

Probable grade IV dextran-induced anaphylactic reaction despite hapten inhibition

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Clinical dextrans with mean molecular weights of 40,000, 60,000, and 70,000 d (dextran 40, 60, and 70) are widely used as plasma volume expanders for improvement of microcirculation and in the prevention of thromboembolic disorders. Dextran and other plasma volume expanders, such as hydroxyethyl starch and gelatin carry the rare risk of anaphylactic or anaphylactoid reactions.¹ The pathogenic mechanism of dextran-induced anaphylactic reactions (DIARs) has been identified as an immune-complex-mediated reaction caused by naturally occurring dextran-reactive antibodies (DRAs).^{2,3} They may be cross-reactive antibodies induced by bacterial polysaccharides from, for example, pneumococci. A DIAR is classified as one of four grades according to the severity of the reaction (Table I).¹

At present Promit (20 ml 15% dextran 1, molecular weight = 1000 d, monovalent hapten dextran) is routinely injected before infusions with clinical dextran to block DRAs. Ten years of postmarketing surveillance of Promit has shown that the incidence of severe DIARs has decreased 100 times from 1/2000 to approximately 1/200,000.³ We report on a patient with a grade IV DIAR to clinical dextran despite pretreatment with dextran 1.

CASE REPORT

A 49-year-old woman was scheduled to undergo surgical correction of a cicatricial hernia. Premedication included ranitidine, thioridazine, chlorazepate dipotassium, lorazepam, and atropine and was tolerated without ill effects. Anesthesia was introduced with etomidate and

Abbreviations used

DIAR: Dextran-induced anaphylactic reaction
DRA: Dextran-reactive antibodies

suxamethonium followed by atracurium, fentanyl, and N₂O. Ten minutes later, 20 ml of Promit was injected, followed after another 10 minutes by an infusion of dextran 70, while the operation was started. After a few minutes, flushing of the face was observed, and despite the dextran infusion being immediately stopped, cyanosis and cardiac fibrillation followed by cardiac arrest ensued. Resuscitation was successful, and the patient recovered completely without sequelae.

There was no history of atopy or adverse reactions to drugs. Four previous surgical interventions performed while the patient was under general anesthesia were tolerated without problems. There was no information on previous dextran infusions.

Results of skin prick tests with common respiratory allergens and latex were negative. Results of intracutaneous tests with dextran 1, 40, and 70; atracurium; and suxamethonium were negative. Serum samples were drawn before surgery and at 3 hours, 24 hours, and 8 days after the episode. Total IgE and specific IgE (as determined by RAST) to latex, suxamethonium, and dextran and tryptase levels were measured. DRAs were determined by passive hemagglutination,⁴ and dextran-specific IgG and IgM were determined by an ELISA method in which dextran was coupled to wells in a microtiter plate. After incubation with the serum sample, enzyme-labeled antibodies with specificities for the human IgG or IgM antibodies were added. After addition of the substrate, the amount of released color, which is proportional to the amount of antibodies in the serum, was measured. The results of the serum analyses are shown in Table II.

DISCUSSION

High titers of DRAs, particularly of the IgG class, have been found in patients with grade III and IV DIARs.² This suggests the pathogenic relevance of antigen-antibody complexes inducing

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TABLE I. Classification of DIARs according to symptoms

Grade of severity	Skin	Gastrointestinal system	Respiratory system	Cardiovascular system
I	Flush, erythema, urticaria	—	—	—
II	Flush, erythema, urticaria	Nausea	Dyspnea	Tachycardia, hypotension
III	Flush, erythema, urticaria	Vomiting, incontinence of stool	Bronchospasm, cyanosis	Shock
IV	Flush, erythema, urticaria	Vomiting, incontinence of stool	Respiratory arrest	Cardiac arrest

Modified from Ring J. Clin Rev Allergy 1991;9:397-414.

TABLE II. Results of laboratory analyses

Analysis	Time at which sample was drawn			
	Before surgery	3 hr	24 hr	8 days
Total IgE (kU/L)	23.6	20.0	18.9	19.9
Latex IgE (RAST class)	0	ND	0	0
Suxamethonium IgE (RAST class)	0	ND	0	0
Dextran IgE (RAST class)	0	ND	0	0
Dextran IgG (OD)	0.405	ND	ND	ND
Dextran IgM (OD)	0.088	ND	ND	ND
DRAs (titer)	1:256	1:128	0	1:128
Tryptase levels	0	0	0	0

ND, Not determined; OD, optical density.

an immune-complex anaphylactic reaction.⁵ The prevention by hapten inhibition supports this concept.

In our patient, cardiorespiratory arrest occurred during the initial phase of a surgical intervention immediately after the infusion of approximately 100 ml of dextran 70. An adverse reaction to another drug is unlikely because the other drugs were not given immediately before the episode and results of skin and in vitro tests with selected drugs were negative. The negative tryptase levels in all serum samples indicate that mast cell degranulation was not involved. Results of skin tests with dextrans and dextran-specific IgE were both negative, which is in accordance with the results of other studies,² rendering a type I hypersensitivity reaction unlikely. DRA titers were elevated before surgery, were decreased 3 hours later, and were negative 24 hours after the incident (Table II), indicating the consumption of antibodies. Dextran-specific IgG was identified in high titers in the preoperative serum sample, whereas the IgM titers were low, as observed in earlier studies.² DRAs of the IgG class played the most important role in the induction of severe DIARs.²

Flushing and cardiovascular reactions are typical for severe DIARs. In our patient a diagnosis of DIAR is further supported by the temporal relationship and by the consumption of DRAs after the episode. Therefore the adverse reaction was classified as a probable grade IV DIAR, despite hapten inhibition with dextran 1. A higher dose of dextran 1 could have mitigated or prevented the reaction.³

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