

Acute Severe Alcohol-induced Bronchial Asthma

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Abstract

We report the case of a severe bronchial asthma attack 15 minutes after the ingestion of food containing small amounts of alcohol. Although an ethanol inhalation test was negative, an acetaldehyde inhalation test was positive. Furthermore, it was discovered that the patient was homozygous for a mutation of the aldehyde dehydrogenase-2 (ALDH-2) gene. We subsequently diagnosed his attack as acute severe alcohol-induced asthma. Since bronchial asthma patients who are homozygous for mutant ALDH-2 genes are susceptible to acute severe alcohol-induced asthma attacks, strict clinical attention is thought a necessity. (*Internal Medicine* 40: 643–645, 2001)

Key words: aldehyde dehydrogenase-2, acetaldehyde inhalation test, mutant homozygous

Introduction

Asthma attacks are induced by alcohol intake in about 50% of Japanese patients with bronchial asthma (1). It has been reported that a cause of alcohol-induced bronchial asthma is a higher serum concentration of acetaldehyde brought about by an abnormal metabolism resulting from a mutation in the aldehyde dehydrogenase-2 (ALDH-2) gene (2). Furthermore, it has been reported that the higher concentration of acetaldehyde activates mast cells and consequently induces histamine release (1). In the clinical setting, although we encounter many bronchial asthma patients with alcohol-induced asthma attacks, the severity of the attack is usually mild to moderate and inhibited by a histamine receptor blocker (3, 4). Severe cases of alcohol-induced asthma are rare. We present a patient who is homozygous for a mutation in the ALDH-2 gene and who suffers acute severe alcohol-induced asthma attacks by taking small amounts of foods containing alcohol.

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Case Report

A 68-year-old man had been monitored for bronchial asthma since 1986. In the morning of October 4, 1999, he ingested homemade sandwiches containing small amounts of alcohol. After 15 minutes he suddenly felt dyspnea and wheezing, and was subsequently conveyed to an emergency ambulance after losing consciousness. Upon arrival at our hospital a remarkable wheezing sound emanated from both lungs and tachypnea was also noted, resulting in the patient's admission to the I.C.U. Although he regained consciousness and his dyspnea disappeared following the injection of epinephrine, aminophylline and methylprednisolone one hour after admission, he was re-admitted to our division of respiratory medicine on October 7, 1999 to investigate the cause of this episode. During that second admission, neither physical examination, laboratory data nor chest X-ray showed any abnormalities. His serum IgE level was 1.8 IU/ml and RAST (radioallegosorbent test) scores against house dust, mite, flour and milk were negative. He did not have a past history of other allergic diseases. His pulmonary functions revealed mild obstructive changes as follows; VC 3,670 ml, %VC 117.3%, FEV_{1.0} 2,280 ml, %FEV_{1.0} 106.5%, FEV_{1.0} % 60.6%, TLC 4,910 ml, %TLC 98%, RV 1,240 ml, %RV 82%, DL_{CO} 21.38 ml/m/mmHg, %DL_{CO} 163.3%. The PC20-Mch measurement, which is the concentration of inhaled methacholine required to induce a 20% fall in FEV_{1.0}, was 198.9 µg/ml, indicating moderate bronchial hyperresponsiveness. Both aspirin and tolmetin inhalation tests, for the diagnosis of aspirin-induced asthma, were negative. We then performed ethanol and acetaldehyde inhalation tests according to Myou's methods (5). The patient signed an agreement allowing the acetaldehyde test to be carried out after the risks were explained. Ethanol and acetaldehyde were dissolved in a physiological solution to make concentrations of 5, 10, 20 and 40 mg/ml. Each concentration of ethanol or acetaldehyde was inhaled for 2 minutes by tidal mouth breathing and followed immediately by measurements of FEV_{1.0}. When FEV_{1.0} was decreased by over 20% from baseline, the inhalation test was judged as positive. Although the ethanol inhalation test was negative, the acetaldehyde inhalation test was positive because FEV_{1.0} was decreased by 33.5% following the inhalation of 20 mg/ml of

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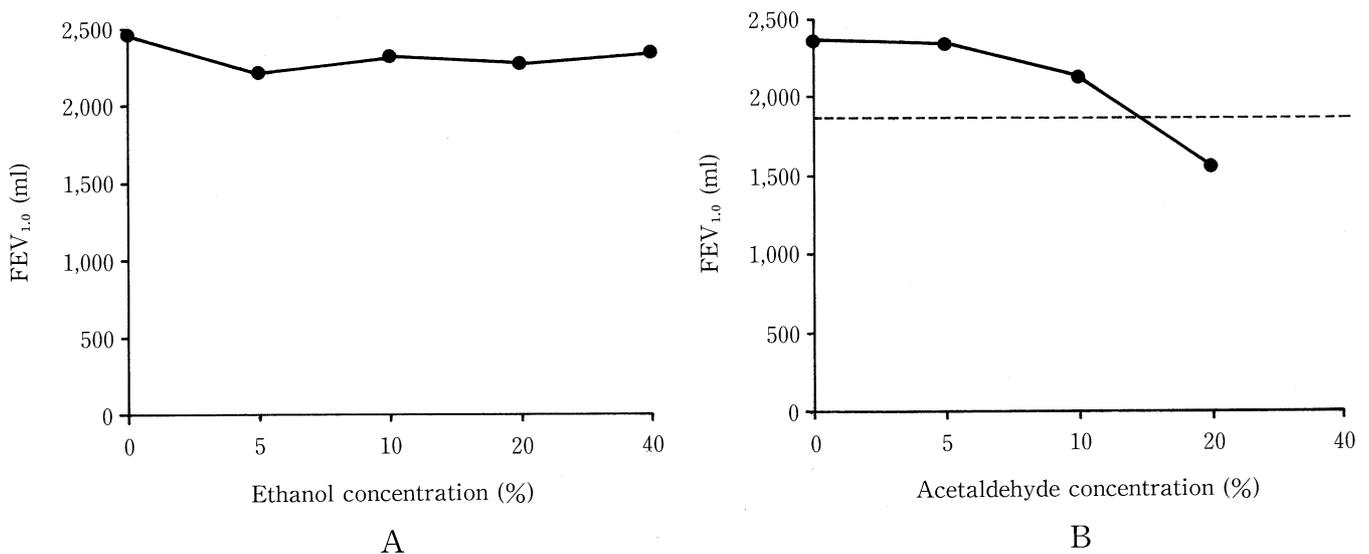


Figure 1. Ethanol (a) and acetaldehyde (b) inhalation test. Dash line indicates 20% fall values from baseline FEV_{1.0}.

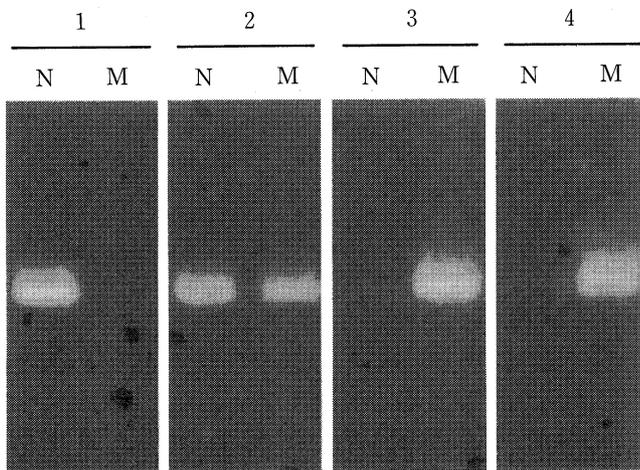


Figure 2. Mutant heterozygous of ALDH-2 gene was shown in the DNA analysis of this patient. 1: normal case, 2: mutant heterozygous case, 3: mutant homozygous case, 4: the patient.

acetaldehyde (Fig. 1). Furthermore, we examined his ALDH-2 genotype by using the polymerase chain reaction according to Takao's methods (3) and found that he was homozygous for the mutant genotype (Fig. 2). From these examinations, we diagnosed his present episode as acute severe alcohol-induced asthma and gave guidance regarding his alcohol intake.

Discussion

Alcohol-induced asthma is often seen in bronchial asthma patients after alcohol intake. It is thought that this phenomenon is absent in Caucasians and is specific to Asians. Shimoda

et al reported that 67% of Japanese patients with asthma experience exacerbation of asthma after alcohol intake (1). Alcohol-induced asthma is thought to be a response to intrinsic histamine released by an increased serum concentration of acetaldehyde, which in turn occurs as the result of a genetic alteration, especially mutation of the ALDH-2 gene, which is involved in the metabolism of alcohol (1, 2). In the case we have presented, the patient had an acute asthma attack within 15 minutes of taking foods containing small amounts of alcohol, but not alcohol by itself. Furthermore, it is not likely that flour which is a component of bread was the cause of his present episode, because the RAST score against flour was negative. Since our examination showed that his acetaldehyde inhalation test was positive, but his ethanol inhalation test was negative and he was homozygous for a mutation of the ALDH-2 gene, his present episode was thought to be alcohol-induced asthma, not an allergy to ethanol. Although a possibility of aspirin-induced asthma by additives was also conceivable, it is unlikely that he is an aspirin-induced asthma patient because both aspirin and tolmetin inhalation tests were negative. Also, although acetaldehyde inhalation tests can give positive results in patients without alcohol-induced asthma as well as in patients with alcohol-induced asthma, Fujimura et al reported that alcohol-induced asthma patients have a selective bronchial hyperresponsiveness to acetaldehyde compared to methacholine (6). The present patient also had a bronchial hyperresponsiveness to acetaldehyde. However, the responsiveness of his airways to acetaldehyde relative to methacholine is bigger than that reported by Fujimura et al (6) (1.899 vs. 1.345 ± 0.093). Since Myou et al reported that there is tachyphylaxis of airways to acetaldehyde (7), it is likely that bronchial hyperresponsiveness to acetaldehyde is reduced by tachyphylaxis in the acetaldehyde inhalation test in this case.

Takeda et al reported that 78% of patients whose asthma

develops within 30 minutes of drinking alcohol have a mutant ALDH-2 gene, with 11.1% of them homozygous for the mutation, but all patients who develop asthma more than 1 hour following alcohol intake do not have the mutant ALDH-2 gene (8). Furthermore, a rapid increase in airway resistance, blood acetaldehyde levels and blood histamine levels is recognized in patients, such as ours, who are homozygous for a mutation of the ALDH-2 gene (8). Although we did not check the blood acetaldehyde or histamine levels by an alcohol-drinking test because the risk was very high in our patient, we were able to diagnose this episode as acute severe alcohol-induced asthma from the other examinations that we have presented. The patient was then instructed not to drink alcohol or eat foods containing alcohol.

In conclusion, we reported acute severe alcohol-induced asthma in a patient homozygous for a mutation of the ALDH-2 gene. Since bronchial asthma patients who are homozygous for this mutation are likely to have acute severe alcohol-induced asthma attacks, strict clinical attention is thought a necessity.

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