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Letter to the Editor

Anaphylaxis caused by maltose solution

Dear Editor,

We report a case of anaphylaxis caused by lactate Ringer's solution with 5% maltose (Potacor®: LRM). Maltose is a biose that consists of two glucose molecule units. It is the main ingredient of starch syrup, and is used as a sweetener for candies or frozen desserts, and occasionally for cosmetics. It can also be made by decomposing starch, a long chain of many glucose units. It is degraded to glucose by maltase in the intestinal tract or renal tubules. Maltose is frequently added to infusion solutions as an energy source that has less influence on blood glucose levels. Maltose administered intravenously is mainly degraded in the renal tubules.

A 30-year-old Japanese female was referred to our department because she had a history of three episodes of anaphylaxis during infusions in our emergency outpatient unit. She also had a history of alcohol intolerance and a delayed allergy to cobalt. She had never used cosmetics including maltose. The first anaphylaxis episode occurred 6 years before the visit, when she had stomachache and nausea that were treated with a mixed solution of LRM and metoclopramide. She developed flushing and itching over her entire body and tachycardia. The second anaphylaxis episode occurred when she had a high fever and anorexia five years previously. Ten minutes after the start of the drip infusion of LRM and a vitamin compound, urticaria appeared over her entire body, followed by dyspnea and a reduction in SpO₂. The third anaphylaxis episode occurred one year ago. She received a drip infusion of LRM and an intravenous injection of scopolamine butylbromide because of a stomachache. Thirty minutes later, anaphylaxis occurred when 150 ml of LRM was administered (amount of maltose administered: 7.5 g). In all episodes, she was administered antihistamines or adrenaline and her symptoms disappeared several hours later.

We performed skin prick tests, scratch tests and intradermal tests with all drugs that were administered on the occasions described (LRM, metoclopramide, vitamin compound, scopolamine butylbromide), all of which showed negative reactions. Challenge tests were positive for only LRM, and negative for the others. The intravenous feeding of LRM began in maltose with an application rate of 0.15 mg/kg/H and 20 min later this was increased to 0.3 mg/kg/H. Urticaria and dyspnea appeared after 27 min (amount of maltose administered: approximately 4 g). Skin prick tests and

scratch tests for the ingredients of LRM were negative [maltose (5%, 10%, 50%), sodium chloride (density in LRM), potassium chloride (density in LRM), calcium chloride (density in LRM), sodium L lactate (density in LRM)]. A Basophil Activation Test for LRM and maltose, and radioallergosorbent test for malt or barley were also negative. A test with intravenous glucose was negative. We performed an oral challenge test using malt extract (containing 60% or more of maltose in 9 g of one package). It was negative until 1 h after taking one package. Subsequently, after 35 min of taking two additional packages, mild flushing with itching appeared on the forearm and neck. These findings led to a diagnosis of anaphylaxis due to maltose in LRM.

There have been 12 cases of anaphylaxis due to medicines containing maltose reported in the past 30 years, including papers and conference reports (Table 1).^{1–5} All were from Japan, where infusion solutions containing maltose are commonly used. More than half of the cases had been repeatedly administered medicines containing maltose several times before the diagnosis was made because of the rarity of anaphylaxis due to maltose. All cases developed anaphylaxis during intravenous drip. In one case, prior to the onset of anaphylaxis, urticaria occurred 1 h after taking a test drug containing maltose for a glucose tolerance test.²

Most cases developed anaphylaxis within a few minutes from the start of administration. In our case, onset of anaphylaxis took 10–30 min to occur. Factors affecting onset may include: the difference in 1) threshold value, 2) administration rate, or 3) maltase activity. For 1), our case did not respond to the skin tests. One of the reasons considered was that her threshold value was high and the antigen amount in the skin test was not reached. For 2), the blood maltose concentration rises faster as the administration rate increases.⁶ If the instillation rate was faster, anaphylaxis in our case might also have developed in a shorter time (Fig. 1). For 3), many previous cases developed rapid symptoms under general anesthesia or states of illness.^{1–5} A fasting state or stressful condition may have an influence on maltase activity or hypersensitivity to maltose.

There have been no reports of hypersensitivity symptoms induced by daily intake of foods containing starch and maltose. It is presumed that the digestive process does not lead to an abrupt increase in blood maltose concentration. However, our case experi-

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Table 1

Case review of anaphylaxis caused by medicines containing maltose for the last 30 years, including our case.

Age Sex (M: male, F: female)	Number of anaphylactic episodes before diagnosis (times)	Time between maltose administration and onset of anaphylaxis or urticaria (times)				Test using maltose solution or maltose				Author
		Within a few mins	10 mins	30 mins or more	Unknown	Skin prick/ scratch test	Intradermal test	Challenge test	Other test	
27 M	2		2				+			Ishii, 1989 ¹
77 F	3	2		1		+			DLST –	Kimura, 1994 ²
28 M	2	1			1	+	+			Enokibori, 1996 ³
12 F	3	3				+				Kakizaki, 1999
30 F	1	1				–	–	+		Nagano, 2000 ⁴
35 F	4	1			3		+		BAT –	Suzukawa, 2006
22 M	1	1								Kanbayashi, 2007 ⁵
44 F	1	1				+	+	+		Hisadome, 2010
23 M	3	1			2	–	+			Umeda, 2014
42 F	1	1				–	+		BAT –	Ono, 2014
14 M	1			1			+		DLST –	Amano, 2015
40 s F	3	1			2		+			Esaki, 2017
30 F	3		1	1	1	–	–	+	BAT –	Our case

Blanks in the test column indicate not done or not described. Reports that are not listed in the references are conference reports in Japanese. DLST, Drug-induced Lymphocyte stimulation test; BAT, Basophil Activation Test.

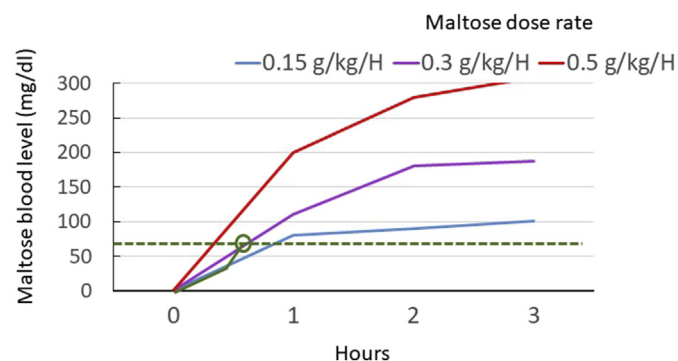


Fig. 1. Blood maltose concentration at the time of intravenous administration of 5% maltose and the estimated anaphylaxis threshold value of our patient. The green circle indicates the estimated blood maltose concentration at the third anaphylaxis episode of our patient, based on the changes in blood maltose concentration during intravenous administration of 5% maltose by eight healthy volunteers, an experiment undertaken by Tahara *et al.*⁶ The green line represents the change in estimated concentration during the patient's drop challenge test. Her expected anaphylaxis threshold value of blood maltose concentration is indicated by the dotted green line.

enced mild urticaria in the oral challenge test. Therefore, we instructed her to refrain from the following: i) high intake of maltose-rich food such as starch syrup; ii) use of testing agents including maltose for glucose tolerance testing; iii) use of α -glucosidase (maltase) inhibitors when suffering from diabetes; and iv) use of cosmetics including maltose.

The sensitization pathway of maltose is unknown, although aggregates of maltose or other minor ingredients might induce anaphylaxis. Our case suggested that hypersensitivity reactions occur when maltose is consumed rapidly and in large quantities beyond the metabolic rate. It is necessary to be aware that anaphylaxis can occur as a result of maltose intake, albeit infrequently. The administration rate should also be noted to prevent the blood maltose concentration from rapidly rising.

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Conflict of interest

The authors have no conflict of interest to declare.

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