

LETTER TO THE EDITOR

Case of anaphylaxis due to carmellose sodium

Dear Editor,

A 67-year-old Japanese woman was referred to us to examine the cause of anaphylaxis. Her past history included hypertension, angina pectoris, diabetes mellitus and hyperlipidemia. Further, she had pollenosis and metal allergy to cobalt, zinc and manganese. She received a joint injection of triamcinolone acetone (Kenacolt A[®], Bristol-Myers Squibb, New York, NY, USA), purified sodium hyaluronate (ARTZ Dispo[®], Seikagaku

Corp., Tokyo, Japan) and lidocaine hydrochloride (Xylocaine[®], Aspen Japan, Tokyo, Japan) for the shoulder pain. Approximately 20 minutes after the injection, urticarial rashes appeared over the whole body. Two hours after the injection, she developed dizziness and nausea. In addition, her blood pressure lowered and she finally became unconscious. She was brought into an emergency room of another hospital with a diagnosis anaphylaxis.

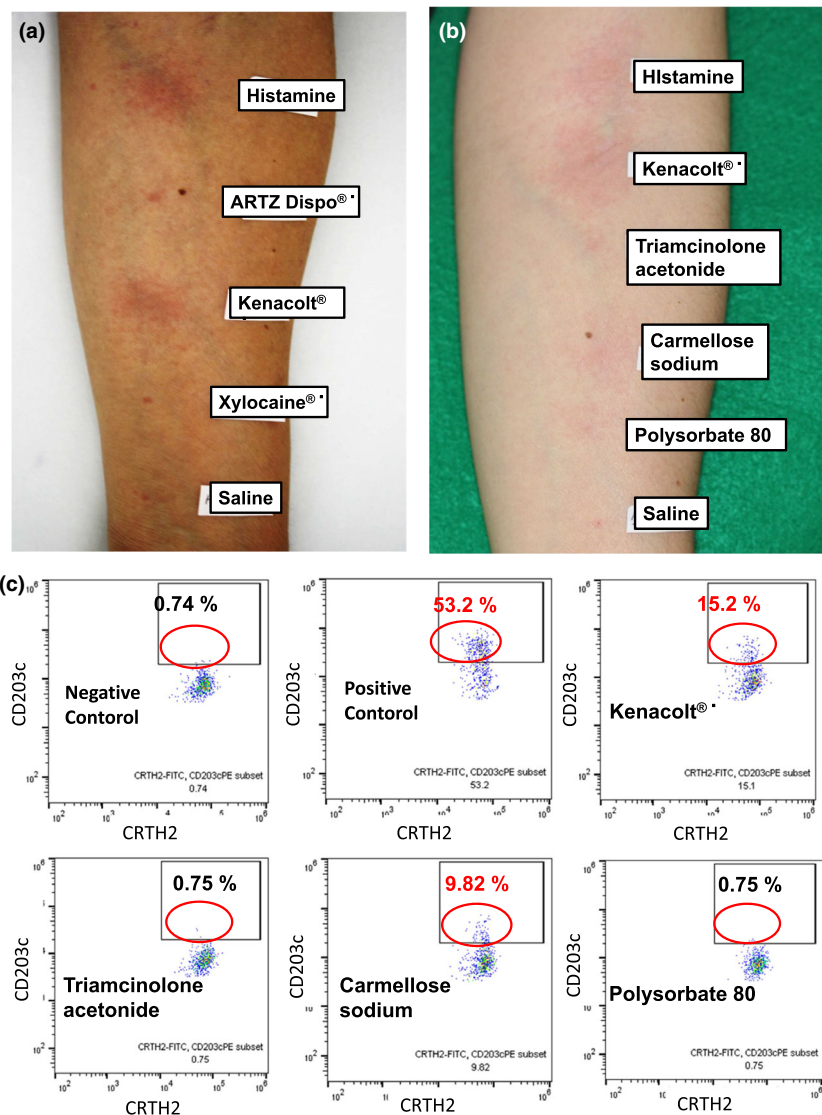


Figure 1. (a) Kenacolt[®] showed a positive reaction (3+; wheal; histamine 6 mm, Kenacolt 6 mm) in a skin prick test. (b) Kenacolt and carmellose sodium showed positive reactions (3+ and 2+; wheal; histamine 10 mm, Kenacolt 10 mm, carmellose sodium 5 mm) in a skin prick test. (c) Kenacolt and carmellose sodium induced basophil activation. Basophil activation was measured by flow cytometry. Peripheral blood basophils were gated as CD203⁺ chemoattractant receptor-homologous molecule expressed on T-helper 2 cells (CRTH2)⁺ cells. Activation of basophils by the indicated antigens was evaluated on the basis of the upregulation of CD203c expression. Stimulation with anti-Fc ϵ RI antibody served as the positive control and culture without stimulation was regarded as the negative control.

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A skin prick test (Kenacolt, ARTZ Dispo, Xylocaine) was performed to determine the cause of anaphylaxis. The patient showed a positive response to Kenacolt (3+; wheal; histamine 6 mm, Kenacolt 6 mm; Fig. 1a). Kenacolt is composed of triamcinolone acetonide (10 mg), benzyl alcohol (9 mg), polysorbate 80 (0.4 mg) and carmellose sodium (7.5 mg).¹ A detailed prick test was conducted using the individual components. Positive responses were observed in Kenacolt (3+; wheal; histamine 10 mm, Kenacolt 10 mm) and carmellose sodium (2+; wheal; histamine 10 mm, carmellose sodium 5 mm; Fig. 1b). We concluded that her anaphylaxis was caused by carmellose sodium. The basophil activation test is a well-known method to measure the activation of basophils through cross-linking of immunoglobulin (Ig)E antibodies bound to the high-affinity IgE receptor (FcεRI) that result from allergen or anti-IgE stimulation.² To verify that this reaction was mediated by antigen-specific IgE, we performed the basophil activation test using triamcinolone acetonide, carmellose sodium and polysorbate 80 diluted to a 1/100 concentration according to a previously described method.³ As shown in Figure 1(c), Kenacolt and carmellose sodium induced substantial activation of basophils from the patient, but triamcinolone acetonide and polysorbate 80 did not, confirming the IgE-dependent reaction of the patient. We also performed the basophil activation test for the same agents in two healthy subjects and observed no reactions (data not shown).

Carmellose sodium (carboxymethylcellulose) is a viscous carbohydrate. It is used as a suspending agent in injectable hormonal preparations. It is also present in many other medical supplies, food and cosmetics as a binding, gliding and anti-adherent substance.^{4,5} There are few reports on anaphylaxis due to injectable drugs containing carmellose sodium.⁵ As carmellose sodium is hardly decomposed or absorbed in the

gastrointestinal tract, it is considered inert in the human body, and sensitization is difficult through ingestion.⁴ This is why anaphylaxis did not appear after the daily intake as a food additive in our patient. However, there have been several reports on anaphylaxis due to ingestion of barium contrast media containing carmellose,³ though the mechanism is unclear. Analyses of further cases of anaphylaxis due to carmellose should lead to better understanding of the disease mechanism. Because carmellose sodium is widely used in various drugs, this agent should be considered as a cause of anaphylaxis.

CONFLICT OF INTEREST: None declared.

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REFERENCES

- 1 A package insert of Kenacolt® in Japan.
- 2 Hemmings O, Kwok M, McKendry R, Santos AF. Basophil activation test: old and new applications in allergy. *Curr Allergy Rep* 2018; **18**: 77.
- 3 Steiner UC, Tomas G, Oliver H. IgE-mediated anaphylaxis to intraarticular glucocorticoid preparations. *AJR Am Roentgenol* 2009; **193**: 156–157.
- 4 Muroi N, Nishibori M, Fuji T, Yamagata M, Hosoi S, Nakaya N, *et al*. Anaphylaxis from the carboxymethylcellulose component of barium sulfate suspension. *N Engl J Med* 1997; **337**: 1275–1277.
- 5 Bircher AJ, Izakovic J, Paul LB. Oral tolerance of carboxymethylcellulose in patients with anaphylaxis to parenteral carboxymethylcellulose. *Ann Allergy Asthma Immunol* 2004; **92**: 580–581.