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Small Bowel Obstruction After FloSeal Use

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ABSTRACT

Objective: FloSeal is a thrombin-gelatin hemostatic matrix that is used to obtain hemostasis. There have been isolated case reports of FloSeal causing bowel obstructions, requiring surgical intervention. We report 3 cases of what we believe were FloSeal-induced small bowel obstructions (SBO).

Methods: We present a series of small bowel obstructions after FloSeal use. Our series includes urology, gynecologic oncology, and general surgery cases at the same institution where the product was appropriately used and resulted in the same complication.

Results: FloSeal was used for hemostasis in all patients. In each instance, a small bowel obstruction developed in 7 days to 9 days. All patients were reexplored laparoscopically and found to have an intense inflammatory reaction at the site of the FloSeal. The adhesions were lysed and the obstructions resolved.

Conclusions: Although further study is needed, the common factor in all these SBOs was a hemostatic agent. In our and others' series, the time to SBO was 7 days to 9 days. If an early postoperative SBO occurs after FloSeal is used, prompt reexploration should be considered.

Key Words: Small bowel obstruction, Hemostatic agents, FloSeal.

INTRODUCTION

Recent advances in biotechnology have led to the development of a range of products designed to prevent intraperitoneal adhesions and excessive bleeding. Usually, hemostasis can be achieved through conventional means, such as suturing and electrocautery. But many adjuvants are available to complement these traditional methods when they fail or in a situation where they are difficult to apply. These tools include hemostatic agents that contain collagen, gelatin, and cellulose products and newer agents that contain components of the coagulation cascade. These intraoperative hemostatic agents have become increasingly used to control intraoperative bleeding in conventional surgery. In addition, these products have been adapted for laparoscopic use and are used more frequently as the complexity of minimally invasive surgery expands. When selecting an intraoperative hemostatic agent, it is important to consider adverse effects and complications due to the use of the agent. Although rare, adverse effects have been reported with the use of hemostatic agents, including anemia, atrial fibrillation, infection, rash, hypotension, respiratory distress, confusion, arrhythmias, thrombi, and fever.[1] Recently, isolated cases of small bowel obstruction (SBO) requiring surgical intervention have been reported.[2,3] These cases have been associated with the use of FloSeal Matrix Hemostatic Agent (Baxter International Inc., Deerfield, IL).

We report a multidisciplinary case series of patients who had FloSeal used and all developed small bowel obstructions. This is the third case report to our knowledge to describe this adverse event resulting from FloSeal use.

CASE REPORTS

The first patient was a 46-year-old male who underwent a laparoscopic-assisted right nephrectomy. Mild hemorrhage was noted in the renal bed, and FloSeal was used to provide hemostasis. The postoperative course was complicated with an SBO by postoperative day (POD) #7. The patient was taken for a diagnostic laparoscopy and was found to have intense inflammatory reaction of the small bowel to the renal bed with a granular material causing a transition point. This was bluntly taken down, and the obstruction resolved.

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The second patient was a 37-year-old female who underwent a laparoscopic gastric bypass. At the conclusion of the case, FloSeal was used on some bleeding near the staple line of the jejujejunostomy. On POD#8, the patient experienced vomiting and intense abdominal pain. Diagnostic laparoscopy showed bowel obstruction with the jejujejunostomy stuck to the anterior abdominal wall, causing the bowel to kink and obstruct. These granular adhesions were taken down and the obstruction resolved.

The final patient was a 63-year-old female who underwent a robotic-assisted laparoscopic hysterectomy, ureterolysis, and bilateral salpingo-oophorectomy for a benign adnexal mass. At the conclusion of the case, FloSeal was used on some bleeding near the left pelvic sidewall. On POD#2, the patient experienced nausea and vomiting, and the diagnosis of SBO versus ileus was entertained. By POD#7, it was apparent that the patient had a bowel obstruction. She was taken to the operating room for a diagnostic laparoscopy and found to have the terminal ileum stuck to the left pelvic sidewall, causing the bowel to kink and obstruct. These granular adhesions were taken down, and the obstruction initially resolved, but then recurred. The patient underwent an exploratory laparotomy on POD#14, and the same granular adhesions were found and taken down, resolving the SBO.

DISCUSSION

Laparoscopic surgery is constantly evolving. More complex procedures are being performed, and novel agents like hemostatic agents are used in these procedures. These agents are also used in open surgery, but their utility in laparoscopic surgery is probably more important, as the surgeon cannot easily stick a finger or gauze over an oozing surface. There has also been an increase in the number of hemostatic agents on the market, some of which are sold with laparoscopic applicators.

Commonly used agents include oxidized cellulose (Surgicel, Ethicon, Somerville, NJ), gelatin sponges (Gelfoam/Surgifoam, Ethicon, Somerville, NJ), and microfibrillar collagen (Avitene, Davol, Warwick, RI). All of these agents are absorbable. Biologic agents include FloSeal, CoSeal, and bovine thrombin. These various products function through different pathways but ultimately increase the body's ability to activate the clotting cascade and increase hemostasis. Thombin is a semi-pure cow thrombin that activates host platelets and fibrin but does have immunologic effects in humans. FloSeal matrix consists of a bovine-derived gelatin matrix component, and a human-derived thrombin component and needs exposure to blood to activate. CoSeal is polyethylene glycol glue that has no obvious biologic or immunologic effect. As mentioned previously, some of the adverse events caused by these agents include anemia, atrial fibrillation, infection, rash, hypotension, respiratory distress, confusion, arrhythmias, thrombi, fever, and postsurgical immune-mediated coagulopathy. Small bowel obstruction has only recently been reported in 2 other case reports, both in the gynecology literature.[2,3]

Usually, postoperative adhesions are a major source of morbidity following laparotomy and are the most common cause of small bowel obstruction in developed countries.[4] Adhesions are fibrous, sometimes vascular bands of scar tissue that connect normally separated organs or tissues and are an almost inevitable result of intraperitoneal surgery.[5] In a prospective analysis of patients undergoing laparotomy after a previous abdominal operation, Menzies and Ellis[6] found that 93% of patients had adhesions resulting from their previous surgery, compared to just 10% of patients undergoing first-time laparotomy. Previous gynecologic surgery is the second most common cause of adhesive SBO after colorectal surgery.[4,7–9] Even though postoperative adhesions are the most common cause of SBO, immediate postoperative bowel stasis in the presence of prothrombotic agents on gelatin matrix (FloSeal) is a reasonable cause for these patients' small bowel obstruction.

FloSeal Matrix Hemostatic Agent (Baxter International Inc., Deerfield, IL) is a relatively new thrombin-based hemostatic adjuvant that is extracted from bovine corneal tissue. It is a dual component system that combines the contact activation properties of a gelatin matrix with human thrombin. The gelatin granules swell as they absorb blood, and fibrin monomers polymerize along this surface. The result is a hemostatic plug that conforms to the shape of the wound. FloSeal requires premixing, activates factors V, VIII, and XIII, converts fibrinogen to fibrin, and is applied from a proprietary syringe. With its paste-like properties and relatively small applicator syringe, FloSeal is easy to use in laparoscopic surgery. Because the product relies on the presence of fibrin to become activated, FloSeal will not work if bleeding is completely absent or if the patient is deficient in fibrin (about 1/1 million people).

Gelatin-based products (like FloSeal) have been implicated as a nidus of infection and abscess formation and have been reported to potentiate bacterial growth. There has also been

a report of microscopic identification of giant cell granulomas in the brain after the use of a gelatin-based product (Gel-foam, Fibrillar, and FloSeal).[1,10,11] Giant cell reaction mimicking an abscess after cardiac surgery has been reported after Surgicel application.[12] There was also a recent report of a caseating granuloma caused by a hemostatic agent that was suspected of being a metastatic leiomyosarcoma.[13] This led to an unnecessary laparotomy.

Hobday et al[2] report an eosinophilic response causing an SBO. FloSeal was used to control hemorrhage, and an SBO resulted on POD #6. Exploration on POD #11 revealed a single area of adhesions associated with the FloSeal. Thomas and Tawfic[3] also reported a case series of 3 patients with postoperative SBO after FloSeal use. Interestingly, they also found an eosinophil-rich inflammatory response that was consistent with a type 1 hypersensitivity response. The strength of their report is that they had resected tissue to examine.

Hoffman et al[14] compared adhesion formation by hemostatic agents in a rat model. The agents studied were Arista, CoSeal, BioGlue, Tisseel, FloSeal, and Surgicel. Arista and CoSeal showed limited adhesion formation, and FloSeal, Tisseel, and Surgicel were not statistically different in adhesion formation. BioGlue promoted adhesions. Although they did not find that FloSeal increased adhesions, it was still present at 7 days in the form of the gelatin matrix. The FloSeal group also showed increased acute inflammation and collagen fibrosis.

Two important events occur in the early postoperative period: adhesiogenesis up to 14 days and the early inflammatory/healing response. The maximum inflammatory response is at 7 days to 10 days. The gelatin matrix is not completely reabsorbed for 6 weeks. There may be a relationship between gelatin matrix and the early inflammatory response that could be the causative factor in SBOs after FloSeal use. Further study is indicated, and it is incumbent on the producer to study and report these events.

Although we feel that the hemostatic agent used contributed to the SBO, there are obviously multiple factors that can affect adhesiogenesis. A combination of electrocautery and ultrasonic dissection were used in all the cases to varying degrees. The type and extent of dissection may have contributed to an increased adhesiogenesis, which could be a confounding factor in these cases. Also, our management was of aggressive and relatively early reoperation once the diagnosis was made. Some surgeons feel watchful waiting is more appropriate for SBOs, but we believe that the clinical picture and a clear transition point on CT is an indication for operation. The argument can be made that this is a resorbable material; however, the time needed to reabsorb the gelatin matrix can extend up to 6 weeks, obviously too long for observation of a bowel obstruction.

This information was presented to our local Baxter representative. We hope that a database of adverse events, funded by industry, can be created. There are very good instances to use all the hemostatic agents involved, but getting a more complete picture of possible adverse outcomes, and the situations surrounding the outcomes, will help surgeons become more comfortable at using the right agent for the right situation. We do not advocate, "throwing the baby out with the bath water," and think a nationwide database would provide even more support for the use of hemostatic agents.

CONCLUSIONS

Although further study is needed, the common factor in all these SBOs was a hemostatic agent. In our and others' series, the time to SBO was 7 days to 9 days. If an early postoperative SBO occurs after FloSeal is used, prompt reexploration should be considered.

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