

A Case of Abnormal Liver Function Tests in a Patient Receiving Total Parenteral Nutrition

Journal of Investigative Medicine High Impact Case Reports
Volume 11: 1–4
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DOI: 10.1177/23247096231181969
journals.sagepub.com/home/hic



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Abstract

Hepatic dysfunction is prevalent in patients receiving total parenteral nutrition (TPN), resulting from steatosis, cholestasis, and cholecystitis. Regular assessments and monitoring of TPN patients are essential, even for clinically stable patients on long-term TPN. Furthermore, it is crucial to establish a differential diagnosis for hepatic dysfunction and investigate for other possible causes of elevated liver enzymes and underlying liver conditions. We present the case of a 56-year-old female patient with severe protein-calorie malnutrition on TPN, who exhibited significantly elevated liver enzymes during the routine periodic assessment. Subsequent investigation revealed that the patient had been taking traditional Chinese herbal medications concurrently with TPN. After discontinuing the herbal medications, the patient's liver enzymes returned to normal levels within 3 weeks.

Keywords

parenteral nutrition, hepatotoxicity, herbal medication, endocrinology

Introduction

Total parenteral nutrition (TPN) involves the intravenous administration of nutrition, which is often necessary when patients cannot obtain adequate nutrition through enteral feeding. Total parenteral nutrition is recommended for patients with various conditions related to intestinal insufficiency resulting from diminished intestinal length or impaired functionality. It is also recommended for individuals who are malnourished as a result of critical illness or are unable to tolerate enteral nutrition. In clinical practice, patients on long-term TPN are frequently monitored for potential adverse events associated with TPN administration. For clinically stable patients receiving long-term TPN, regular assessments of body weight, hydration status, fluid calories and energy balance, and laboratory examination, including liver function tests, should be conducted at scheduled intervals (e.g., every 3–6 months) following established guidelines.^{1,2} In this article, we present the case of a 56-year-old female who exhibited a significant elevation in liver enzymes while undergoing TPN therapy.

Case Report

A 56-year-old woman presented to the outpatient department of our hospital, experiencing nausea, vomiting, and

abdominal discomfort. She underwent right lower and middle lobe resection for lung cancer 7 months prior, and was diagnosed with superior mesenteric artery syndrome, for which she had undergone lysis of the ligament of Treitz and duodenal jejunostomy 4 months prior. Her weight decreased from 55.8 kg (body mass index [BMI] 20 kg/m²) before lung cancer surgery to 39 kg (BMI 14 kg/m²). Due to persistent inadequate enteral intake following the surgery, TPN was initiated, and home TPN was maintained after discharge. The patient was initially prescribed home TPN at a volume and rate of 1440 mL/hour for 12 hours daily. Her TPN order provided 1290 kcal per day, based on estimated calorie requirements of 30 to 35 kcal/kg, and her feeding weight was 39.4 kg. Her TPN also contained 35 g of lipid emulsion,

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Received March 30, 2023. Revised May 15, 2023. Accepted May 29, 2023.

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consisting of soybean oil, medium-chain triglyceride oil, olive oil, and fish oil, administered 7 days per week. After discharge, she was monitored weekly for body weight, hydration status, fluid calories and energy balance, and laboratory tests, including complete blood count, electrolytes, liver, and kidney function at scheduled outpatient visits for a month. Following stabilization, she continued to receive monthly follow-up care. While undergoing TPN treatment, her appetite and body weight both improved, leading to a gradual tapering of TPN. Ultimately, she was able to receive TPN 3 times per week at the same volume.

After 4 months of TPN therapy, the patient visited the outpatient department for periodic monitoring. Contrary to previous visits, she complained of decreased appetite along with nausea, vomiting, and abdominal discomfort. Routine blood tests revealed that aspartate aminotransferase (AST) and alanine transaminase (ALT) levels, which had been within the normal range in previous tests, had acutely increased to 444 and 418 U/L, respectively. Total bilirubin level was normal (0.9 mg/dL; reference range = 0.2-1.2 mg/dL), and alkaline phosphatase (ALP) was mildly increased (196 U/L; reference range = 35-104 U/L). She had no history of liver disease or alcohol consumption, and her physical examination was unremarkable. She was taking omeprazole, dronabinol, megestrol, and ondansetron, and there were no changes in the type or dosage of medication within 3 months before the event. At the time, she was reducing the frequency and volume of TPN, suggesting that TPN was unlikely to be the cause of the sudden increase in her liver enzymes. During regular monitoring while the patient was receiving TPN, abnormal test results were discovered, prompting a repeat blood test 2 days later. The results showed elevated levels of total bilirubin (0.8 mg/dL), AST (117 U/L), ALT (434 U/L), and ALP (239 U/L). After considering the improving pattern in the AST, the patient's somewhat improved symptoms, unremarkable physical examination, and the recent abdomen computed tomography results that indicated no hepatobiliary disease, we suspected alternative medicine supplements-induced hepatotoxicity and refrained from conducting any further tests at that time. Through patient interviews and a comprehensive review of her medical history, it was discovered that she had started taking a mix of Chinese herbal supplements 2 weeks prior. The patient's regimen of Chinese herbal medication included *Trichosanthes kirilowii*, *Atractylodes japonica*, *Glycyrrhiza uralensis*, *Platycodon grandiflorus*, *Areca catechu*, *Codonopsis pilosula*, *Foeniculum vulgare*, *Zingiber officinale*, *Citrus unshiu* or *Citrus reticulata*, *Cannabis sativa*, *Perilla frutescens*, *Wolfiporia extensa*, *Hematite*, *Pinellia ternata*, *Elettaria cardamomum*, *Aucklandia lappa*, *Aconitum carmichaelii*, *Senna obtusifolia*, and *Rheum palmatum* (Figure 1). However, due to worsening symptoms, such as decreased appetite and nausea, she discontinued the supplements 3 days prior to her clinic visits (Figure 1). She denied any other alternative medication. The patient was advised to discontinue the use of herbal medications, and TPN was

continued. In the follow-up examination after 2 weeks, both AST and ALT had returned to within the normal range. The patient's nutritional status further improved with adequate enteral intake, and she was eventually weaned from TPN after 2 months.

Discussion

Total parenteral nutrition represents a mode of nutrition administered intravenously to patients incapable of acquiring adequate nutrition via the digestive tract.^{2,3} Although TPN serves as a life-saving treatment for numerous patients, it can also manifest several side effects, such as liver failure.⁴ Hepatic dysfunction is prevalent among TPN recipients, presenting various forms, including steatosis, cholestasis, and cholecystitis. Two risk factors associated with hepatic dysfunction during TPN are the duration of TPN administration and overfeeding. Overfeeding transpires when patients receive excessive energy from macronutrients, predominantly carbohydrates or lipids.⁵ Fatty acid deficiencies, which may induce liver alterations, can arise when TPN formulations lack lipids. Conversely, TPN containing excessive lipids and soybean-based lipid emulsions rich in linoleic acid have been correlated with liver injury. To mitigate the risk of liver injury during TPN therapy, maintaining a lipid dosage of 1 g/kg/day and employing lipids composed of a blend of soybean oil, medium-chain triglycerides, and long-chain triglycerides may prove beneficial.⁶

In TPN-dependent patients presenting with abnormal liver enzymes, TPN is often considered the initial culprit. Nevertheless, when TPN can be ruled out, a comprehensive examination of other potential causes is warranted. Diagnosing hepatic dysfunction during TPN primarily relies on exclusion. This includes considering various risk factors commonly observed in hospitalized TPN patients, such as critical illness, postsurgery recovery, septic shock, hypoxia, hepatobiliary tract dysfunction, and the use of hepatotoxic medications. Given the multifactorial causes of hepatic dysfunction, the differential diagnosis and work-up encompass evaluations for other possible triggers of elevated liver enzymes, pre-existing liver disease, and medication or supplementations. In the process of determining hepatic dysfunction diagnoses in TPN patients, the pattern of liver chemistry abnormalities provides useful information for conducting additional tests or differential diagnoses. When there is a severe elevation in transaminases, particularly above 1000 IU/mL, the likelihood of diagnosing conditions, such as viral hepatitis, ischemic hepatitis, or drug-induced hepatic injury significantly outweighs other potential diagnoses. Conversely, when transaminases exhibit a moderate elevation, that is, less than 1000 IU/mL, a substantial increase in ALP and bilirubin levels can provide further clues. These changes might suggest the presence of cholestasis, indicating potential factors like sepsis, biliary causes, or medications. The degree of bilirubin elevation and fractionation may also

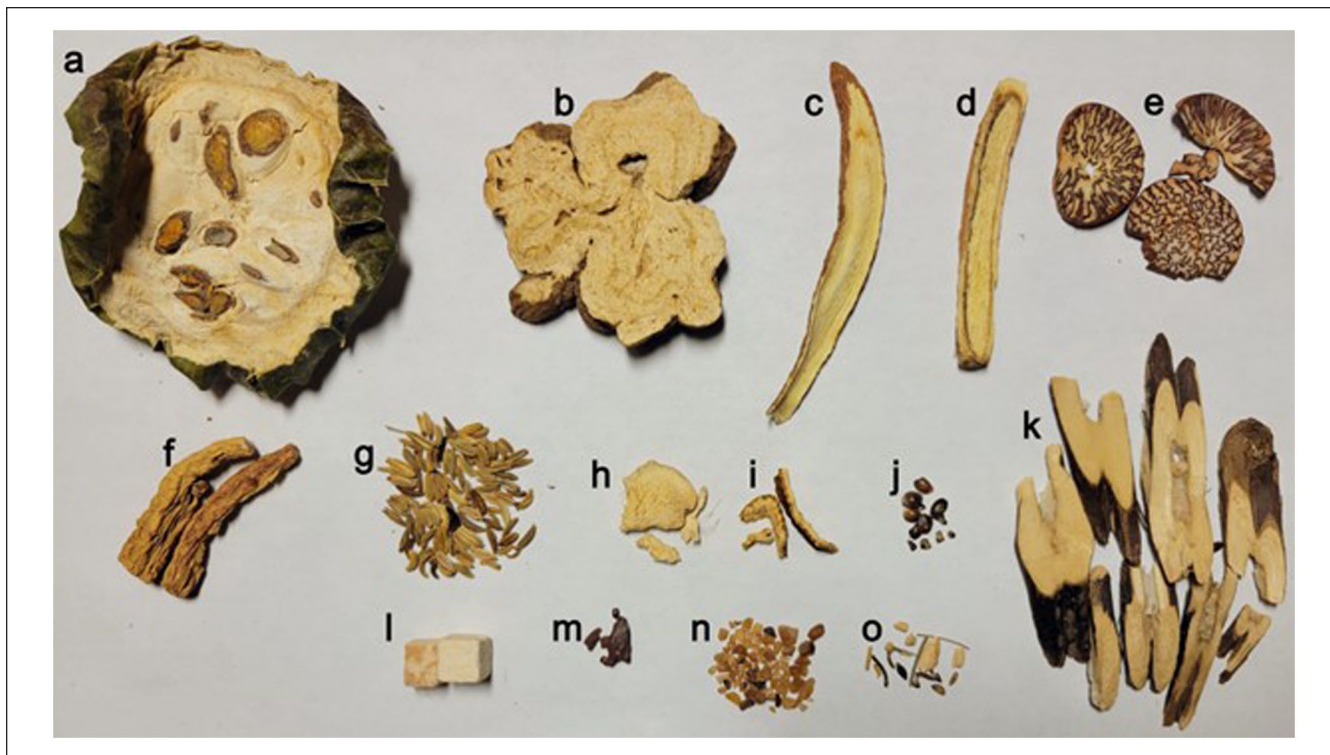


Figure 1. Photo of patient's Chinese herbal medication regimen. (a) *Trichosanthes kirilowii*, (b) *Atractylodes japonica*, (c) *Glycyrrhiza uralensis*, (d) *Platycodon grandiflorum*, (e) *Areca catechu*, (f) *Codonopsis pilosula*, (g) *Foeniculum vulgare*, (h) *Zingiber officinale*, (i) *Citrus unshiu* or *Citrus reticulata*, (j) *Cannabis sativa*, (k) *Perilla frutescens*, (l) *Wolfiporia extensa*, (m) Hematite ($\text{Fe}_2\text{O}_3 \cdot n\text{H}_2\text{O}$), (n) *Pinellia ternata*, (o) and so on, *Elettaria cardamomum*, *Aucklandia lappa*, *Aconitum carmichaelii*, *Senna obtusifolia*, and *Rheum palmatum* not shown in figure (unidentifiable or not found in sample).

indicate hemolysis, potentially resulting from medications or infections, among other causes. Imaging plays a crucial role in distinguishing between biliary and nonbiliary processes. Liver biopsy can serve as a valuable adjunct in evaluations, particularly in clarifying causes of chronic liver disease or cirrhosis that may be newly detected.⁷

Chinese herbal medicine has gained popularity in the United States, yet the usage of these herbs is not stringently monitored or regulated for safety. Clinical experience has demonstrated that herbal medications may induce medical conditions that occasionally necessitate hospitalization and close monitoring.⁸ The incidence of herbal hepatotoxicity remains uncertain, but it is frequently reported. Approximately, 5% to 10% of patients with drug-induced liver failure have been associated with the utilization of herbal products.⁹ In the present case, the patient had been consuming traditional Chinese herbal medicine concomitantly with home TPN. Following the cessation of the herbal mixture, her liver enzymes returned to normal levels. It is less probable that TPN was the primary cause for the elevated liver enzymes, given that the patient was in the process of gradually reducing her dependence on TPN at that time.

Identifying a single ingredient in an herbal medicine mix that may cause hepatotoxicity is challenging; however, among the 20 herbs, *P grandiflorum*, *A japonica*, *W extensa*,

C pilosula, *S obtusifolia*, and *T kirilowii* have been previously reported as potentially hepatotoxic.¹⁰ The patient was consuming a mixture of 20 herbs (Figure 1). Like the patient in this report, many individuals often do not perceive herbal supplements as actual medications and remain unaware of their potential health risks. Clinical diagnosis of hepatic injury related to herbal medicine use is complicated, as other causes must be ruled out and patients do not always voluntarily disclose their use of herbal supplementation to health-care providers. It is crucial for clinicians to conduct thorough medical histories and inquire about supplement use when clinical suspicion is high. Vigilance for adverse side effects is essential for both the patient and care provider.

Conclusion

Hepatic dysfunction is a common occurrence in patients receiving TPN; therefore, consistent monitoring is essential. When elevated liver enzymes are observed among TPN-dependent patients, a thorough differential diagnosis and work-up should be conducted to identify various potential causes. Furthermore, a comprehensive evaluation of dietary supplements, including herbal remedies and other over-the-counter products, should be undertaken and considered as a possible cause of hepatic dysfunction.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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