

# Caseating Granulomata Caused by Hemostatic Agent Posing as Metastatic Leiomyosarcoma

Abraham R. Shashoua, MD, Diana Gill, MD, Ramon Barajas, MD, Morteza Dini, MD, Carey August, MD, Gary L. Kirschenbaum, MD, Liza Escuardo, MD

## ABSTRACT

**Background:** As the number of minimally invasive and laparoscopic procedures increases, hemostatic agents are becoming more popular as a means of achieving rapid hemostasis.

**Case Report:** The patient is a 61-year-old woman who underwent a laparoscopic supracervical hysterectomy. FloSeal Hemostatic Matrix (Baxter Healthcare, Deerfield Illinois) was used at the conclusion of the procedure.

**Results:** Pathology unexpectedly revealed high-grade leiomyosarcoma of the uterus. The patient then presented to our facility for consultation and was scheduled for robotic trachelectomy and lymphadenectomy. Laparoscopy revealed nodular lesions throughout the abdomen and pelvis. Biopsies were performed and the case aborted. Final pathology however showed caseating foreign body giant cell granulomata in all specimens. No malignancy was found. The patient then underwent exploratory laparotomy, trachelectomy, and a staging procedure. All pathology specimens and pelvic washings were negative for malignancy.

**Conclusions:** Use of gelatin-thrombin hemostatic agents may elicit a foreign body reaction leading to large giant cell granulomata. In this case, the presence of these granulomata mimicked metastatic disease.

**Key Words:** Laparoscopic hysterectomy, Hemostatic agents, Foreign body granuloma, Leiomyosarcoma.

## INTRODUCTION

Egyptians used various high-temperature cautery, waxes, and poultices to obtain hemostasis, Native Americans applied scrapings from animal hides to wounds, and the Greek scholar Hippocrates described the use of high-temperature cautery and various topical hemostatic agents to stop bleeding. In the modern era, fibrin used as a topical hemostatic agent was introduced in the early 1900s. In 1940, the use of Gelfoam in neurological procedures was popularized. More recently, multiple new products have entered the market. FloSeal Hemostatic Matrix (Baxter Healthcare, Deerfield, Illinois) consists of a bovine-derived gelatin matrix component, a human-derived thrombin component, applicator tips, and several mixing accessories. It is approved by the FDA for broad applications in surgical care as an adjunct to hemostasis when control of bleeding by ligature or conventional procedures is ineffective or impractical. There is scant literature regarding complications with the use of FloSeal.

## CASE REPORT

The patient is a 61-year-old female with a 2-year history of postmenopausal bleeding. She underwent hysteroscopic resection of a submucosal leiomyoma at the age of 59. She presented again for postmenopausal bleeding. An ultrasound showed a large 5-cm subserosal leiomyoma and several new submucosal leiomyomata. An endometrial biopsy was negative for malignancy. Cervical cytology examinations including human papilloma virus testing were negative. The patient underwent a laparoscopic supracervical hysterectomy and bilateral salpingo-oophorectomy. The specimen was removed by morcellation. According to the operative report, FloSeal was applied to the cervical stump for adhesion prevention. The specimen weighed 229 grams and showed fragments of intermediate to high-grade leiomyosarcoma. Trachelectomy and a staging procedure were advised soon after the initial surgery, but the patient desired a second opinion.

At our facility, the patient was offered trachelectomy and robotic-assisted laparoscopic staging versus exploratory laparotomy and staging. She opted for the robotic approach. Upon introduction of the laparoscope, extensive

Advocate Illinois Masonic Medical Center, Department of Obstetrics and Gynecology, Chicago, Illinois USA (Drs Shashoua, Gill, Barajas, Dini).

Advocate Illinois Masonic Medical Center & The University of Illinois at Chicago, Department of Pathology, Chicago, Illinois, USA (Drs August, Kirschenbaum, Escuardo).

Address correspondence to: Abraham Shashoua, MD, Director of Minimally Invasive and Robotic Gynecologic Surgery, Assistant Professor of Obstetrics and Gynecology, University of Illinois at Chicago, Advocate Illinois Masonic Medical Center, 3000 N Halsted St, Ste 405, Chicago, IL 60657, USA. Telephone: (773) 296-7300, Fax: (773) 296-7390, E-mail: ashashoua@yahoo.com

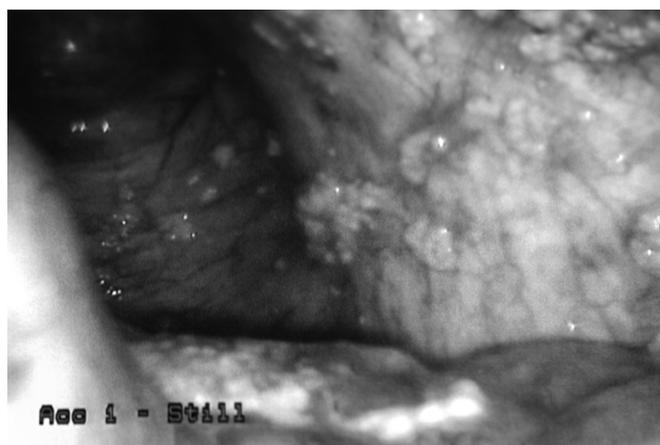
© 2009 by JLS, *Journal of the Society of Laparoendoscopic Surgeons*. Published by the Society of Laparoendoscopic Surgeons, Inc.

nodular lesions throughout the abdomen and pelvis were noted, involving the bowel, omentum, abdominal wall, and cervical stump (**Figures 1, 2, 3**). Several biopsies were obtained, and the case was aborted assuming advanced metastatic leiomyosarcoma. The final pathology revealed caseating giant cell granulomata without evidence of malignancy (**Figures 4, 5, 6**).

The patient subsequently underwent exploratory laparotomy, trachelectomy, and staging. Operative findings were unchanged from the previous procedure. The pathology revealed extensive caseating granulomata, a lower uterine segment and cervix with leiomyomata, but no evidence of malignancy. All lymph nodes and biopsies were negative. The postoperative course was uncomplicated. Adjuvant chemotherapy was offered but the patient declined.

## DISCUSSION

FloSeal Matrix Hemostatic Agent (Baxter HealthCare, Deerfield, IL) is composed of thrombin and a proprietary gelatin matrix that is manufactured by extracting collagen from bovine corneal tissue. The collagen then undergoes gelatinization and cross linking/stabilization with glutaraldehyde. This compound is ground into 500- $\mu\text{m}$  to 600- $\mu\text{m}$  particles. The thrombin component, Thrombin-JMI (King Pharmaceuticals, Inc., Bristol, TN), is of bovine origin and is supplied as a sterile freeze-dried powder that is reconstituted in 0.9% sodium chloride and mixed with the gelatin matrix in the operating room just before use. Bovine thrombin directly activates fibrinogen and converts it into fibrin monomers, bypassing the intrinsic and extrinsic systems.<sup>1</sup>



**Figure 1.** Caseating granuloma caused by hemostatic agent posing as leiomyosarcoma laparoscopic image of lesions involving cul de sac and right pelvic sidewall.

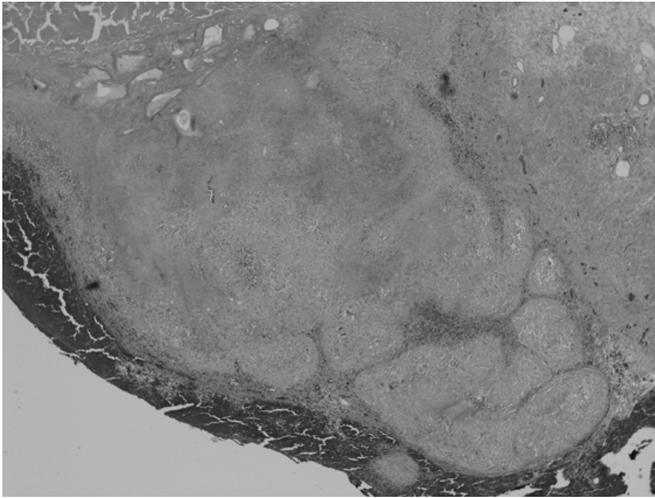
Because FloSeal contains no fibrinogen, contact with blood is required for thrombin to convert endogenous fibrinogen to fibrin. The combination of thrombin and gelatin matrix creates a granular hemostat that uses both active and mechanical components to achieve hemostasis.<sup>2</sup> As blood percolates through the matrix in the presence of bleeding, the granules swell approximately 20% within 10 minutes, conforming to the shape of the wound and forming fibrin polymers. Gelatin matrix is therefore used best as a pure hemostatic agent, not as tissue glue, urinary tract sealant, or for adhesion prevention. The matrix is applied to a source of bleeding and kept in place for approximately 2 minutes. Excess FloSeal should be removed by gentle irrigation. FloSeal is resorbed by the



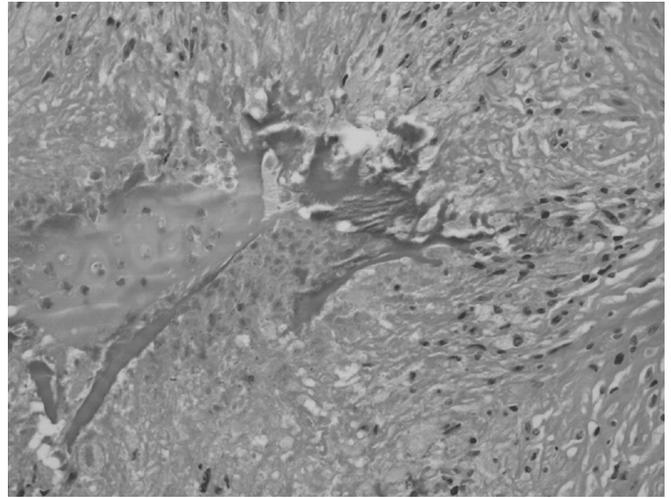
**Figure 2.** Caseating granuloma caused by hemostatic agent posing as leiomyosarcoma laparoscopic image of lesions involving right abdominal wall peritoneum.



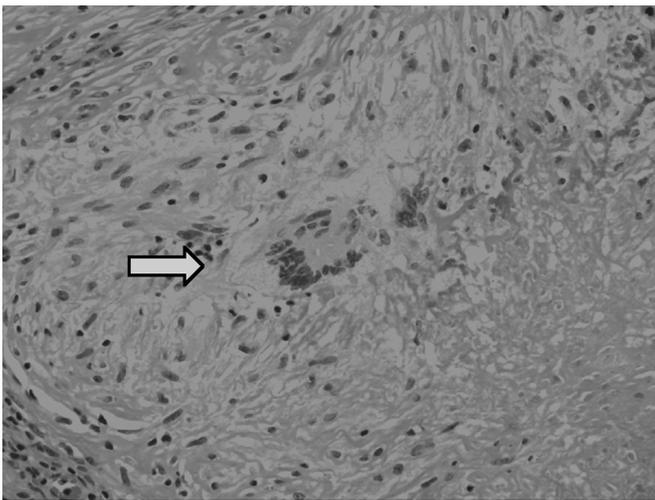
**Figure 3.** Caseating granuloma caused by hemostatic agent posing as leiomyosarcoma laparoscopic image of lesions involving cervical stump, omentum and peritoneum overlying bladder.



**Figure 4.** Caseating granuloma caused by hemostatic agent low power image of caseating granuloma.



**Figure 6.** Caseating granuloma caused by hemostatic agent pathology showing foreign material within granuloma.



**Figure 5.** Caseating granuloma caused by hemostatic agent multinucleated giant cell within granulomata.

body within 6 weeks to 8 weeks, consistent with the time frame of normal wound healing.<sup>3</sup>

Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth. Giant cell granulomas, as presented in this case, have been observed at implant sites when used in the brain.<sup>4</sup> In a case reported by Nakajima et al,<sup>5</sup> granulomatous masses secondary to microfibrillar collagen hemostat (Avitene, Davol, Inc, Cranston, RI) were thought to be metastatic mucinous cystadenocarcinoma.

## CONCLUSION

In the case presented, giant cell granulomas secondary to the use of FloSeal Hemostatic Matrix were mistaken for metastatic leiomyosarcoma. This led to cancellation of the planned procedure and need for a second procedure. This product should be used only when control of bleeding is needed and conventional procedures are ineffective or impractical. It should not be used as a prophylactic measure or for adhesion prevention. When using all gelatin-based hemostatic agents, excess material, not incorporated in the clot, should be removed to prevent foreign body reactions.

## References:

1. Oz MC, Rondinone JF, Shargill NS. FloSeal Matrix: new generation topical hemostatic sealant. *J Card Surg.* 2003;18:486–493.
2. Spotnitz WD, Burks S. Hemostats, sealants and adhesives: components of the surgical toolbox. *Transfusion.* 2008;48(7):1502–1516.
3. FloSeal [package insert]. Deerfield, IL: Baxter; 2005.
4. Knowlson GT. Gel-foam granuloma in the brain. *J Neurol Neurosurg Psychiatry.* 1974;37:971–973.
5. Nakajima M, Kamei T, Tomimatu K, Manabe T. An intraperitoneal tumorous mass caused by granulomas of microfibrillar collagen hemostat (Avitene). *Arch Pathol Lab Med.* 1995;119(12):1161–1163.