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Prolonged life-threatening anaphylaxis to Floseal during partial nephrectomy: A case report

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Abstract

Floseal Hemostatic Matrix is a topical hemostatic agent used across specialties and commonly applied to the renal bed during partial nephrectomy. Here we present the first adult case of Floseal allergy in the literature. A 62-year-old man underwent partial nephrectomy for a Bosniak type IV cyst. After unclamping the kidney, the patient declined precipitously, later determined due to an anaphylactic reaction to the Floseal placed on the renal bed. The patient had a prolonged anaphylactic reaction that required ionotropic support for over 24 h, possibly due to continued exposure. His tryptase level was elevated, and allergy testing revealed an allergy to the gelatin matrix component of the Floseal. Floseal anaphylaxis should be considered during episodes of cardiovascular collapse after drug administration. However, consideration should be given to removing it to prevent continued exposure and weighed against the risk of prolonged surgery in an anaphylactic patient.

Keywords: Allergy; Anaphylaxis; Floseal; Gelatin; Partial nephrectomy

1. Introduction

Hemodynamic instability during surgery has many causes that must be determined quickly to ensure correct management. Although rare (occurring in only 1:10,000 cases), anaphylaxis is an important cause of cardiovascular collapse during surgery.

Here we present a case of anaphylaxis to Floseal Hemostatic Matrix during robotic partial nephrectomy. Previous reports of anaphylaxis to gelatin-based products are briefly reviewed, and the intraoperative management of such cases is discussed.

Minimally invasive nephron-sparing surgery for renal tumors is now the standard of care in the developed world, with the European Association of Urology guidelines recommending it in all T1a and feasible T1b renal tumors.[1] Hemostasis of the renal bed can be a major issue in these cases, and topical hemostatic agents are commonly used in open and especially laparoscopic cases [2]; as far back as 2010, they were used in more than half of partial nephrectomies,[3] a number that is almost certainly higher now.

Allergies to gelatin-based hemostatic agents are uncommon. Here we present the first case in the literature of anaphylaxis to Floseal outside of pediatric spinal surgery (in which 7 cases have been reported to date) and, to our knowledge, the second adult reaction to any gelatin-based topical hemostatic agent. Given the widespread use of Floseal and its regular use in partial nephrectomy, surgeons and anesthetists should be aware of this important cause of intraoperative hypotension.

2. Case report

The patient was a 62-year-old man with a medical history of obesity, hypertension, and hypercholesterolemia. He had no history of allergies or atopy. He presented with an incidental finding of a 23-mm Bosniak IV cyst in the upper pole of the right kidney, for which he underwent a robotic-assisted partial nephrectomy.

Prior to this case, midazolam and antibiotic prophylaxis with cefazolin were administered. Standard monitoring was performed, including an arterial line. Propofol and fentanyl were used for induction with rocuronium for paralysis and desflurane maintenance. Tramadol and dexamethasone were administered shortly after induction. The patient was placed in the right lateral position.

The case was initially challenging due to the patient's weight and indurated vascular fat surrounding the upper pole of the kidney. A clamp was placed on a single renal artery, and the warm ischemia time was 19 minutes. The estimated blood loss until clamp removal was approximately 400 mL. Floseal was used on the renal bed for hemostasis and around the hilum due to venous ooze.

Fifteen minutes after first Floseal administration and 10 minutes after clamp removal, the robotic surgery patient cart was in the process of being undocked when the patient became hypotensive to a systolic blood pressure of 80 mm Hg that rapidly fell to 60 mm Hg. Accordingly, 4 mg of metaraminol was given in boluses without effect. Owing to concerns about major hemorrhage, the endoscope was reintroduced but found no concerning bleeding. It was then noted that the patient had an urticarial rash on the arms

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and facial swelling. No respiratory compromise or wheeze was noted. Two 100-μg boluses of adrenaline were administered with improvement in blood pressure to a systolic blood pressure of 160–170 mm Hg. The surgery was finished, and the wounds closed. During this time, the urticarial rash worsened and spread to cover the remainder of the body (Fig. 1). Three further 100-μg boluses of adrenaline were required before a central line could be inserted, and an adrenaline infusion was commenced. The patient was then admitted to the intensive care unit (ICU).

No new drugs were given for 2 hours prior to the reaction, and the last agent administered was rocuronium 45 minutes prior to surgery. Floseal was recognized as a possible causative agent during the case, and consideration was given to its removal from the renal bed, but prolonging the operation was thought to be too high a risk given the patient's hemodynamic instability.

In the ICU, the patient required adrenaline and noradrenaline infusions to maintain his hemodynamics. A PiCCO was inserted; readings indicated distributive shock with an early period of low cardiac output consistent with anaphylaxis. Transthoracic echocardiography showed normal, if hyperdynamic cardiac function. At 24 hours after ICU admission, the adrenaline was ceased; however, 25 minutes later, the patient's facial rash returned, and his oxygen saturation and blood pressure decreased. This was resolved after adrenaline was restarted at a low dose. Noradrenaline and adrenaline ceased at 32 and 34 hours post-exposure, respectively. The patient gradually improved, was extubated on day 3 post-operative, and was discharged on day 8 post-operative without further complications.

The tryptase level obtained 15 minutes after the reaction was 7.8 g/L, followed by a second reading at 5 hours post-exposure (26.2 g/L), indicating a high probability of an anaphylactic reaction. At 24 hours post-exposure, the tryptase level had fallen to 5.1 μg/L.

Follow-up testing revealed that the patient had reacted to the gelatin matrix component of Floseal. The patient consented to the publication of this case report and had been educated about future Floseal administration and gelatin-containing immunizations.

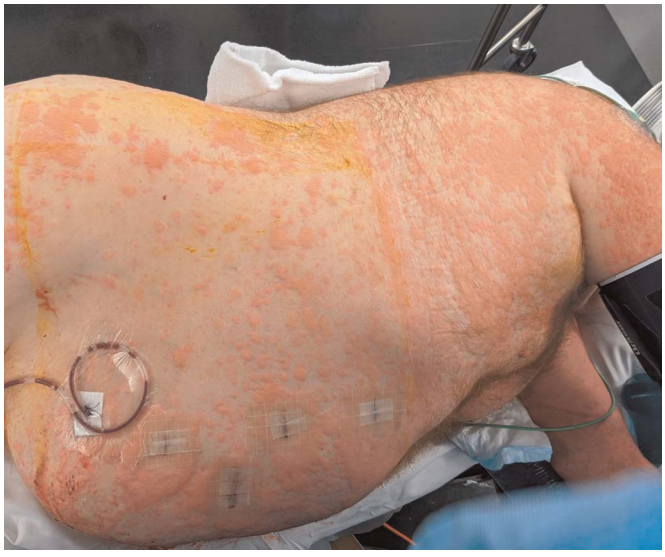

Figure 1. Cutaneous reaction following the end of partial nephrectomy.

3. Discussion

Topical hemostatic agents are increasingly used in the surgical discipline. They are particularly useful near delicate structures or in vascular tissue beds where traditional mechanical or heat-based methods of coagulation are unsuitable.[4] Floseal is composed of human plasma thrombin in combination with bovine gelatin.[4] Together, these components cause hemostasis via a combination of direct coagulant and mechanical action.

Intraoperative anaphylaxis is dangerous for a number of reasons: it is difficult to diagnose but must be promptly recognized and treated. The initial signs of anaphylaxis can be subtle, and the patient is often covered, which masks external signs and adds to the difficulty of examining them during a procedure. Multiple other causes of cardiovascular instability are potentially present, and anaphylaxis can easily be confused with excessive depth of analgesia, surgical factors such as large vessel compression, or, in this case, hemorrhage.[5] Barriers to treatment can also contribute, including surgical factors such as pneumoperitoneum, positioning, and the inability to stop the surgery at critical points. It has a mortality rate of approximately 4%, although estimates vary widely among studies with additional morbidity such as hypoxic brain injury.[6–8]

Gelatin has been widely reported as a causative agent of type 1 hypersensitivity reactions to vaccines in children, in which it is used as a stabilizer; however, in adults, reactions to it are rare.[9] The only previous adult case of a reaction to a topical hemostatic agent was reported in a patient with a pre-existing meat allergy who underwent atrial septal defect closure using a CellSaver reinfusion device to infuse blood mixed with SurgiFlo intravenously.[10] Our patient did not report a history of meat allergies.

It is unknown why there is a preponderance of cases of anaphylaxis to gelatin-containing agents in pediatric spinal surgery. However, patients who have undergone multiple operations, especially children with spina bifida, are at high risk for anaphylaxis and likely to have undergone multiple procedures using topical hemostatic agents.[11]

The patient had a prolonged reaction period following the procedure, which is not typical of anaphylaxis. Prolonged anaphylaxis, a well-described syndrome,[12] is most likely to occur when the triggering agent is orally ingested,[13] which given the ongoing nature of the exposure is probably most analogous to this clinical situation. No alternative sources of ongoing shocks were identified during or following the case.

Given this patient's prolonged high-dose inotrope requirement, consideration should be given in the future to removing the triggering product if it is safe to do so. This patient required high-dose vasopressors for an extended period instead of the more typical hours long course of anaphylaxis, possibly due to continuous exposure to Floseal on the renal bed.

At the time, in addition to concerns about prolonging the procedure it was thought that, irrigating and suctioning to remove the product would result in greater exposure in the short term; it is difficult to know if this is true and whether, given anaphylaxis' dose-independent nature,[14] this would have been a worthwhile trade-off.

Floseal is often used in situations in which the risk of bleeding is lower than that of partial nephrectomy, and, in future cases, the patient's decline may not be so precipitous. In these cases, the potential risk of bleeding and prolongation of the surgery should be considered to potentially shorten the course of illness post-operatively. This should be weighed against the fact that prolonged anaphylaxis is rare, even with ongoing exposure.[12] Little is known about whether removal of the triggering agent improves outcomes in anaphylaxis, and currently inducing vomiting or gastric lavage are not recommended for oral ingestion.[15]

4. Conclusions

Although rare, Floseal anaphylaxis should be considered in episodes of cardiovascular collapse following its administration. Consideration should be given to its removal weighed against the risk of prolonging surgery in an anaphylactic patient.

Acknowledgments

None.

Statement of ethics

As the patient directly consented for the publication of this case, this work is exempt from a Human Research Ethics Committee review at our institution. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflicts of interest statement

The authors declare no conflicts of interest in relation to this work.

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Author contributions

GM, PM: Study concept and design;
GM: Data acquisition, drafting of manuscript;
GM, DF, YL, PM: Critical revision of the manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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