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CASE REPORT
Craniofacial/Pediatric

Intraoperative Anaphylaxis to Gelatin during Alveolar Bone Grafting for Cleft Palate

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Summary: Intraoperative anaphylaxis can be life threatening. Anaphylaxis to gelatin-based topical hemostatic agents is an underrecognized hypersensitivity. To date, only 21 cases of intraoperative anaphylaxis have been reported for gelatin-based hemostatic agents. In this article, we report the case of a 10-year-old male patient who sustained anaphylaxis after the use of Gelfoam during harvest of a bone graft. Rapid diagnosis and treatment of intraoperative anaphylaxis is imperative to prevent adverse outcomes. Referral to an allergist for identification of the allergen and appropriate notation in the medical record are paramount to avoid future anaphylactic events. Surgeons should avoid gelatin-based hemostatic agents, such as Gelfoam, in patients with reported intolerance of gelatin-based foods and medicines. *(Plast Reconstr Surg Glob Open 2024; 12:e5636; doi: 10.1097/GOX.0000000000005636; Published online 1 March 2024.)*

Gelatin hypersensitivity may be an underrecognized allergy. Mammalian gelatin (bovine or porcine), derived from purified collagen, is a common agent used in topical hemostatic surgical products. Gelatin allergy is well described as a type-1 hypersensitivity reaction to vaccines, but only a few cases of anaphylaxis to hemostatic agents have been reported.[1] It is unknown whether the paucity of published cases is due to rarity of the allergy, or if it is an underrecognized allergy.[2] We describe intraoperative anaphylaxis to Gelfoam (Pfizer) in a 10-year-old male patient who presented for alveolar bone grafting from the iliac crest.

CASE PRESENTATION

Operative Timeline

The patient had a complete heart block and was pacemaker dependent. Preoperatively, his pacemaker was set to 80 beats per minute (bpm) and an asynchronous setting. He underwent induction of general anesthesia without complication, and the right iliac crest was infiltrated with 0.25% bupivacaine with 1:200,000 epinephrine. Cancellous bone graft was harvested from the right iliac crest through a "treasure-chest-type" osteotomy approach. A strip of Gelfoam soaked in 0.25% bupivacaine was placed in the donor cavity to facilitate analgesia and hemostasis. The cartilage cap was replaced, and the incision was closed in layers.

At this point, the patient arched his back and was noted to be hypotensive (MAP 30 mm Hg and oxygen desaturation to 70%). End-tidal CO_2 rapidly decreased (Fig. 1). The patient did not respond to recruitment maneuvers or albuterol treatment. Therefore, the surgical drapes were removed and revealed a truncal rash, as well as facial edema. Intramuscular epinephrine was given, and a central venous and arterial line were placed for blood pressure monitoring and resuscitation. Cardiology came to the operating room and increased the pacemaker rate to 100 bpm with no improvement in blood pressure. A transthoracic echocardiogram demonstrated normal biventricular function. Arterial blood gas results are shown in Table 1. A tryptase level was obtained within an hour of the reaction and was 69.9 ng/mL (normal < 11.5 ng/mL).

Given the temporal association of acute hemodynamic decompensation, the leading diagnosis was anaphylaxis. Once the patient was stabilized, the surgical site was reopened, the Gelfoam was removed, and the site was copiously irrigated with normal saline. The bone graft was placed in a sterile container and banked in a freezer. The remainder of the surgery was aborted, and the patient was kept intubated due to airway edema concern. On postoperative day 1, all vasoactive pressors were weaned off, and the patient was extubated. The facial edema and truncal

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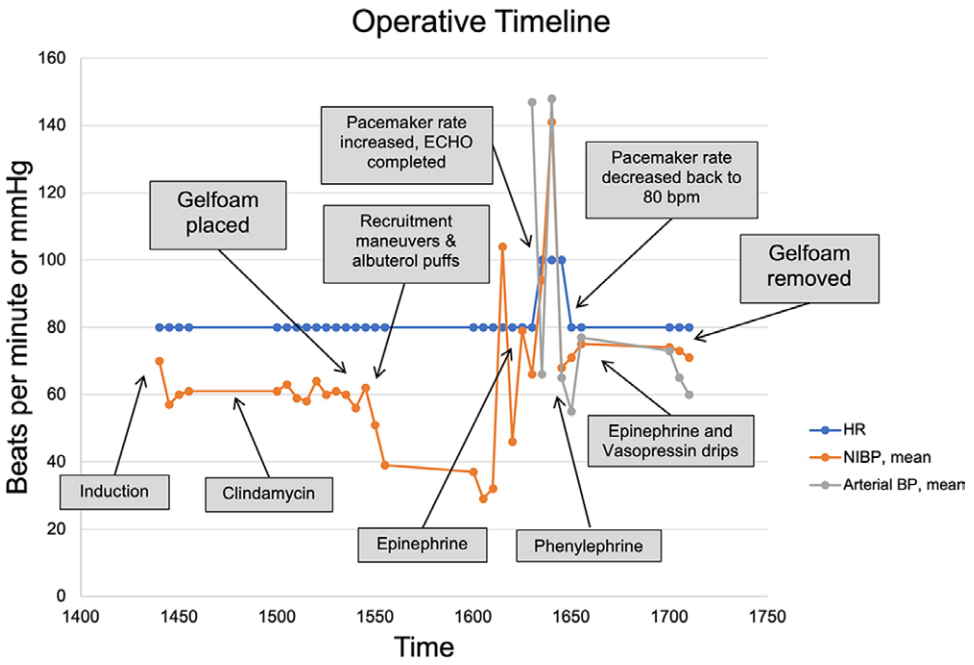

Fig. 1. A timeline illustrating the intraoperative course of events during alveolar bone grafting surgery in a 10-year-old male patient who sustained anaphylaxis after placement of Gelfoam. HR, heart rate; NIBP, noninvasive blood pressure; BP, blood pressure.

Table 1. Intraoperative Arterial Blood Gas Results

pH	7.23
$PaCO_2$	56 mm Hg
PaO_2	232 mm Hg
HCO_3	23 mEq/L
Base excess	–4.0 mml/L
SaO_2	100%
Lactate	2.20 mml/L

rash gradually resolved, and he was discharged home on postoperative day 2.

Outcome

Two weeks after surgery, the patient followed up with an allergist, and a gelatin allergy was confirmed. The patient's skin test demonstrated sensitization to porcine gelatin and had positive IgE levels to bovine gelatin (2.65 kU/L). The patient was cleared for repeat surgery with recommendation to strictly avoid all medical sources of gelatin. Two weeks later, he underwent successful grafting of his maxillary alveolus with the banked graft. At 1-month follow-up, the graft was stable, and the incisions were healing appropriately.

DISCUSSION

This case report describes rapidly identifying and accurately treating a pediatric patient with an acute intraoperative anaphylactic reaction. The incidence of intraoperative anaphylaxis is estimated to occur between one in 4000 and one in 25,000 cases, and many cases are attributed to muscle relaxants.[3] Anaphylaxis is a serious event, with mortality rates approaching 4.3% under general anesthesia.[4] Gelatin has been implicated in approximately 0.34% of perioperative anaphylaxis cases.[5] The degree of gelatin allergenicity varies greatly depending on its derived source and processing.[6] Although gelatin allergy has been well described in reactions to foods, few publications describe the anaphylactic potential of gelatin as a component in hemostatic agents.

A systematic review by White et al identified 21 cases and 19 articles reporting intraoperative anaphylaxis to gelatin-based hemostatic agents with evidence of hypersensitivity confirmed after the anaphylactic episode (ie, tryptase/IgE levels, skin prick testing).[2] Fifty-seven percent of cases involved pediatric patients, and 57% percent involved spinal surgery. Only one case also occurred during an alveolar bone grafting. Thirty-three percent of cases had a known contraindication to gelatin-based hemostat before surgery.[2] Hence, increased awareness and better identification of allergy to gelatin-based hemostatic agents is imperative to avoid life-threatening anaphylactic events.

After surgery, the patient's mother did report that the patient had indigestion with gelatin-containing foods, like Jell-O. However, previous publications reported that oral tolerance to gelatin-containing food products and vaccines did not predict hypersensitivity to Gelfoam or other gelatin-based hemostatic agents.[7] This may be attributed to the different routes of administration, with increased allergen exposure due to contact with a vascular space. This patient previously had Gelfoam applied during a dental procedure without complication. This was likely the sensitization event, inducing the formation of antibodies to gelatin antigens.

Not only is perioperative anaphylaxis to gelatin rare, but it is also likely underrecognized. This is attributable to difficulty with identification of a causative agent in the operating room, where several drugs may be given in rapid

succession. Additionally, exposure to various substances through the perioperative course further confound identification of the offending agent.[2]

Cost and product availability likely play a role in continued use of gelatin-based topical hemostatic agents. Alternative agents devoid of gelatin include absorbable products such as oxidized cellulose and microfibrillar collagen. However, cost among these products varies greatly with additional variations by region, purchase quantity, and healthcare systems.[8,9] Despite its allergenicity, Gelfoam is otherwise safe and inexpensive compared with other hemostatic agents, costing on average $85 for an 8×12.5 cm sponge, further contributing to its common and widespread use.[9]

Gelatin allergy should be suspected in cases of intraoperative anaphylaxis when topical gelatin-based hemostat agents are used. The triggering substance should be removed, and the operation should be paused or aborted. An allergist should be consulted to objectively diagnose the hypersensitivity. After the patient has been stabilized and the gelatin allergy has been confirmed, the patient may safely return to surgery, with strict avoidance of all sources of gelatin.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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