

Table 1Summary of Patients With Clinical Symptoms of Allergy Attributable to Alcoholic Beverages and Positive Prick Test Results to Acetic Acid^a

Study	Patient no.	Age, y	Sex	Atopy	Alcohol symptoms	Vinegar symptoms	Prick acetalddehyde and ethanol	Ethanol challenge	Others
Karvonen and Hannuksela, ³ 1976	1 (case No. 3)	28	F	–	Urticaria	Urticaria	–	Urticaria	+ Challenge acetic acid – Challenge acetalddehyde
Przybilla and Ring, ⁴ 1983	1	22	F	+	Anaphylaxis	Anaphylaxis	–	Anaphylaxis	+ Prick vinegar
Kelso et al, ⁵ 1990	1	14	M	–	Anaphylaxis	No	–	Anaphylaxis	Histamine normal
Sticherling et al, ⁶ 1995	3	65	F	–	1 Urticaria/AE	Asthma	ND	Urticaria	
		62	F	–	1 Anaphylaxis	Anaphylaxis	ND	Anaphylaxis	
		22	F	–	1 Anaphylaxis	No	ND	Urticaria	
Boehncke and Gall, ⁷ 1996	1	68	F	–	Anaphylaxis	Anaphylaxis	–	Anaphylaxis	– IgE acetic acid – IgG acetic acid
Emonet et al, ⁸ 1998	1	48	M	–	Urticaria	No	ND	Urticaria	Serum tryptase, 3.8 ng/mL
Nakagawa et al, ⁹ 2006	1	47	M	–	Anaphylaxis	No	–	Urticaria	+ Pachtest ethanol
Fernando and Clarke, ¹⁰ 2009	2	58	F	–	Anaphylaxis	No	–	Urticaria/AE	Serum tryptase, 13.5 ng/mL
		22	F	–	Anaphylaxis	No	–	Urticaria	Serum tryptase, 14.2 ng/mL
Current report	1	40	F	+	Urticaria/AE	No	–	Urticaria/AE	Serum tryptase normal
Total	12	Mean age: 47	9 F 3 M	10 – 2 +	8 Anaphylaxis 2 Urticaria/AE 2 Urticaria	5 Yes 7 No	8 – 4 ND	4 Anaphylaxis 6 Urticaria 2 Urticaria/AE	

Abbreviations: AE, angioedema; ND, not done.

^aPlus sign indicates positive; minus sign, negative.

It is possible that the small amount of vinegar consumed was not sufficient to trigger symptoms. We have not performed a challenge test with acetic acid because it is corrosive and irritant (doses of 60–70 mL of concentrated acetic acid can be fatal).

In summary, we suggest that skin prick tests with the beverage, pure ethanol, and acetic acid should be performed in those patients with allergic reactions after consuming alcoholic drinks. If a positive skin test result to acetic acid is detected, a challenge test with pure ethanol may be performed, with written patient approval and taking maximum precautions because severe reactions in sensitized patients are common.

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Venom anaphylaxis can mimic other serious conditions and disclose important underlying disease



Systemic allergic reactions to venoms are common and there is a known association between venom anaphylaxis (VA) and systemic mastocytosis (SM).¹ SM is diagnosed (or ruled out) by a bone marrow (BM) examination, but this procedure is considered unfeasible in the large number of patients with venom allergy and complete absence of other signs or symptoms indicative of mastocytosis. Current recommendations suggest the use of baseline serum tryptase to screen for underlying SM in patients with VA.² However, a substantial fraction of patients with SM have a normal baseline tryptase level, and a diagnosis of mastocytosis could be overlooked using only this screening approach, with potentially severe implications.^{3,4}

A recently developed mutation-specific quantitative polymerase chain reaction (qPCR) method for *KIT* D816V mutation detection in peripheral blood (PB) has been demonstrated to represent a highly specific and (compared with baseline tryptase) sensitive screening tool for SM in patients with anaphylaxis.^{4,5} We present a case of VA initially interpreted as a cerebral stroke in which the underlying SM was diagnosed solely based on this qPCR mutation analysis.

An otherwise healthy 49-year-old man suddenly feels a stinging pain on his back while driving alone in his car. Within minutes, he feels severely ill with nausea and visual disturbances, has difficulty breathing, but manages to phone his wife who calls for an ambulance. Despite his condition, he drives his car a few hundred meters back home but past his house and into a nearby garden because of a deteriorating level of consciousness, followed by loss of bladder control and loss of consciousness.

Paramedics arriving at the scene find the patient in his car, unconscious with perioral cyanosis. Blood pressure is not recorded instantly, but oxygen treatment is initiated immediately and shortly after the patient regains consciousness. Because blood pressure, heart rate, and oxygen saturation at this time are normal, the patient is rushed to the emergency department with no additional treatment given.

At arrival to the hospital, the patient is still confused, answers with latency, and is found to have decreased muscular strength in his left leg. On suspicion of a cerebral stroke, acute computed tomography of the brain is planned and a thrombolysis team is called, but a neurologic re-evaluation finds only speech latency and concludes there is no suspicion of stroke. Then, because an epileptic seizure is suspected to have caused the symptoms, electroencephalography and magnetic resonance imaging of the brain are performed the following day; the results are normal. The patient feels better and can state he suspected an insect sting on his back minutes before symptoms occurred the previous day. Physical examination confirms a red, swollen area with a diameter of approximately 5 cm on his upper right back. The patient is discharged and referred for allergy evaluation on suspicion of VA as the cause of the event.

Immunoglobulin E specific to yellow jacket is 36.9 kIU/L (reference <0.35 kIU/L) and main allergen components for yellow jacket are positive (Ves v 1 2.97 kIU/L; Ves v 5 49.9 kIU/L). Immunoglobulin E specific to honeybee and honeybee allergen components are negative. Baseline serum tryptase is 9.2 ng/mL (normal). Serum tryptase was not measured during the acute phase because anaphylaxis was not suspected.

As an integral part of our evaluation of patients with venom allergy, mutation-specific qPCR for the presence of *KIT* D816V mutation was performed in PB. The test result was positive (allele burden 0.001%), thereby strongly implying a diagnosis of underlying SM.⁴ BM examination showed infiltrates of CD25⁺, CD117⁺, and tryptase-positive spindle-shaped mast cells, thereby confirming a diagnosis of indolent SM with the major and 3 minor diagnostic World Health Organization criteria fulfilled.⁶ Other symptoms and signs of mastocytosis including skin lesions were completely absent. Before the anaphylactic event, the patient had never had any allergic reactions or mast cell mediator-related symptoms.

This case report has 2 important key messages.

First, VA should be considered as a differential diagnosis in cases with sudden and otherwise unexplained loss of consciousness even in the absence of other symptoms of anaphylaxis such as urticaria or angioedema. Such skin symptoms are absent in up to 15% to 20% of cases of VA, and if the patient cannot report the stinging incident during the acute course, then a correct diagnosis of anaphylaxis can be very difficult and the outcome could be fatal. Absence of skin symptoms during the anaphylactic episode has even been suggested to be indicative of underlying mastocytosis.⁷ Venom-related fatalities can be underestimated; a study reported the presence of venom-specific immunoglobulin E in 23% of serum samples from subjects who died outdoors suddenly of unexplained cause during the summer season.⁸

Second, SM should be considered in cases of VA even in the absence of other signs and symptoms of mastocytosis and a normal baseline serum tryptase level.^{3,9} Often, a BM examination would not be performed in those circumstances. Therefore, in addition to measurement of baseline tryptase, we recommend screening for the presence of the *KIT* D816V mutation in PB by highly sensitive mutation-specific qPCR in all patients with VA. This approach has

been shown to disclose underlying mastocytosis in a significant fraction of patients in whom the diagnosis otherwise would have been missed.³ The method is not only sensitive and highly specific but also simple and cheap (cost of reagents <US\$50). A positive *KIT* D816V mutation analysis in PB should always be followed by a BM examination to confirm the diagnosis of SM. Significant clinical suspicion of SM with more signs or symptoms of the disease also should prompt the clinician to perform a BM examination even if the *KIT* D816V mutation is not found in PB, because the mutation-specific qPCR can produce false negative results in patients with very low *KIT* D816V levels and because a small fraction of patients with SM carry another mutation.³ In these patients, the REMA score proposed by the Spanish Network for Mastocytosis could aid the clinician in deciding which patients should undergo BM examination despite a negative screening result for *KIT* D816V mutation in PB.¹⁰

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