Anaphylactoid reaction to maltose 5% solution during spinal anaesthesia

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Purpose: A rare case of an anaphylactoid reaction to maltose solution is presented.

Clinical features: A 28-yr-old man underwent repair of bilateral inguinal hernia under spinal anaesthesia with dibucaine. At the end of operation, he developed generalized flush and circulatory collapse immediately after receiving Na acetate solution containing maltose, 5%, *iv*. The reactions were treated with 32 mg ephedrine and 250 mg methylprednisolone *iv*, and rapid infusion of 1,000 ml acetated Ringer's solution. The skin tests provoked positive responses to maltose solutions.

Conclusion: The clinical features and skin tests suggested that the episode was an anaphylactoid reaction to maltose. Maltose is one of the dissacharides (MW: 342) produced from starch and glycogen. Maltose solutions are used frequently in Japan as a carbohydrate source. Further study is required to confirm whether maltose has an immunological antigen-eliciting activity.

Objectif : Présenter une rare observation de réaction anaphylactoïde au maltose.

Éléments cliniques : Un homme de 28 ans a subi une cure bilatérale de hernie inguinale sous rachianesthésie à la dibucaïne. À la fin de l'intervention, il a présenté un érythème généralisé et un collapsus circulatoire après l'administration d'acétate de Na contenant du maltose à 5% *iv*. La réaction a été traitée avec 32 mg d'éphédrine et 250 mg de méthylprednisolone *iv* avec une perfusion rapide de 1 000 ml d'une solution de Ringer avec acétate. L'intradermoréaction était positive aux solutions de maltose.

Conclusion : Les élément cliniques et les épreuves cutanées suggèrent une réaction anaphylactoïde au maltose. Le maltose est un dissacharide (PM : 342) provenant de l'amidon et du glycogène. Au Japon, on administre souvent des solutions de maltose comme sources d'hydrates de carbone. Des épreuves supplémentaires sont nécessaires pour confirmer l'action antigénique du maltose.

ANAESTHETISTS may encounter acute life-threatening allergic reactions, i.e., anaphylaxis or anaphylactoid reactions, during anaesthesia. The incidence is increasing recently because of use of a greater number of drugs perioperatively.[1,2] Allergic reactions to intravenous infusion are, however, rare. Maltose solution has been used widely in Japan as a carbohydrate source, which provides energy of twice the mass of sugar (and of calories) per millilitre as an equimolar solution of glucose.[3] More than 15 million litres are estimated to be consumed each year, without serious adverse reactions. The present report is a case of anaphylactoid reaction to maltose solution.

Case report

A 28-yr-old man, weight 60 kg, height 172 cm, was scheduled for repair of bilateral inguinal hernias. Four months before the present admission, the patient was given 2 g cefotiam (antibiotics), and 250 ml lactated Ringer's solution with maltose 5% *iv*, for acute epididymitis. This infusion was followed by swelling and erythema over the face and legs, for which 250 mg methylprednisolone, and 20 mg glycchizinate *iv*, were effective. No cardiovascular and respiratory changes were noted during this reaction. Intradermal testing of cefotiam before surgery was negative. Physical examination and laboratory tests revealed no abnormalities.

No preanaesthetic medication was given. Electrocardiographic leads, a blood pressure cuff, and a transcutaneous pulse oximeter were placed on arrival at the operating room and an intravenous infusion of acetated Ringer's solution was started. Blood pressure was 120/70 mmHg and heart rate 72 beats·min⁻¹. Dibucaine, 7.2 mg in 3 ml (of glucose 10%), was injected intrathecally at the L 3-4 interspace. Analgesia to pinprick reached T6 at five minutes. Blood pressure and heart rate were stable at 100/58 mmHg and 80 beats·min⁻¹. Midazolam, 5 mg, was administered *iv* for sedation. Ephedrine, 8 mg *iv*, was given to maintain blood pressure 15 min later. The patient was fully stable for one hour. After the operation was over at 1 hr 15 min, 0.3 mg flumazenil *iv* was administered and the patient regained consciousness. The Ringer's acetate solution, 1,000 ml, was followed by Na acetate solution containing maltose 5%. A few minutes later, blood pressure decreased precipitously to 70/36 mmHg and heart rate slowed to 40 beats·min⁻¹. Oxygen was administered via face mask, 400 ml maltose-containing solution was infused rapidly and a total of 32 mg ephedrine was given *iv*, but blood pressure further decreased to 46/20 mmHg. A gener-

alised erythematous rash was noted at that time, and anaphylaxis was suspected. Methylprednisolone, 500 mg, was administered *iv* and the maltose-containing solution was replaced with acetated Ringer's solution, 1,000 ml, which was infused rapidly. Blood pressure and heart rate returned close to the control level within 15 min. During this episode, the patient was conscious and did not complain of dyspnea. There was no audible wheezing, and SpO_2 remained at 99–100% with 1.0 of F_IO_2. Vital signs remained stable over the next 30 min. The erythema persisted for five hours and faded gradually.

The patient consented to skin tests with prick and intradermal injection to Na acetate solution with maltose 5%, lactated Ringer's solution with maltose 5%, maltose 10% solution, dextrose 10% solution, cefotiam, dibucaine, and flumazenil which were performed four weeks later by a dermatologist. Each solution was prepared with undiluted and tenfold serial dilution. Normal saline solution served as a negative and histamine solution (0.01 mg·ml⁻¹) as a positive control. In the prick tests, the patient demonstrated positive responses to maltose solutions: flare of 10 × 15 mm in diameter to 0.1 mg·ml⁻¹ maltose solution and 15 × 20 flare to 100 mg·ml⁻¹ maltose solution (the photographs were poor in quality and are not shown). Prick tests to the other agents were all negative. In the intradermal tests to serial diluted maltose solutions, the patient demonstrated negative responses to 0.1 and 1 mg·ml⁻¹ solutions, and positive responses to a 10 mg·ml⁻¹ solution; a wheal of 7 × 10 mm and flare of 17 × 20 mm in diameter (see Figure).

A whole-blood histamine-release test was performed. Results expressed as a percentage of total histamine are considered positive when >20% of total histamine has been released.[4] In this case, maltose released 3.8, 4.2 and 4.1% of total histamine from whole blood in the presence of 10, 1 and 0.1 mg·ml⁻¹ maltose solutions, respectively.

Discussion

The patient demonstrated rapid development of generalised flush and hypotension after receiving Na acetate solution containing maltose 5% *iv*. He had suffered a similar though milder reaction to lactated Ringer's solution with maltose 5% on a previous occasion. The clinical features and history indicated that the episode was an anaphylactic or anaphylactoid reaction to *iv* maltose.

Skin testing is most frequently used for identifying the causative agent of allergic reactions.[5–9] In the present case, even the most dilute concentration of
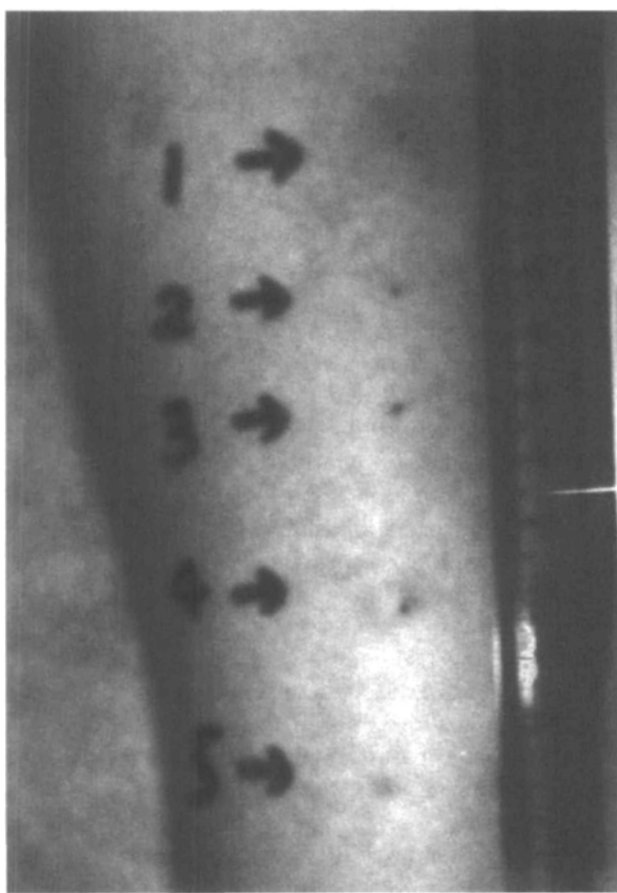
FIGURE Intradermal testing on the right arm of the patient.
Arrow 1 represents a positive reaction to 10 mg·ml⁻¹ maltose
solution; arrows 2 and 3 negative reactions to 1 and 0.1 mg·ml⁻¹
solution respectively; arrow 4 the positive control to histamine
solution; and arrow 5 a negative one to normal saline solution.

maltose produced positive responses in the prick test,
while only the highest concentration produced posi-
tive response in the intra-dermal test. It is generally
agreed that the intradermal test gives positive, or more
correctly false-positive response by a direct pharmaco-
logical histamine release. This was not the case in pre-
sent study, and the intradermal tests gave negative
results to the concentration that provoked positive
response in the prick test. No explanation is available
for these paradoxical findings. Although the prick test
appears to be less sensitive, it seeks essentially anti-
genic recognition from sensitised lymphocytes,[7,8,10]
and the positive response in the prick test in the pre-
sent patient confirmed maltose as the causative agent.

The histamine-release test was negative in the pre-
sent study. The concentration of maltose used in the
test, i.e., 10, 1 and 0.1 mg·ml⁻¹, was based on an

assumption that the reaction begins to occur when
approximately 50 ml maltose 5%, i.e., 2.5 g of mal-
tose, is administered to a man of 60 kg. In most clin-
ical studies, a close correlation has been noted
between the results of skin tests and the histamine-
release test.[4] The failure of the present histamine-
release test may possibly be referred to the difficulty to
perform, and furthermore, to the possible presence of
antibodies that compete for antigen and prevent it
from reaching the IgE-sensitised basophils.[4] The rate
of false-negative has been reported 20%.[4]

Airway maintenance, oxygen administration, rapid
intravenous infusion of crystalloid and/or colloid solu-
tions of >10 ml·kg⁻¹, and epinephrine are the mainstay
of treatment. The severity of symptoms reflects the
quantity of mediators released.[1] Beta-adrenergic recep-
tor stimulation increases the intracellular cyclic AMP of
the basophils and mast cells, which phosphorylates the
Ca^{2+} pump protein, and suppresses the mediator
release. Intravenous epinephrine, initial dose 50–100
µg in adults, 10 µg·kg⁻¹ in children, should be given
immediately. Repeated administration or infusion of
epinephrine, 0.05–0.10 µg·kg⁻¹·min⁻¹, may also be
required.[2,11] Subcutaneous or intramuscular injection of
50 µg·kg⁻¹ epinephrine, is an alternative to intravenous
administration in less severe reactions[1] as arrhythmias
occur. The arrhythmias are caused by an H_2 dysrhyth-
mogenic effect of histamine on the atria and ventricles.[2]
In the present case, at the initial stage of the reaction,
we could not realize the occurrence of anaphylaxis or
anaphylactoid reaction, and ephedrine was given in the
usual dose for mild hypotension induced by spinal
anaesthesia. Consequently, a considerable dose of
ephedrine was required. Hypotension in this case was
mild and rapid intravenous volume expansion with
Ringer's acetate solution restored BP to the control
level. Although corticosteroids are often administered
for the treatment of allergic reaction, their theoretical
value in acute phase is, at present, difficult to defend.

The patient had stable blood pressure without
vasopressors under spinal anaesthesia to T6 for over
one hour. However, the peripheral sympathetic block
would prevent compensatory vasoconstriction and
thus exaggerate the magnitude of hypotension as sug-
gest by Stoelting.[1]

Several reviews have appeared on the use of maltose
infusions.[3,13,14] It is a disaccharide and is found in cere-
al products and glucose syrups.[12] Intravenously admin-
istered maltose is transported into the cells partly
independent of insulin, and then gradually hydrolysed
to two glucose molecules.[3,14] In Japan, maltose solution
is commercially available and is used frequently, approx-
imately >15 million litres per annum. The incidence of

adverse responses is extremely low, and only two cases have been reported.[15,16] Both occurred following repeated administration, developed serious reactions, and skin tests indicated that maltose was responsible. No study has succeeded in identifying the antigenicity of maltose. Further investigation is required to confirm whether maltose has an immunological antigen-eliciting activity. Anaesthetists must always be alert to the possible occurrence of such allergic reactions even to the components of intravenous infusion.

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