftriaxone as the likely causative agent. Total bilirubin remained within the normal range throughout hospitalization. The international normalized ratio (INR) was 1.0 on day 3, and creatinine levels remained stable (0.52-1.07 mg/dL). Hepatitis B/C serologies, ANA, and ceruloplasmin were negative at admission, further supporting the exclusion of alternative etiologies.

DISCUSSION

Ceftriaxone-induced liver injury is a rare but clinically significant adverse drug reaction that necessitates careful consideration, particularly in patients with recurrent antibiotic exposure. While DILI is often a diagnosis of exclusion, certain characteristics of ceftriaxone-induced hepatotoxicity set it apart from other drug-related liver injuries. The underlying mechanism has been linked to both direct hepatocyte toxicity and immune-mediated responses.[6] This dual mechanism may explain why some patients exhibit transient enzyme elevations while others, as in this case, experience pronounced hepatocellular damage.

One distinguishing feature of this case is the hepatocellular pattern of liver injury, which contrasts with the more commonly reported cholestatic, or mixed-type injury associated with ceftriaxone. Previous studies have documented that ceftriaxone-induced hepatotoxicity is often associated with biliary pseudolithiasis and sludge formation, leading to a predominantly cholestatic injury pattern.[7] In a study by Yoshida et al, CT imaging of patients receiving ceftriaxone revealed sludge formation in the biliary tree, which correlated with liver function abnormalities.[7] However,

imaging in our patient showed no evidence of biliary obstruction or sludge, suggesting that ceftriaxone may cause hepatotoxicity through alternative pathways.

In patients with altered gastrointestinal anatomy, such as those who have undergone Roux-en-Y gastric bypass, ascending cholangitis must be considered in the differential diagnosis for liver enzyme abnormalities. The patient's symptoms of abdominal pain, subjective fevers, and chills raise concern for this; however, several findings argue against cholangitis in this case. The patient did not have leukocytosis, hypotension, or jaundice; her bilirubin and INR remained within normal limits, and imaging showed no biliary dilatation or sludge. While MRCP may have limited sensitivity in detecting biliary abnormalities in patients with Roux-en-Y anatomy,[8] the clinical and laboratory data in this case did not support acute infectious cholangitis.

Notably, our patient developed significant transaminitis following a single 1-g dose. While high-dose ceftriaxone (≥ 4 g/day) has been more frequently associated with liver injury,[9] our case highlights an atypical reaction occurring at a standard therapeutic dose, suggesting an idiosyncratic response. A recent study by Hayahide et al found that higher doses increased the risk of liver enzyme elevations, particularly in patients with impaired hepatic reserve.[1]

While ischemic hepatitis due to sepsis or shock can lead to acute transaminase elevations, our patient did not consistently demonstrate clinical or laboratory evidence of systemic hypoperfusion. In prior ED visits, liver enzyme elevations were observed shortly after ceftriaxone administration despite the absence of overt hypotension or significant leukocytosis (eg, blood pressure 155/80 mm Hg, heart rate 130 beat per minute, temperature 101 °F, and white blood cell count 6000–10 000/μL followed by AST 185 U/L, ALT 254 U/L, and ALP 190 U/L within 24 hours). The reproducibility of enzyme elevations in close temporal relation to ceftriaxone use without consistent signs of systemic illness makes ischemic hepatitis less likely. Coupled with the exclusion of other hepatic etiologies, this pattern supports a diagnosis of drug-induced liver injury. These observations align with prior reports highlighting the idiosyncratic nature of antibiotic-related hepatotoxicity, including ceftriaxone.[4]

Age and sex also have been identified as potential risk factors for DILI, with older patients and females being at greater risk.[5] Lucena et al found that older patients were more likely to develop cholestatic liver injury, while younger patients more frequently exhibited hepatocellular injury patterns.[5] Our patient's profile aligns with this trend, underscoring the importance of patient-specific factors in predicting susceptibility.

The prognosis of ceftriaxone-induced liver injury varies widely. In most cases, liver function abnormalities resolve following drug discontinuation, as observed in our patient. However, severe DILI cases can progress to acute liver failure requiring transplantation.[10] Reuben et al reported that antibiotics, including cephalosporins, were among the leading culprits of acute liver failure.[10] Although our patient experienced full recovery within weeks, the potential for severe outcomes highlights the need for vigilance in monitoring hepatic function during ceftriaxone therapy, even at low doses.

Additionally, the rapid improvement in liver enzyme levels over a few days is atypical for DILI, which more commonly resolves over weeks.[1,5] However, previous episodes in this patient followed a similar pattern of transient transaminitis that normalized without intervention after ceftriaxone cessation. The reproducibility of these episodes across multiple hospitalizations lends credence to an idiosyncratic hepatotoxic response to ceftriaxone. While rechallenge testing is not ethically justifiable, a future episode with baseline normal LFTs followed by ceftriaxone administration and subsequent enzyme spikes could offer stronger causal evidence.

Labeling ceftriaxone as an allergen must also be weighed carefully. Ceftriaxone is a cornerstone in managing several infections, and its exclusion may lead to the use of broader-spectrum or less effective agents, such as vancomycin or fluoroquinolones, which carry additional risks.[10] Documentation of suspected ceftriaxone-induced hepatotoxicity should include details on the severity and reversibility of prior reactions to inform future prescribing decisions. Inappropriate or unverified allergy labeling has been linked to worse antimicrobial stewardship outcomes and higher rates of resistant infections.[11]

Finally, consultation with a bariatric surgeon not involved in the patient's care could provide further insight into whether the patient's Roux-en-Y anatomy could predispose her to atypical biliary complications. While such input was not obtained during this case, it may represent a valuable addition to future evaluations of similar presentations.

CONLCUSIONS

This case underscores the importance of considering drug-induced liver injury, even at standard doses of commonly used antibiotics like ceftriaxone. In patients with Roux-en-Y anatomy, alternative causes such as ascending cholangitis must be considered; however, the reproducible elevation and subsequent normalization of liver enzymes support a diagnosis of idiosyncratic ceftriaxone-induced liver injury. These recurring episodes emphasize that a thorough review of patient history is vital to identifying DILI risk factors. Clinicians should maintain a high index of suspicion for antibiotic-induced hepatotoxicity and carefully weigh the risks of prematurely documenting antibiotic allergy labels, which may compromise future care. Broader multidisciplinary evaluation, including surgical expertise, may further improve diagnostic accuracy in complex postoperative patients.

Financial disclosures: None declared.

Funding/support: None declared.

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