



Letter

Intraoperative anaphylaxis induced by the gelatin component of thrombin-soaked gelfoam in a pediatric patient

Intraoperative anaphylaxis is relatively rare, with an estimated incidence of 1:25,000 to 1:4,000.¹ A 2½-year-old girl with a history of tetralogy of Fallot status post repair underwent tethered spinal cord repair in a latex-free environment. She was orally premedicated with midazolam and ketamine and received intraoperative fentanyl, sevoflurane, etomidate, dexamethasone, cefazolin, and a crystalloid infusion (lactated Ringer's). Two and a half hours later, thrombin-soaked Gelfoam was applied on the dura, and her wound was irrigated with 50,000 units of bacitracin solution. Within 2 to 3 minutes, she developed generalized urticaria, a drop in her systolic blood pressure from 110 to 50 mmHg, and a decrease of her oxygen saturation from 99% to 90% with marked difficulty in ventilation. She responded quickly to immediate high-pressure manual ventilation, albuterol, diphenhydramine, intravenous fluids, and ephedrine, which was readily available for instant use.

After the allergy service was consulted, it was revealed postoperatively that a few months prior the patient developed generalized hives, lip swelling, and abdominal pain 20 minutes after ingesting Spam, which is canned pork meat with a characteristic gelatinous glaze, also known as aspic. Her condition required epinephrine administration in an outside emergency room. She had since tolerated pork, milk, egg, wheat, seafood, peanut, and treenuts and had not eaten soy.

Gelfoam is an absorbable gelatin sponge intended for application to bleeding surfaces as a hemostatic agent and prepared from purified pork skin gelatin. It can be used alone or in combination with topical thrombin. For this patient, given that the thrombin-soaked Gelfoam and Spam have porcine gelatin as a common ingredient, it was highly suspected that the antigen inducing these 2 anaphylactic reactions was gelatin.

Patient under skin-prick testing was performed on the back to histamine (Hollister-Stier, WA, 6 mg/mL histamine base, 10 mg/mL histamine dihydrochloride), preservative-free porcine gelatin (College Pharmacy, Colorado Springs, CO), full-strength bacitracin solution (1,000 units/mL), MMR-II (Merck Pharmaceuticals, full-strength solution, containing 14.5 mg of hydrolyzed porcine gelatin per dose), soy (Greer Laboratories), and normal saline (0.9%). She was positive to gelatin (wheal 15, flare 40) and histamine (wheal 7, flare 30) and negative to normal saline, bacitracin, MMR-II, and soy. Specific immunoglobulin E was positive to porcine gelatin (1.81 kU/L) and negative to bovine gelatin (ARUP Laboratories). Given her cardiac condition, intradermal testing for MMR II was performed and was positive at 1:10 dilution. (wheal 9, flare 15, with a nonreactive intradermal normal saline). This concentration was found to be nonirritant in 20 healthy volunteers.² The patient received uneventfully

MMR-II vaccine using a stepwise protocol involving 6 incremental doses given subcutaneously with a 20-minute interval between each dose (0.05 mL 1:100 dilution, 0.05 mL 1:10 dilution, 0.05 mL full-strength, 0.1 mL full-strength, 0.15 mL full strength, 0.2 mL full-strength). This protocol is similar to the algorithm recommended by Wood et al³ for patients with immediate-hypersensitivity reactions to vaccines or their components. Although our patient may have been desensitized MMR-II, it is also possible that she has tolerated the small amount of hydrolyzed gelatin present in the vaccine. She has since tolerated midazolam, fentanyl, sevoflurane, ketamine, cefazolin, and lactated Ringer's.

Topical bovine thrombin has been used therapeutically since the 1940s. It may be applied alone, but it is often used in conjunction with other hemostatic aids, including absorbable agents (such as Gelfoam, collagen, and cellulose).⁴ Although the extent of the utilization of topical bovine thrombin with or without gelatin sponge is not known precisely, an estimated 1 million patients per year receive these hemostatic agents in the United States.⁵ Anaphylaxis to these products is rare overall. Clark et al⁶ performed a 21-year review of topical bovine thrombin spontaneous case safety reports submitted to FDA's adverse event reporting system, from 1986 to 2006. Of 41 cases spontaneously reported, 19 were classified as anaphylactic or anaphylactoid, although no further information was provided. Anaphylaxis to thrombin-containing preparations was otherwise reported in more details in only a few patients. Rothenberg and Moy⁷ described a patient with an anaphylactic reaction within minutes of the application of surgical gelatin sponges soaked with topical bovine thrombin. Four weeks later, this patient showed a positive skin prick test to topical bovine thrombin. Three other patients were reported in Japan in 1991 with a positive radioallergosorbent test to bovine thrombin, although the radioallergosorbent inhibition test suggested that the antigenic substance was mainly found in the contaminant rather than in the bovine thrombin itself.⁸

Gelatin, a derivative of animal skin and bones, may be a component of multiple products, including food, medications, cosmetics, and vaccines. Intraoperative anaphylaxis to gelatin-containing products is rare and has been reported in a few papers. In a French study, 7 of 15 cases were reported to have immunoglobulin E-mediated anaphylaxis to gelatin colloids, and the overall frequency of anaphylaxis to these products was estimated to be 0.345%.⁹

We report the first case of anaphylaxis from thrombin-soaked Gelfoam application, which was secondary to porcine gelatin hypersensitivity. In addition, it is also the first report describing

anaphylaxis to aspic. We recommend inquiring about gelatin allergy not only in drugs but also in food as part of the preoperative assessment when the use of gelatin-containing products is anticipated. If suspected, an allergy service consultation would be warranted before surgery.

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