

We recommend that all radiopaque foreign bodies in the cervical esophagus have their location confirmed by repeated physical examination and fluoroscopy just prior to induction of anesthesia. Secondly, fluoroscopy should be done with the patient in the same position that will be required for anesthetic induction and endotracheal intubation. Finally, the anesthetist must be willing to alter the anesthetic technique if it can be demonstrated that the foreign body has migrated to an unsafe position.

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A Severe Reaction to Dextran Despite Hapten Inhibition

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Prevention of deep vein thrombosis, thromboembolism, and fatal pulmonary embolism is a major consideration in the perioperative period. Dextran, a polysaccharide with an average molecular weight of 40,000 (dextran 40) or 70,000 (dextran 70), is used to decrease the incidence of perioperative thromboembolic morbidity and mortality.¹ However, severe anaphylactic reactions to dextran can occur.² Hapten inhibition with dextran 1 (MW 1000—Promit® Pharmacia) prior to the administration of dextran 40 or dextran 70 has decreased the incidence of adverse reactions.³⁻⁵ However, we describe a severe reaction to dextran 40 after hapten inhibition by dextran 1 in a patient who had previously received this combination 9 months earlier without complication.

REPORT OF A CASE

A 69-yr-old hypertensive male was scheduled for a right total hip replacement (THR) 9 months after a left THR. The patient had received dextran 1 and dextran 40 in the operating room without complication, and had received dextran 40 daily until discharge without adverse reaction. During his current admission, review of systems was negative except for hypertension treated with furosemide 40 mg po daily and oral potassium supplementation. Preoperative laboratory studies were normal. EKG demonstrated bifasicular block, left ventricular hypertrophy, and an anteroseptal infarct of undetermined age. Preoperative vital signs included an arterial blood pressure of 170/100 mmHg, a heart rate of 80 bpm, and a respiratory rate of 18 breaths per minute. Premedication consisted of meperidine 75 mg, hydroxyzine 25 mg, and glycopyrrolate 0.2 mg im. Electrocardiographic monitoring and an indwelling arterial line were placed. Anesthesia was induced with fentanyl 100 µg, thiamylal 500 mg, and succinylcholine 100 mg iv, and maintained with nitrous oxide and enflurane. Skeletal muscle paralysis was maintained with iv atracurium. A deliberate hypotensive technique was employed to decrease bleeding and produce a more secure cement-bone interface. Because of the history of hypertension, the mean arterial blood pressure was only decreased to 70-90 mmHg by a nitroglycerin infusion. (In normotensive patients, the mean arterial pressure is usually decreased to 60 mmHg.) Acetabular and femoral components were cemented without hypotensive, cardiac, or pulmonary complications. During placement of the trochanteric wires, at which time the arterial blood pressure was 110/70 mmHg, 20 cc of dextran 1 were administered iv. Five minutes later, dextran 40 was started, and after 2-3 drops, the systolic arterial blood pressure fell precipitously to 35 mmHg, accompanied by a junctional rhythm at 50 bpm. Facial flushing and wheezing were absent. A diagnosis of an anaphylactic reaction to dextran was made. Dextran, as well as the anesthetics, were discontinued; ephedrine 10 mg and neosynephrine 100 µg were administered iv. The systolic blood pressure increased to 65 mmHg. Diphenhydramine 50 mg, administered iv, resulted in a dramatic rise in arterial blood pressure to 110/70 mmHg and a return to sinus rhythm. The remainder of the case proceeded uneventfully.

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DISCUSSION

Patients undergoing orthopedic surgical procedures are at risk for developing deep vein thrombosis, thromboembolism, and fatal pulmonary embolism. After hip surgery, the incidence of deep venous thrombosis occurs as frequently as 68%.⁶ Fatal pulmonary embolism occurs much less frequently than deep venous thrombosis. In a prospective multicenter study of surgical patients not receiving thromboembolism prophylaxis, the incidence of fatal pulmonary embolism was 0.77%.⁷

Prophylaxis against thromboembolism has successfully decreased the incidence of postoperative deep venous thrombosis and fatal pulmonary embolism.⁷⁻⁹ Current methods of prophylaxis include dextran, heparin, oral anticoagulants, platelet inhibitors, dihydroergotamine, and lower limb compression devices.^{8,9} Many orthopedic surgeons include dextran in their regimen of thromboembolism prophylaxis because dextran decreases viscosity, dilutes the clotting factors, and inhibits platelet aggregation. Dextran therapy is preferred because of its ease of administration without need to continuously monitor clotting functions. Acetylsalicylic acid is utilized by some orthopedic surgeons as their major method of thromboembolism prophylaxis. Heparin and oral anticoagulants can cause postoperative bleeding, are difficult to control, and are usually not considered by the orthopedic community.

After reports of adverse reactions to dextran appeared, a multicenter study by Ring and Messmer reported four anaphylactoid reactions to dextran 40 in 51,261 infusions (0.007% incidence).¹⁰ Reactions ranged from mild discomfort to respiratory arrest, cardiac arrest, and death. Patients at risk tended to be older, male, and had respiratory or cardiac disease. In a 10-yr study in Sweden involving over 1.3 million units of dextran, Ljungstrom reported an incidence of dextran-induced anaphylactic/anaphylactoid reactions (DIAR) of 0.013% for dextran 40 and 0.025% for dextran 70.² The symptoms were graded from I to V: I—skin manifestations (flush, erythema, urticaria) and lumbar pain; II—mild to moderate hypotension (lowest recorded BP 40–60 mmHg depending on duration), gastrointestinal disturbances, respiratory distress; III—severe hypotension, shock BP < 40–60 mmHg, bronchospasm; IV—cardiac and/or respiratory arrest; and V—fatal reaction).^{2,10} Fatal DIAR occurred in 0.003% of patients receiving dextran 40, and 0.004% of patients receiving dextran 70. Reactions occurred with as little as 0.5–1.0 cc of dextran.

DIAR are mediated by dextran reactive antibodies which are IgG immunoglobulins.^{9,11,12} Dextran reactive antibodies (IgG molecules) are formed in response to

dextran polysaccharides, which can result from exposure to dextran contaminants of sugar, dextrans in dental plaque, and from crossreactivity with bacteria.^{9,11,13} Therefore, dextran reactive antibodies are present in the general population, and this places many patients at risk for a dextran reaction.^{9,11}

When dextran is infused, it acts as an antigen and combines with the dextran reactive antibodies. Dextran has many antigenic sites that can react with dextran reactive antibodies, allowing for crossbridging of antibodies and formation of antigen-antibody immune complexes.^{9,11,12} These can form on or adhere to the cell membrane IgFc receptors, and result in the local release of pharmacologic mediators. Immune complexes can deposit in various organs in the body, and result in tissue damage and severe systemic reactions, such as anaphylaxis.¹¹ The dextran immune complexes deposit in the lung, activate complement *via* the classical pathway with release of vasoactive substances such as histamine and bradykinin, and produce an anaphylactic reaction.^{9,11}

This entire process can be prevented if the potentially reactive sites on the immunoglobulin, dextran reactive antibody, are blocked before the antigen is administered. By prior administration of a hapten, a substance capable of combining with immunoglobulins but not producing a reaction, the immunoglobulin reactive sites are occupied and unable to react to the antigen.^{3-5,9,14} Dextran 1 (MW 1000) has proven effective as a hapten in decreasing the incidence of adverse reactions.³⁻⁵

While hapten inhibition has significantly decreased the incidence of DIAR, it has not eliminated them. The patient in this report had a grade III reaction. While there is one report of a grade III reaction after dextran 1, this case is especially unique, since prior administration of dextran 1 and multiple administrations of dextran 40 were uneventful. With the introduction of dextran 1 and its use in our institution in over 1,000 cases without a severe reaction, we have considered dextran administration to be a safe procedure.

We are concerned that a patient who previously was a non-reactor would react on a subsequent challenge. Perhaps the patient formed a higher level of antibodies between the two operations. Although there is supposedly no antibody formation with lower weight dextran infusions, there is one study to counter this opinion.¹⁵ Antibody formation to dextran is more common with molecular weights greater than 90,000, but also occurs, although infrequently, with lower molecular weights.¹⁵ The possibility also exists that the patient had dextran reactive antibodies present prior to his first challenge with dextran, but these were sufficiently blocked by dextran 1. However, after the course of dextran, the immunoglobulin levels may have increased *via* an an-

amnestic response, and the usual dextran 1 dose became insufficient to inhibit a response when the patient was rechallenged, since hapten inhibition is a dose-related phenomenon. Dextran 1 (20 ml) administered iv prior to dextran 40 or 70 decreases the incidence of severe anaphylactic reactions (grades III-V) to 0.003%.⁵ The incidence of mild reactions is unchanged. Dextran 1 in doses of 10 ml has been shown to be less effective in preventing severe reactions than the now-utilized 20-ml dose.⁵ The reaction might have been much worse had the patient not received any dextran 1 prior to the infusion of dextran 40. This case may present a situation where larger doses of hapten inhibition, perhaps 30 ml, would be required.

In order to identify individuals at risk for dextran-induced anaphylactic/anaphylactoid reactions, it would be necessary to determine titers of dextran reactive antibodies prior to infusion, since patients with high titers of dextran reactive antibodies are more susceptible to reactions. Antibody determinations prior to infusion may have demonstrated high antibody levels in the case presented; however, these determinations are not routinely performed. Ring and Messmer define the severity of reactions to dextran with hypotension considered to be a major component of Grade II and Grade III reactions.¹⁰ These authors do not require measurement of mediators or histamine to diagnose an anaphylactic reaction.

This acute hypotensive episode could have resulted from an acute myocardial infarction, a pulmonary embolus, a massive cerebral hemorrhage, or an inadvertent injection of a vasodilating agent. The nitroglycerin, which had been used for deliberate hypotension, had been discontinued and disconnected from the iv 20 min prior to the episode of hypotension. Since the patient was stable hemodynamically until a few seconds following the administration of two to three drops of dextran, and since no other drugs were given, it was evident that the reaction occurred as a result of the dextran. In the previous cases of anaphylactic reaction to dextran that we observed, as well as those described prior to the introduction of hapten inhibition, the onset of hypotension was exactly the same. We do not feel that the patient suffered from primary myocardial dysfunction, since the hemodynamic changes occurred suddenly and were directly related to the administration of dextran.

Phenylephrine, ephedrine, and diphenhydramine were administered to combat this acute hypotensive episode, although epinephrine is the drug of choice for anaphylactic reactions.

Dextran is a very important and effective agent in the prevention of thromboembolic events. Hapten inhibition has played an important role in decreasing the incidence of dextran-induced anaphylactic/anaphylactoid reactions, but has not eliminated them. DIAR have a very low incidence, but vigilance is important to ensure prompt treatment should a reaction occur.

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