

A Case of Idiopathic Anaphylaxis Followed by Acute Liver Injury

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Idiopathic anaphylaxis is characterized by recurrent anaphylaxis without a known trigger. The coexistence of acute liver injury with idiopathic anaphylaxis is rare, even in cases of severe anaphylaxis such as shock. An unusual case involving repeated episodes of anaphylactic shock accompanied by acute liver injury is described here. A 36-year-old woman who experienced anaphylaxis due to an unknown cause was referred to our hospital because of marked elevations in her liver enzyme levels. After a thorough evaluation to determine the cause of the acute liver injury, viral infection, drug use, and autoimmune hepatitis were excluded. The episodes were accompanied by elevated liver enzymes, which suggested that this was a case of anaphylaxis followed by acute liver injury. The patient will have to use self-injectable epinephrine to prevent future hepatic failure.

Key Words: Idiopathic anaphylaxis; acute liver injury

INTRODUCTION

Idiopathic anaphylaxis is characterized by recurrent anaphylaxis that is not associated with a known trigger. This diagnosis can only be made after excluding possible exogenous and endogenous causes such as anaphylaxis caused by food, exercise, medications, insect stings and bites, and illnesses such as mastocytosis and C1 esterase inhibitor deficiency and/or dysfunction.¹⁻³ The most common clinical symptoms of idiopathic anaphylaxis are identical to those of anaphylaxis with a known cause, namely generalized urticaria, angioedema, gastrointestinal symptoms, upper and lower respiratory obstructions, and vascular collapse. However, the coexistence of acute liver injury is rare in patients with anaphylactic shock.⁴

Here, we report a rare case of idiopathic anaphylaxis followed by acute liver injury.

CASE REPORT

A 36-year-old woman was admitted for evaluation due to recurrent anaphylaxis. Three days before her hospital visit, the patient drank about 2,000 mL beer because of heavy stress. Normally she drank 1,500-2,000 mL beer twice a week. Two days later, she ate fried chicken for lunch and after 1-2 hours generalized urticaria and lip swelling developed, accompanied by dyspnea and light-headedness. However, there was no loss of consciousness. The patient recovered after a few hours of rest, although pruritus and general weakness remained. The following

day, the patient underwent blood tests at a local hospital and marked elevations in her aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were noted. When the patient arrived at the hospital, her blood pressure was 110/70 mmHg and urticaria with pruritus observed. She was treated with an antihistamine and steroids and referred to the emergency department at our hospital for further evaluation.

The patient had experienced five similar episodes in the past. The first episode occurred 10 years previously. At that time, the patient was suffering from stress brought on by overwork. The next day, 3 or 4 hours after eating black bean sauce with noodles, the patient developed generalized urticaria, lip and periorbital swelling, and nausea. At the same time, her throat felt constricted and she was short of breath. She recovered after treatment in the emergency department; however, it was difficult to determine the exact therapeutic regimen. The second episode occurred 3 years later. Generalized urticaria, lip swelling, and dyspnea developed after eating chicken stew. When the patient visited the emergency department of another hospital, her serum aminotransferase levels were between 1,000 and

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2,000 IU/L and she was admitted. She was negative for hepatitis virus markers, and an abdominal ultrasound detected no abnormal findings. Her serum aminotransferase levels quickly dropped below 200 IU/L over the following week and she was discharged. About a month later, at a follow-up visit, her serum aminotransferase levels had returned to normal values. The third and fourth episodes, which occurred 3 years ago and 7 months ago, respectively, were similar except that neither was associated with specific foods. Worthy of note is that during the fourth episode, which was treated at another hospital, it was initially suspected that her blood pressure was low. In both the third and fourth episodes, her serum aminotransferase values rose to 5,000 IU/L and then improved rapidly. The fifth episode occurred 6 months ago after the patient ate noodles. These episodes had increased in frequency over the past year from approximately once every 3 or 4 years to twice a year.

The patient had no history of bronchial asthma or drug or food allergies. She also had not been taking any medicine or herbal supplements for several months. Her family history was unremarkable. The patient was a married housewife who had a regular menstrual cycle. She had been living in urban areas and had never had pets.

At the present admission, the patient was alert. Her blood pressure was 145/87 mmHg, and her other vital signs were normal. Neither urticaria nor angioedema was present because they had already resolved. Her abdomen was soft, without tenderness, distension, or organomegaly. Laboratory testing revealed that her complete blood count and differential were normal without peripheral eosinophilia (white blood cell, 9,400/ μ L; total eosinophil count, 47/ μ L). Her serum creatinine level was normal, and her blood glucose concentration was mildly elevated (177 mg/dL). In addition, her AST and ALT levels were markedly elevated (681 and 1,337 IU/L, respectively). Her levels of alkaline phosphatase, gamma-glutamyl transpeptidase, and lactate dehydrogenase were also elevated to 122, 129, and 339 IU/L, respectively; however, there was no hyperbilirubinemia. Serological analyses for hepatitis A, B, and C viruses and tests for autoantibodies such as anti-nuclear antibody, anti-mitochondrial antibody, and anti-liver kidney microsomal type 1 antibody were all negative. Furthermore, her serum ceruloplasmin level was normal. Serum tryptase and histamine or its urinary metabolites were not measured. Testing for metanephrine or catecholamines and other hormonal studies was not performed because of a low probability of pheochromocytoma or carcinoid syndrome. Abdominal computed tomography demonstrated mild periportal edema of the liver. There was no evidence of abnormal focal lesions in the liver or biliary dilatation. A liver biopsy was not performed.

Initially, we suspected food-induced anaphylaxis, specifically wheat-induced anaphylaxis, because the intake of wheat-containing foods was a common feature in several episodes. Although her total serum IgE levels were 297 kU/L (reference range

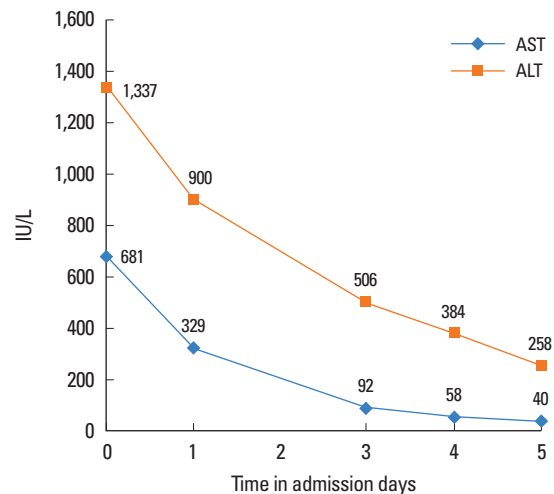


Figure. Course of the aminotransferase levels in the present case. AST, aspartate aminotransferase; ALT, alanine aminotransferase.

≤ 100), wheat-specific IgE antibodies were not detected. Moreover, a skin prick test with a large panel of commercial extracts of food allergens, including wheat, returned negative results. The skin panel also contained extracts of apple, banana, grape, orange, peach, pineapple, tomato, beef, cabbage, carrot, celery, chicken, chicken egg, milk, codfish, crab, lobster, shrimp, oyster, peanut, walnut, hazelnut, and mushroom (Allergopharma, Reinbek, Germany). The skin test results were confirmed by a multiple allergen simultaneous test (Advansure Allergy Screen, LG Life Sciences, Seoul, Korea). In addition, when an oral provocation test with noodles was performed under controlled conditions and monitoring, no reaction was observed over the course of 1 hour. The patient then underwent a 20-minute exercise challenge test. The patient experienced no symptoms either during or after exercise, which suggested that the attacks were not caused by wheat or exercise. No association between the previous episodes and foods, medications, or other triggers could be identified.

Her AST and ALT values improved rapidly without specific treatment, and on day 5 of her hospital stay her values were 40 and 258 IU/L, respectively (Figure). Self-injectable epinephrine was prescribed and the patient was discharged.

DISCUSSION

The present report describes a case of repeated episodes of anaphylaxis with concomitant acute liver injury. Given that the anaphylaxis-triggering stimulus could not be identified, a diagnosis of idiopathic anaphylaxis was made.

The etiology of acute liver injury in this case was neither viral nor drug related. Her episodes were characteristically accompanied by elevated liver enzymes, which suggests an etiological relationship between the acute liver injury and idiopathic anaphylaxis. Consequently, ischemic hepatitis was thought to be a

possible etiology. Ischemic hepatitis, also known as hypoxic hepatitis or shock liver, is characterized by centrilobular liver cell necrosis and sharply increasing serum aminotransferase levels in a clinical setting of cardiac, circulatory, or respiratory failure.^{5,6} Liver biopsy is not mandatory for the diagnosis if her clinical and laboratory features are typical and when other causes of acute hepatitis have been excluded. Hypotension, especially shock, appears to be an important but not essential condition for the development of ischemic hepatitis.⁵ Other important conditions leading to ischemic hepatitis include hepatic injury resulting from a low-flow state secondary to congestive heart failure, hypoxia from sepsis or respiratory failure, and hypoxemia due to a variety of etiologies.⁷ In the present case, the data were consistent with ischemic hepatitis because her serum aminotransferase levels increased rapidly to more than 1,000 IU/L and then quickly returned to normal. The histological features of her liver were unknown because a biopsy specimen was not obtained. However, systemic hypotension, severe hypoxemia, and other risk factors for hypoxic hepatopathy were not clearly documented in several episodes, although according to the patient, low blood pressure was suspected during the fourth episode.

Alcohol intake was also considered as a cause of the acute liver injury in our patient, but her reported alcohol intake alone could not have caused acute liver disease given that the development of alcoholic liver disease in females generally requires a daily intake of alcohol exceeding 20-40 g/day for 10-12 years.^{8,9} None of the laboratory abnormalities or physical signs were sufficient to make a diagnosis of alcohol-related liver injury. In addition, because the vast majority of patients with alcoholic steatohepatitis have higher AST levels than ALT levels, with both being below 300 IU/L,¹⁰ the possible contribution of alcohol to the liver injury in this case was minimal.

We suggest that idiopathic anaphylaxis induced the acute liver injury in the present case. Because the patient in this case exhibited acute liver injury during anaphylaxis, self-injectable epinephrine was prescribed to prevent acute liver injury after anaphylaxis in the future.

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