

# Urticarial Reaction Caused by Ethanol

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## ABSTRACT

**Background:** We report a case of an urticarial reaction after drinking alcohol beverages. The patient was a 47-year-old man suffering urticarial and anaphylactoid reaction to alcohol for two years. These reactions were observed at every alcohol beverages intake.

**Case Summary:** We performed a prick test with diluted ethanol, alcohol beverages and their metabolites (acetaldehyde, acetic acid). Only acetic acid showed a positive result. Oral challenge test with diluted-ethanol caused pruritus and swelling of his lips. An oral challenge test with 8% diluted Shochu (Japanese distilled alcohol from rice or wheat) caused wheals on his upper back.

**Discussion:** Only acetic acid, a metabolite of alcohol, induced a positive prick test in the patient with alcohol-induced urticaria. This result was not observed in normal volunteers. An oral challenge test with diluted-alcohol or Shochu showed a positive wheal reaction in a dose dependent-manner which suggests that urticaria seen in this patient might be induced by alcohol-intolerance. However possible allergic reaction to acetaldehyde could not be excluded.

## KEY WORDS

acetic acid, ethanol, IgE, intolerance, urticaria

## INTRODUCTION

Alcohol beverages are commonly consumed in the world and known to lead to a variety of adverse effects in humans. Acute and chronic effects of alcohol as well as alcohol addiction are well known. Other effects including, intolerance syndrome (flushing syndrome), oriental syndrome, which is a genetic, drug-alcohol flush reaction, and contact urticaria are known generally.<sup>1</sup>

On the contrary, urticarial and anaphylactoid reactions caused by alcohol are very rare and the cause of these reactions has remained unclear. We have experienced one patient who developed urticarial and anaphylactoid reactions after consumption of alcohol beverages.

## CLINICAL SUMMARY

A 47-year-old Japanese man presented with anaphylaxis, including generalized urticaria and swelling of the lips after intake of alcohol beverages since 2003. Various types of alcoholic beverages caused these

symptoms. Previously, he had been able to consume alcoholic beverages without problems. In his past history, intake of mackerel caused urticarial reaction in childhood, but this reaction had not occurred recently.

Laboratory tests showed normal levels (complete blood counts, liver and renal function). Serum IgE level was slightly over the border-line (210 IU/ml).

Twenty-minute closed patch tests, prick tests and scratch tests with diluted ethanol, alcohol beverages (beer, Shochu, brandy, as control) and their metabolites (acetaldehyde; 9.5%, 95%, acetic acid; 0.96%, 9.6%) were performed. Twenty-minute closed patch tests with different concentrations of ethanol showed positive reactions (Fig. 1a). In the prick test, acetaldehyde showed erythema slightly, but only acetic acid showed positive wheal reaction in the patient but not in normal volunteers (Fig. 1b). On the other hand, ethanol only showed erythema and no wheal reaction even in the scratch test (Fig. 1c).

The mouthwash test with diluted ethanol was negative. This result suggested that these urticarial reac-

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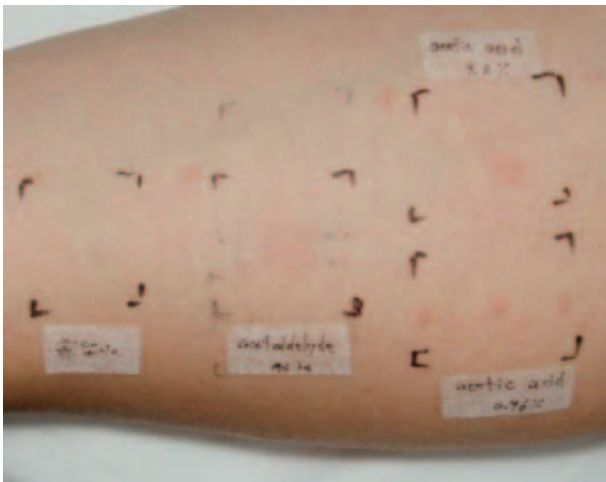
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**Fig. 1a** Closed patch test of ethanol and alcohol beverages showed positive reactions in all chambers.



**Fig. 1b** In the prick test wheal reaction advanced on his forearm. Only acetic acid was positive.

tions were not due to contact urticaria. Oral challenge test was performed with 10 ml of 2.5%, 5%, 10%, 20% ethanol at intervals of 15 minutes, as previous report has shown that the plasma acetic acid concentration ascends rapidly in humans within 15 minutes after oral administration of ethanol.<sup>2</sup> The administration of 20% ethanol caused pruritus of his lips after 7 minutes and this symptom diminished within 30 minutes. After oral challenge test, it became difficult for the patient to continue administration of ethanol because of its irritation to his tongue and the following oral challenge test was performed by using 8% diluted Shochu unwillingly.

The administration of 60 ml of 8% diluted Shochu caused pruritus of his lips after 10 minutes. As the symptom began to decrease slowly for a little while,



**Fig. 1c** No wheal reaction was seen in scratch test of ethanol.

another 60 ml Shochu was added and this caused swelling of his lips and pruritus of the oral cavity. These symptoms began to decrease again after several minutes and another 20 ml of 8% diluted Shochu administration induced itchy erythema on his upper trunk and wheals on his upper back. All of these effects faded within 1 hour (Fig. 2).

## **PATHOLOGICAL FINDINGS**

Skin biopsy was not performed.

## **DISCUSSION**

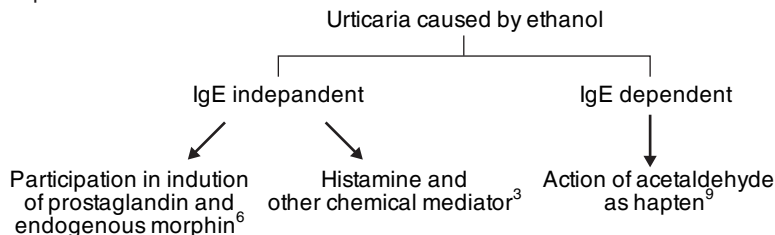
We analyzed nine previously reported patients with urticarial and anaphylactoid reaction caused by ingestion of alcoholic beverages where ethanol itself had been demonstrated to be the causative agent.<sup>3-8</sup> The reactions ranged from swelling of the lips, urticaria to anaphylactoid reaction. Six out of 9 patients were positive in prick test to acetic acid.<sup>5,7,8</sup> Ethanol, alcohol beverages and acetaldehyde were all negative. Our patient showed positive reaction in 20 minute closed patch tests. It is considered that the erythema is caused by accumulation of acetaldehyde because healthy volunteers with flushing syndrome (two individuals) showed the same reaction and others (five individuals) showed negative reactions. Although the mechanism of urticarial reaction by alcohol is unclear, it seems to be important to decide whether this reaction is mediated by type I allergic reaction or not. If this reaction is due to type I allergic reaction, the patient must take care of the anaphylactic shock. It has been shown that acetaldehyde functions as a hapten and specific IgE against acetaldehyde. The protein complex is detected in the serum of non-Oriental patients with severe hypersensitivity reaction to alcohol (Table 1).<sup>9</sup> This method may be useful to decide whether the reaction is type I or not, but we could not demonstrate this in our laboratory.

A previous report showed that the urticarial reaction to ingested alcohol is inhibited by indomethacin and naloxone but not by H1 or H2 antihistamines and suggested that the reaction was mediated through



**Fig. 2** After drinking 20 ml of Shochu furthermore, he developed itchy erythema on his upper trunk (right window) and wheals on his upper back. (left window). These reactions vanished within 1 hour.

**Table 1** It is not well known whether the urticaria caused by ethanol is IgE dependent or not. A few theories are discussed. In the IgE-dependent theory, acetaldehyde acts as a hapten. In contrast, in IgE-independent theory, induction of prostaglandin and endogenous morphine as well as histamine and other chemical mediators participate in the urticarial reaction.



endogenous prostaglandins and opiates.<sup>6</sup> However, another report showed that the reaction was inhibited by neither indomethacin and naloxone nor H1 or H2 antihistamines. This report mentioned that the level of plasma histamine rises after the oral challenge test and possibility in the presence of other mediators.<sup>3</sup> Moreover, it was also reported that H1 antihistamines alone blocked the reaction.<sup>4</sup> The concentration of plasma histamine after induction of the urticarial reaction is not always increased which may influence the contradictory effect of antihistamines on the urticarial reaction. In our case, the patient abstained from intake of alcohol and these urticarial reactions were abolished without antihistamines and other drugs.

At present, it is difficult to draw any conclusion that these anaphylactoid reactions to alcohol observed in our case are allergic or not, because the reaction was dependent on the concentration or volume of alcohol. It is possible that the patient could have chronic urticaria because urticarial reactions are easily induced in patients with chronic urticaria by ingestion of alcoholic beverages. However, he had no history of chronic urticaria and dermatography was negative when he was free from alcohol. From these results, it

is likely that urticarial reactions were caused by alcohol intolerance rather than allergic reaction. The exact candidates of alcohol-induced urticaria in the present case and the reason why only acetic acid was positive in the prick test are obscure in this observation. More investigation should be required to answer these unexplained questions.

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