

Hepatotoxicity caused by bay leaf (*Laurus nobilis*): A case report

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Abstract

Introduction: In recent years, an increase in the use of herbal supplements, natural products, and traditional medicines has been observed. These herbs and herbal products have been associated with complications, such as liver injury, causing high mortality and morbidity.

Case Report: A 51-year-old female presented to the emergency department with a 2-week history of abdominal pain, vomiting, and nascent jaundice. In the detailed history of the patient, the daily consumption of *Laurus nobilis* tea was reported for 1 month at home. On physical examination, she was icteric and ill-looking. Mild right upper quadrant discomfort with tenderness was noted, but no rash or hepatosplenomegaly was observed. The laboratory tests results were as follows: serum AST/ALT ratio 1.2 (908/744 U/L), gamma-glutamyl transferase 63 U/L, ALP 124 U/L, bilirubin (total/direct) 27.0/14.0 mg/dL, and lactate dehydrogenase 420 U/L. Prothrombin time international normalized ratio was 2.77. The gastroenterology department considered fulminant hepatitis in the patient and recommended liver transplantation. The patient died while preparations for the transplant were ongoing.

Conclusion: Many herbal products are known to be hepatotoxic. *Laurus nobilis* is a commonly consumed herbal product, and the potential of this herb to cause hepatotoxicity should be considered.

Key Words: herbal products, traditional medicine, bay leaf, hepatotoxicity

Introduction

Interest in natural therapies has increased significantly in recent years. Herbs and herbal products are widely consumed worldwide and are generally considered safe. However, many cases of herbal liver injury are reported each year. Because the liver is the primary organ responsible for the metabolism and detoxification of drugs and herbal supplements, toxicities can accumulate in the liver, causing injury. These types of hepatotoxicity can lead to severe liver injury, which can result in acute liver failure and ultimately cause serious mortality. Liver toxicity can be determined by measuring enzyme activities, such as serum alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT), and determining the total bilirubin concentration¹. *Laurus nobilis* is a perfumed evergreen tree or large bush with dark-green, smooth leaves and is native to countries in the Mediterranean region and Europe. Known as a bay leaf in English and laurel in Turkish, *Laurus nobilis* is one of the oldest known spices and is commonly used as a condiment and spice in traditional meat dishes, rice, stews, and soups. *Laurus nobilis* is an aromatic substance with industrial importance that is used in medicine and cosmetics, in addition to consumption as food². For the first time, we report a case of toxic hepatitis caused by consuming *Laurus nobilis* for 1 month in a 51-year-old

female, which ultimately led to progressive liver failure and death over the course of 3 weeks.

Case Presentation

In February 2021, a 51-year-old female with no other history of underlying chronic liver disease presented to the emergency department with a 2-week history of abdominal pain, vomiting, and nascent jaundice and was hospitalized. In the detailed history of the patient, the daily consumption of *Laurus nobilis* tea was reported for 1 month at home. On physical examination, she was icteric and ill-looking. Initial vital signs in the emergency department were blood pressure of 110/80 mmHg, pulse of 101 beats per minute, respiratory rate of 22 breaths per minute, oxygen saturation at 94% on room air, and temperature of 36.8 °C. Mild right upper quadrant discomfort with tenderness was noted, but no rash or hepatosplenomegaly was observed. In our case, no chronic drug usage by the patient was reported. The laboratory tests results were as follows: hemoglobin 14.2 g/dL, white blood cells (WBC) 5,700/mm³ (segment 67.3%, lymphocytes 19.7%, and eosinophils 2.9%), platelets 300,000/mm³, serum AST/ALT ratio 1.2 (908/744 U/L), gamma-glutamyl transferase (GGT) 63 U/L, ALP 124 U/L, bilirubin (total/direct) 27.0/14.0 mg/

dL, and lactate dehydrogenase (LDH) 420 U/L. Prothrombin time international normalized ratio (INR) was 2.77. Serologic tests for viruses causing acute hepatitis, such as anti-hepatitis A virus (HAV) Ab IgM, hepatitis B surface antigen (HBs Ag), anti-hepatitis B core protein (HBc) IgM, anti-hepatitis E virus (HEV) Ab IgM and IgG, anti-hepatitis C virus (HCV), and anti-human immunodeficiency virus (HIV), were all negative. Ultrasonography examination was normal. The gastroenterology department considered fulminant hepatitis in the patient and recommended follow-up for the patient at the liver transplantation center, according to King's College Criteria. The transplantation center was contacted, and they stated that the patient received an organ transplant order, and a live donor was present, but the patient died while preparations for the transplant were ongoing.

Discussion

Currently, herbal products are used primarily for weight loss and bodybuilding but are also to improve general well-being and the symptoms of chronic diseases. Herbal products that are referred to as natural are generally considered safe and without any side effects. However, various herbal products, especially dietary supplements and herbal preparations, can cause liver injury. Each year, many cases of herb-induced liver injury are reported. Among these, liver injury, sometimes severe enough to cause death, has been described³.

Liver injury associated with the consumption of herbal products is referred to as "herb-induced liver injury" (HILI) and is rarely observed in susceptible individuals. The clinical signs of HILI are the same as those for drug-induced liver injury (DILI)⁴. HILI is typically self-limiting. However, continual liver injury, acute liver failure, death, and liver transplantation have been indicated. A diagnosis of HILI can be difficult to make because none of the traditional assessment methods can accurately assess hepatotoxicity associated with herbs⁵.

Hepatotoxicity generally occurs when the ALT level rises three-fold, the serum ALP level rises two-fold, and the serum bilirubin level rises two-fold (serum ALT and ALP levels also rise). Hepatotoxicity can be divided into three main classes: hepatocellular injury is indicated when serum ALT levels increase; cholestatic injury is indicated when ALP and bilirubin levels increase; and mixed liver injury is indicated when both ALT and ALP levels increase⁶. Our case was evaluated as mixed hepatocellular–cholestatic liver injury due to there was more than three-fold rise in ALT, more than two-fold rise in bilirubin and mild rise in ALP. The degree of liver enzyme elevation is poorly correlated with the severity of liver disease. The cholestatic pattern of hepatitis has the lowest mortality, but liver tests require a longer time to normalize. In addition, the cholestatic and mixed patterns of hepatitis are associated with a small but definite risk of evolution to chronicity⁷.

Not all herbs are harmless. In recent years, many cases of HILI have been reported, including direct confirmations of hepatic fibrosis, portal inflammation, cholestasis, chronic hepatitis, hepatic venous-occlusion, and focal hepatic necrosis. Today, the dried leaves of *Laurus nobilis* are commonly used as a spice or flavoring in the kitchen and food industry. Essential oils prepared from the leaves have antibacterial, antioxidant, and anti-inflammatory activities. As a traditional medicine, a decoction or tea made from laurel leaves is often used therapeutically, providing antispasmodic effects in the intestines and stomach to counteract diarrhea and easing the symptoms of rheumatic pain, respiratory diseases, cough, asthma, and heart diseases^{2,8}.

Many studies have been published in the literature describing HILI^{3,9,10}. Among the English language literature, *Laurus nobilis* extract has been described as having strong free radical scavenging properties that prevent the effects of toxicity and provide hepatoprotective effects in experimental animal models¹¹. Interestingly, we noticed that only the hepatoprotective properties of *Laurus nobilis* were investigated in the literature. However, we found no studies in which hepatotoxicity has been investigated. The hepatotoxicity that may occur when *Laurus nobilis* is consumed by humans for any purpose depends on several factors, such as the dosage of the product, the user's age, health, and other conditions. Currently, insufficient scientific information exists to determine the appropriate dosage range for *Laurus nobilis*; however, herbal products are not necessarily safe, and the dosages used can be important.

We did not find any studies in the literature examining hepatotoxicity associated with the use of *Laurus nobilis*. Therefore, this report appears to describe the first case of death following fulminant hepatic failure due to the use of *Laurus nobilis*. In our case, no chronic drug use was reported by the patient, and the observed increase in liver enzymes was attributed to hepatotoxicity due to the use of herbs and herbal products.

In summary, many herbal products are known to be hepatotoxic. Unfortunately, with the increased interest in the use of herbal products, the risk of developing hepatotoxicity also increases. *Laurus nobilis* is a commonly consumed herbal product, and the potential of this herb to cause hepatotoxicity should be considered. Emergency physicians should be alert to the clinical presentation of HILI in patients using herbal supplements. Acute hepatocellular damage that may occur in these patients is characterized by elevated serum aminotransferases and bilirubin levels.

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