

Anaphylaxis to Surgiflo During Posterior Spinal Fusion in an Adolescent Status Post Truncus Arteriosus Repair: A Case Report

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Anaphylactic reaction to gelatin-containing hemostatic agents has been reported in the orthopedic literature, most commonly during scoliosis repair in adolescents. However, the risk, differential diagnosis, and management of anaphylaxis in patients with complex congenital heart disease undergoing noncardiac procedures have not been previously reported. We describe the case of an adolescent with a history of repaired truncus arteriosus undergoing posterior spinal fusion who developed sudden and profound hypotension that was ultimately confirmed to be an anaphylactic reaction to Surgiflo. Echocardiography was used to aid in diagnosis and management of the cardiovascular effects of anaphylaxis in this patient with residual cardiac pathophysiology. (A&A Case Reports. 2017;XXX:00–00.)

Intraoperative anaphylactic reactions are rare, with an estimated incidence of 1:4000 to 1:25,000.¹ We report a case of an anaphylactic reaction to Surgiflo (Hemostatic Matrix; Ethicon Inc, Somerville, NJ), a hemostatic agent containing partially reconstituted porcine gelatin used to decrease surgical bleeding. This agent has been reported to cause anaphylaxis previously, but this case was unique in that it presented as sudden and profound hypotension during posterior spinal fusion in an adolescent with a history of repaired truncus arteriosus. Diagnosing anaphylaxis as a cause of hypotension in an anesthetized patient undergoing major spine surgery can be difficult. Complex congenital heart disease and underlying pathophysiology secondary to residual cardiac defects make it even more difficult to make the correct diagnosis. Successful treatment can also be a challenge if the patient is receiving cardiovascular medications to manage the underlying condition that can alter the expected hemodynamic response to treatment.

We obtained writing consent from patient's family for publication.

CASE DESCRIPTION

A 16-year-old, 56-kg girl presented for a T3 to L3 posterior spinal fusion to treat syndromic kyphoscoliosis. Her

medical history was significant for 22q11.2 deletion syndrome (DiGeorge Syndrome, characterized by the presence of congenital heart defects, hypoparathyroidism, and immunodeficiency),² asthma, atopic dermatitis, and celiac disease. She had a history of allergy to gluten. Her congenital heart defect was truncus arteriosus, which was repaired primarily when she was a neonate. At age 6 years, her right ventricle to pulmonary artery (RV-PA) conduit was replaced.

The preoperative evaluation revealed a slender, healthy appearing adolescent with good exercise tolerance. A preoperative transthoracic echocardiogram (TTE) revealed mild RV-PA conduit stenosis (estimated peak gradient of 32 mm Hg), mild conduit insufficiency, dyskinesia of the ventricular septum with normal biventricular contractility, no intracardiac shunts, and an estimated RV pressure of one-third of systemic pressure.

On the morning of surgery, the patient received oral gabapentin 600 mg and acetaminophen 325 mg in accord with the institution's spinal surgery pathway. The patient was premedicated with oral midazolam 10 mg before intravenous (IV) catheter placement followed by midazolam 2 mg IV. Anesthesia was induced IV using propofol 200 mg and fentanyl 100 µg. Endotracheal intubation was accomplished without the use of muscle relaxant. Right internal jugular central venous and radial arterial catheters were placed. Cefazolin 30 mg/kg was administered IV before skin incision. A loading dose of aminocaproic acid 100 mg/kg IV was given followed by an infusion of 30 mg/kg/h for the remainder of the procedure. Anesthesia was maintained with propofol and fentanyl infusions to enable continuous monitoring of sensory and motor evoked potentials. Vital signs remained stable when the patient was turned prone. In the prone position, the patient required an intermittent infusion of nicardipine to maintain the mean arterial pressure between 60 and 70 mm Hg to minimize blood loss. The nicardipine infusion was ultimately not required to maintain the target blood pressure and was discontinued before the onset of hypotension.

Eighty-five minutes into the procedure, the patient's blood pressure fell suddenly from 80/50 to 50/30 mm Hg accompanied by an increase in heart rate from 80 to 140

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Accepted for publication August 23, 2017.

Funding: None.

The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.cases-anesthesia-analgesia.org).

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DOI: 10.1213/XAA.0000000000000646

beats per minute. Ephedrine 10 mg was given IV without effect. There were no changes in pulmonary compliance, end-tidal CO₂, systemic oxygenation or ventilation, temperature, or continuous neuromonitoring parameters. Resuscitation was continued with administration of phenylephrine 100 µg, a dopamine infusion escalated to 8 µg/kg/min, and bolus administration of lactated Ringer's. When blood pressure did not respond, an epinephrine bolus of 50 µg was given followed by an infusion of epinephrine, which was rapidly escalated to 1.0 µg/kg/min before seeing evidence that the blood pressure was increasing to near the values present just before the event. The only surgical change that preceded the abrupt hypotension was the start of spine instrumentation with the placement of 2 L3 pedicle screws. The pedicle screw tracts and intraosseous spaces had been injected with Surgiflo.

The surgeon was made aware of the hemodynamic changes and the team quickly decided to close the incision and turn the patient supine for evaluation and continued resuscitation. Once the patient was turned supine, blood pressure increased further, and patchy erythema was noted on her palms, soles of her feet, and chest wall. The surgical team cited previous reports in the orthopedic literature implicating Surgiflo as a cause of anaphylaxis and this became the primary diagnosis. A TTE was performed to rule out other possible etiologies for the hypotension including pulmonary embolism, right ventricular dysfunction, or worsening of RV-PA conduit obstruction. The TTE showed adequate biventricular contractility and function. Maximum velocity across the right ventricular outflow tract was 3.4 m/s with a peak gradient of 46 mm Hg, unchanged from the preoperative echocardiogram. Blood samples for tryptase and histamine levels were obtained about an hour after the event, and the patient was given a bolus of 10 mg of dexamethasone. Over the ensuing 30 minutes, epinephrine was weaned, the patient was awakened and extubated in the operating room and transferred to the intensive care unit. On arrival in the intensive care unit, vital signs were stable, and the patient had a normal neurologic examination and cognition.

The next day the patient was returned to the operating room to complete the procedure. Continuous transesophageal echocardiography (TEE) monitoring was added to the previous day's monitoring. Initial echo images were obtained in the supine position when the central venous pressure measured 3 mm Hg, again showing normal biventricular filling and function (Supplemental Digital Content 1, Video 1, <http://links.lww.com/AACR/A134>). When the patient was turned prone, central venous pressure increased to 17 mm Hg and TEE showed compression of the right ventricle without a change in contractility. The RV outflow tract was open without significant obstruction by gradient or color Doppler (Supplemental Digital Content 2, Video 2, <http://links.lww.com/AACR/A135>). Surgiflo was not used and the procedure was completed uneventfully.

Consultation with an allergist confirmed the high suspicion of an anaphylactic reaction to Surgiflo. It took several days for the tryptase and histamine levels to be available and both were elevated at 17.3 µg/L (normal: below 10 µg/L) and 19 nmol/L (normal: 0–8 nmol/L), respectively. The patient was discharged to home on the seventh postoperative day

and had a full recovery at her postoperative visit. On further questioning regarding gelatin allergy, the patient reported a cutaneous reaction (redness, swelling) to several immunizations. We reviewed the records of the prior cardiac surgical procedures but could not determine if the patient had been exposed to Surgiflo during either procedure. The consulting allergist advised that skin testing would not be productive and recommended avoiding future exposure to products derived from bovine or porcine gelatin.

DISCUSSION

Acute hypotension in the setting of posterior spinal fusion surgery is often due to bleeding with inadequate volume replacement. However, the differential diagnosis of hypotension in patients with complex congenital heart disease can be challenging due to the underlying pathophysiology (eg, residual shunts, diastolic or systolic dysfunction, outflow obstruction) and the potential for unexpected response to medical management.

Truncus arteriosus is a rare congenital heart lesion where the embryological single great vessel fails to divide into the pulmonary artery and aorta. The neonate presents with a single arterial trunk with a truncal valve straddling the 2 ventricles and a ventricular septal defect providing mixed blood to the coronary and pulmonary arteries and systemic circulation. Repair, commonly in the neonatal period, consists of ventricular septal defect closure, detaching the pulmonary arteries from the common artery and associating them with the RV using a RV-PA conduit. The common artery now separated from the pulmonary circulation serves as the aorta and truncal valve as the aortic valve. Long-term survival and functional status after repair are excellent; however, the RV-PA conduit does not grow as the patient grows and it is almost inevitable that the RV-PA conduit will need to be replaced due to conduit stenosis. RV-PA stenosis leads to increased RV end diastolic volume and hypertrophy. This results in impaired ventricular filling, ventricular enlargement, and ultimately diastolic and systolic dysfunction.³

The preoperative evaluation was reassuring with a TTE showing good biventricular function in the face of a moderate but chronically obstructed RV-PA conduit.

Nevertheless, given the existing RV outflow obstruction and resulting RV hypertrophy, the patient would be more sensitive to a decrease in preload, or an increase in pulmonary vascular resistance flow through the stenotic RV-PA conduit exacerbating the clinical presentation of anaphylaxis.

The impact of the prone position is an additional factor to consider in this case. To the extent that prone positioning may reduce preload or increase RV outflow obstruction, it would adversely impact the pathophysiology of anaphylaxis. We were unable to demonstrate an increase in the gradient through the RV-PA conduit in the prone position with the TEE during the second procedure, although a change in the shape of the RV was observed suggesting that the pulmonary flow could be reduced, if for example venous return acutely diminished. The increase in central venous pressure from 3 to 17 when moving from the supine to prone position suggests a change in RV compliance which may have made it easier to maintain ventricular wall tension and RV output despite the reduced venous return.

VIDEO+

VIDEO+

There are previous case reports, mostly in pediatric patients and in the orthopedic literature, of intraoperative anaphylaxis to the gelatin in topical hemostatic agents.⁴⁻⁷

Gelatin reaction may be immune or nonimmune. Immune anaphylaxis or type I allergic reaction is mediated by immunoglobulin E (IgE), IgG, and complex/complement. IgE-mediated type can be detected with in vitro immunoglobulin testing. Tryptase level is increased in this type of hypersensitivity due to a release of proinflammatory substances from the mast cells stimulated by IgE. Highest levels of tryptase are detected between 60 and 120 minutes after exposure.⁸⁻¹⁰ Inflammatory mediators released by the mast cell may also exert a direct negative inotropic effect worsening the condition in patients with prior myocardial dysfunction.^{11,12}

Anaphylaxis was high on the list of differential diagnoses given the sudden, marked hemodynamic changes, how refractory the hypotension was to therapies and the temporal relationship to the administration of Surgiflo in the surgical field. Estimated blood loss at the time of the event was relatively modest. Conduit obstruction because of thrombosis or air embolism was considered, but the end-tidal CO₂. Neurogenic shock from a spinal injury is another possibility but was unlikely for several reasons. First, the surgeon had only instrumented the spinal cord at L3 and had not done any corrective maneuvers. Second, intraoperative imaging, used to guide screw placement, reduced the risk of placing a screw into the spinal cord. Finally, motor and sensory evoked potentials were unchanged and normal. Surgiflo seemed the most likely culprit since other medications administered during the case with potential for an anaphylactic reaction had been delivered much earlier.

Prompt diagnosis and treatment of anaphylaxis are critical and initial treatment requires both administration of fluid to maintain preload in the face of vasodilation, and epinephrine to effect vasoconstriction, positive inotropy and chronotropy, and bronchodilation. In this particular patient, one would expect her to be especially dependent on an adequate preload in order for epinephrine to be effective at restoring cardiac output. The lack of response to the initial doses of epinephrine may have reflected the time needed to administer sufficient volume to restore preload sufficiently. As noted previously, as long as the prone position did not increase the RV-PA conduit gradient or impair venous return, it may have helped the resuscitation by its impact on RV compliance.

It is also possible that the increased RV pressure impaired filling of the left ventricle (LV) due to septum displacement and a decrease in the transeptal gradient will decrease the contractile performance of the LV, lower the blood pressure and impair the cardiac output, and as a consequence the RV will experience more ischemia. The increased pulmonary vascular resistance from hypoxemia and high-peak pulmonary pressures from the bronchospasm could impair further the RV performance. The immediate management strategies in this scenario are directed to increase the systemic vascular resistance and the LV pressure and to lower the pulmonary vascular resistance to allow the reestablishing of the transeptal gradient.

Epinephrine may be the inotrope of choice, independent of the benefits regarding anaphylaxis, since epinephrine

will increase afterload and contractility of both ventricles. Experimental data show that in RV failure from an intentionally created pulmonary artery band, inotropic support from inodilators (eg, milrinone) in conjunction with catecholamines (eg, dopamine, epinephrine) provide the best support to improve biventricular performance.¹³ However, in the setting of severe systemic vasodilation from any type of shock, it seems reasonable to increase blood pressure to maintain contractility and end-organ perfusion pressure. Use of vasopressin and methylene blue has been suggested in anaphylactic shock refractory to catecholamine treatment.^{14,15} Vasopressin would likely be useful as an adjunct to epinephrine because it increases systemic vascular resistance without any impact on pulmonary vascular resistance but epinephrine would still be important for inotropic support.¹⁶

There are other issues to consider when treating anaphylaxis in a patient with congenital heart disease. Patients on β -blockers or vasodilators may have a refractory response to anaphylaxis treatment by blocking the compensatory response to hypotension and/or blunting the response to inotropes and vasoconstrictors.¹⁷ A severe decrease in systemic vascular resistance may produce reversal of left to right shunting or increase a preexisting right to left shunt leading to aggravated cyanosis and hypoxemia increasing the difficulty in the management.

Prior reactions to gelatin or bovine or porcine products, including immunizations, gelatin, and gummy candy should be considered a contraindication to the use of gelatin-containing hemostatic agents. Patients with congenital heart disease and prior exposure to gelatin-containing agents are at increased risk of anaphylaxis that may be refractory to treatment. TEE should be considered as another monitor to aid with diagnosis and management of adverse hemodynamic changes in patients with congenital heart disease undergoing a major surgical procedure, especially if they have residual pathophysiology. ■■

DISCLOSURES

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