

Intraoperative Anaphylaxis Secondary to Intraosseous Gelatin Administration

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Background: FloSeal and SurgiFlo Hemostatic Matrices are commonly used in surgical procedures to promote coagulation and minimize blood loss. They are composed of bovine and porcine gelatin matrix, respectively, that can be injected into pedicles to stop osseous bleeding during pedicle screw insertion.

Methods: This report details 2 pediatric spinal deformity reconstructive surgery patients who experienced intraoperative cardiovascular events after the intraosseous administration of animal-derived gelatin.

Results: Case #1 is an 11-year-old female with adolescent idiopathic scoliosis who was undergoing routine posterior spinal instrumentation and fusion. During placement of the fourth pedicle screw, the patient developed profound hypotension, tachycardia, and elevated airway pressures requiring intravenous epinephrine and phenylephrine for hemodynamic support. Surgery was aborted. Postoperative work-up demonstrated a positive ImmunoCAP study for bovine gelatin. Surgery was repeated 1 week later, without the use of FloSeal, and no episodes of hemodynamic instability. Case #2 was a 9-year-old female with juvenile idiopathic scoliosis who was undergoing a growing spine construct. As in Case #1, SurgiFlo was placed into 2 pedicle tracts after which there was profound hypotension, tachycardia, and elevated airway pressures. Resuscitative efforts included intravenous atropine and epinephrine with resolution. Surgery was aborted. Surgery was repeated 2 weeks later, without the use of SurgiFlo, with no episodes of hemodynamic instability.

Conclusions: Given that the patient's symptoms were classic for anaphylaxis, and that the timing of the anaphylaxis immediately followed the administration of FloSeal and SurgiFlo we believe that FloSeal and SurgiFlo were the causes of the reactions. These are the first known reported cases of intraoperative anaphylaxis associated with FloSeal and SurgiFlo. On the basis of our experience, in order to avoid intraoperative cardiovascular events, we obtain preoperative ImmunoCAP testing and elicit-

ing a thorough preoperative history about bovine-derived and porcine-derived gelatin products.

Key Words: scoliosis, gelatin allergy, anaphylaxis

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FloSeal and SurgiFlo Hemostatic Matrices are commonly used in surgical procedures to promote coagulation and minimize blood loss (<http://www.baxterbiosurgery.com/us/products/floseal/index.html>; <http://www.ethicon360.com/products/surgiflo-hemostatic-matrix>). They are composed of bovine and porcine gelatin matrix, respectively, that can be combined with thrombin and is a latex-free product. We report 2 surgical cases with intraoperative anaphylaxis secondary to a gelatin allergy.

CASE #1

The patient is an 11-year-old white female with a past medical history of well-controlled intermittent asthma, seasonal allergic rhinitis, and kyphoscoliosis. Preoperative magnetic resonance imaging of the spinal cord demonstrated a holocord syrinx involving the entire thoracic spine and a type I Arnold-Chiari malformation. After neurosurgical evaluation she underwent a posterior fossa decompression with a duraplasty utilizing Durepair graft, which is composed of type 1 and 3 bovine collagen. Two months postoperatively, she was readmitted for presumed chemical meningitis, which was successfully treated with intravenous steroids.

Five months after posterior fossa decompression, she underwent a posterior spinal fusion from T3-L2 for her kyphoscoliosis. Anesthesia was induced with 450-mg doses of propofol followed by a continuous propofol infusion at 100 mcg/kg/h. The patient received 2 doses of rocuronium as well as fentanyl (single dose followed by continuous infusion). In addition, she received single doses of midazolam and clindamycin. A routine midline incision was carried out and followed by exposure of the posterior elements and facetectomies over the operative levels. Placement of pedicle screws were started at L2 and proceeded cephalad on the left side. After creation of the pedicle channels, FloSeal was gently injected into the osseous channel to stop/diminish bleeding from the pedicle.

The patient was hemodynamically stable during the spinal fusion procedure until placement of the fourth pedicle screw at T11. Within seconds of FloSeal placement, the patient's mean arterial blood pressure fell to 40 and 50 mm Hg, the heart rate increased to 120 beats/min, and peak airway pressures reached 41 cm of water. The patient received 300 mcg of intravenous (IV) phenylephrine which did not improve her status, and then was

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given 10 mcg of IV epinephrine which increased her mean arterial pressure to 70 and 80 mm Hg. The surgical wound was rapidly packed, emergently closed with surgical staples, and then covered with sterile Ioban. The patient was then turned quickly to the supine position and it was noted that her trunk was erythematous with some mottling in the extremities. The patient was given a second 10 mcg of IV epinephrine and then was started on a continuous infusion of epinephrine and her status continued to improve, with the anesthesiologist noting that it was easier to provide manual breaths to the patient after the epinephrine drip was started. A total of 4000 mL IV crystalloid fluids were given to the patient as well. An emergent intraoperative echocardiogram was interpreted as normal. A subclavian central line was inserted to assess central venous pressure, which demonstrated adequate intravascular volume. No change in neuromonitoring occurred during this event. After discussions between the anesthesiology and surgical team, the decision was made to abort the surgical procedure due, in part, to the lack of an identifiable cause of the hemodynamic instability. All pedicle screws were removed. The surgical wound was closed in the routine, layered manner and she was then transferred from the operating room to the intensive care unit (ICU) for hemodynamic monitoring and continued treatment. Of note, a second dose of clindamycin was given 2 hours after the adverse event without complication.

Upon further history, the patient reported episodes of perioral edema, facial swelling, and urticaria immediately after eating blue suckers, blue Jell-O, or blue cake frosting, and these episodes have been treated successfully with hydroxyzine. However, she did report being able to eat other flavors of "Gummi candies" without adverse reactions.¹ The patient also reported a history of penicillin allergy, manifest by rash, and urticaria.

After stabilization in the ICU, allergen-specific immunoglobulin (Ig)E levels (ImmunoCAP) were obtained to latex and bovine gelatin to determine the source of patient's intraoperative anaphylactic reaction. Her latex-specific IgE was undetectable at <0.34 IU/mL, but the bovine gelatin-specific IgE was elevated at 1.90 IU/mL. Evaluation of food colorings did not identify any causative agent. These findings led to the diagnosis of intraoperative anaphylaxis because of the bovine gelatin in the FloSeal preparation. She had no reactivity with immunizations prior to the spine fusion, however, postoperatively when immunized with a Tdap booster she developed a systemic allergic reaction.

CASE #2

This patient is a nearly 9-year-old female who presented with a kyphoscoliosis. She was born prematurely at 24 weeks from maternal preeclampsia and has bronchial pulmonary dysplasia, but has no oxygen requirements. She is slightly developmentally delayed, but does well in school and is cognitively essentially normal. There was no history of allergic reaction to porcine gelatin products. The deformity consisted of a left-sided thoracic curve measuring 75 degrees with a kyphosis of 70 degrees. She is neurologically intact and the preoperative spinal magnetic resonance imaging was normal. She was placed into halo-gravity traction for 25 months to improve the 70-degree kyphosis, in hopes of getting this corrected enough to allow placement of a growing rod construct.

On the day of surgery, she had an uneventful inhalation induction of general anesthesia with sevoflurane, nitrous oxide, and oxygen. Following intravenous access, she was maintained on an intravenous general anesthetic of propofol, sufentanil, and

dexametomidine. She was placed prone on the OSI table (Modular Table System; Mizuhosi, Union City, CA) and 20 pounds of traction was applied through the halo and 20 pounds on her legs (similar to her presurgery weight). There was good baseline neuromonitoring data prior to and after traction was applied. The back was sterilely prepped and draped. A midline incision was centered over the T12 and L1 levels. On the left side, subperiosteal dissection was carried out at the T12-L1 level and exposing the T12-L1 joint. Pedicle screws were placed with the free-hand technique at T12 and L1 by burring the posterior cortex, followed by a pedicle finder to localize the pedicle channel. All 5 walls were palpated, a guidewire was placed then the tract was untapped by 1 mm. In between placing the pedicle finder and the guidewire, we placed a small quantity of SurgiFlo due to significant venous bleeding from the bone. The left-sided T12 and L1 screws were placed without problem, and at this time anesthesia reported a significant drop in blood pressure and tachycardia, with concomitant difficulty in ventilating the patient, and quickly thereafter had an undetectable arterial line tracing. The surgical incision was quickly closed with a running suture in the skin, turned supine, and chest compressions were initiated. After administration of intravenous epinephrine and atropine, there was return of sinus rhythm, decrease in peak airway pressures, and stabilization of systemic blood pressure.

The surgery was aborted and she was kept intubated and transferred to the ICU. She remained in the ICU for 24 hours and then was extubated without difficulty. The growing rods were placed 2 weeks later without problems and without the use of SurgiFlo. After discharge, the patient tested positive for a porcine gelatin allergy (13.13 kU/L, reference interval <0.35).

DISCUSSION

Gelatins come from different sources and have differing degrees of allergenicity. Gelatins are high-molecular-weight peptides derived from various animal collagens, and are used in several foods, medications, cosmetics, and vaccines as stabilizers. Differing degrees of allergenicity from different types of gelatin may be because of its processing, molecular weight, melting point, and dosage.^{2,3} Furthermore, lack of reactivity by oral exposure (such as gummy candies) does not preclude development of allergic symptoms following systemic exposure, such as inadvertent intravascular (or, as in this case, intraosseous) administration. Furthermore, the severity of an allergic reaction may vary with subsequent exposures.²

FloSeal and SurgiFlo are topical hemostatic agents composed of bovine and porcine gelatin matrices, respectively, with or without bovine thrombin. The gelatin matrix in this product is made of cross-linked gelatin granules of collagen origin and is manufactured as a sterile gel in a disposable syringe. In the operating room, the FloSeal and SurgiFlo matrix component are mixed with saline diluent (sodium chloride USP 0.9%) just prior to use. The gelatin matrix and the thrombin work individually, as well as synergistically, to provide assistance in clotting and minimize blood loss.³ A previous report on 2 surgical cases documented the development of neurological deficits attributed to the use of FloSeal in decreasing pedicle tract bleeding.⁴ In these cases the FloSeal was able to enter the spinal canal by pedicle

breeches and upon its expansion, due to imbibing of water, applied a compressive effect on the spinal cord with a secondary loss of neurological function.

Given that the patient's symptoms were classic for anaphylaxis, and that the timing of the anaphylaxis immediately followed the administration of FloSeal and SurgiFlo, we believe that FloSeal and SurgiFlo were the causes of the reactions. Additional testing with an elevated ImmunoCAP to the gelatins help support these diagnoses in both cases. These patients remind us of the importance of eliciting a thorough allergy history prior to beginning new therapies. These are the first known reported cases of intraoperative anaphylaxis associated with FloSeal and SurgiFlo.

Preoperative history of reactions to bovine or porcine gelatin (ie, immunizations or Jell-O) may not be sensitive enough to prevent these intraoperative reactions. Neither of these cases had preoperative reactions to immunizations and only case #1 had previous history of reaction to Jell-O. Of note, the lead author has identified another patient, who was scheduled for a spine surgery, with a "+" ImmunoCAP to bovine gelatin. FloSeal was not used during the surgery and no cardiovascular events occurred. Also, this additional patient also had no history of immunization or Jell-O reactivity preoperatively.

Surgery was performed without the use of FloSeal and no intraoperative problems were encountered. Interestingly since the spine surgery, the patient in case #1 has had a systemic reaction to a tetanus immunization. The rapid intraosseous, and possibly intravascular, exposure may have amplified this patient's allergic sensitivity to bovine gelatin. On the basis of our experience, in order to minimize the likelihood of intraoperative cardiovascular events, we obtain preoperative ImmunoCAP testing and eliciting a thorough preoperative history about bovine and porcine-derived gelatin products. It must be emphasized that even with these screening methods the possibility of an intraoperative allergic reaction cannot be eliminated.

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