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# Practical Suggestions for Prevention of Complications Arising from Oxidized Cellulose Retention: A Case Report and Review of the Literature

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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**Conflict of interest:** None declared

**Patient:** Male, 51  
**Final Diagnosis:** Oxidised cellulose retain  
**Symptoms:** Abdominal pain • nausea • vomiting  
**Medication:** —  
**Clinical Procedure:** Laparoscopic abdominal exploration and drainage  
**Specialty:** Surgery

**Objective:** Challenging differential diagnosis

**Background:** Bleeding is a major intraoperative complication during surgical procedures. When conventional methods such as ligation and diathermocoagulation are ineffective for bleeding management, hemostatic agents should be used. Oxidized cellulose is one of the major hemostatic agents used worldwide. Oxidized cellulose is often left *in situ* after hemostasis because of its high level of reabsorption that lasts up to 8 weeks. However, 38 cases of retaining-associated complications are reported in the literature.

**Case Report:** A 51-year-old male patient presented in our emergency department with acute abdominal pain, nausea, and vomiting. The patient had been admitted in our department for laparoscopic cholecystectomy for acute cholecystitis 25 months previously. Abdominal ultrasound and CT scan showed the presence of a cystic circular mass, with homogeneous fluid content, close to the surgical clips of the previous surgery, resembling a “neogallbladder”. Laparoscopic abdominal exploration and drainage were performed. Histological examination reported protein-based amorphous material with rare lymphocytes and macrophages. Culturing was negative for bacterial growth. The patient was discharged uneventfully on the 4<sup>th</sup> postoperative day. The primary surgical report was evaluated with evidence of application of Gelita-Cel® Standard for hemostatic purposes. Results of 12-month follow-up were normal.

**Conclusions:** Herein, we report the first case of a complication associated with the use of Gelita-Cel® Standard. We reviewed the literature to better define the purpose and limits of oxidized cellulose use as a hemostatic agent. Despite the fundamental role of oxidized cellulose as a hemostatic agent, we provide some practical suggestions to prevent the reported severe complications and surgical overtreatments.

**MeSH Keywords:** Cellulose, Oxidized • Cholecystectomy, Laparoscopic • Diagnosis, Differential • Hemostasis, Surgical • Postoperative Complications

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## Background

Successful hemostasis has always been fundamental in all surgical procedures. Ligature and diathermocoagulation are the main hemostatic methods; however, since 1909, with the use of fibrin [1], numerous hemostatic agents (HA) have become available. In 1945, oxidized cellulose (OC) was introduced in surgery and it has become one of the major HAs because of its ease of use, favorable biocompatibility, and bactericidal properties [2–4]. Several OCs are available and classified in regenerated oxidized cellulose (ROC; e.g. Surgicel® – Johnson and Johnson, Somerville, NJ, USA) and non-regenerated oxidized cellulose (nROC; e.g., Oxycell® – Becton Dickinson, Franklin Lakes, NJ, USA). Although the manufacturers recommend the OC removal after its use, it is generally left *in situ* because of its high level of reabsorption that lasts up to 8 weeks. However, several cases of retained OC with severe complications have been reported in the literature. Here, we describe a complication that was associated with the use of Gelita-Cel® Standard (ROC; Gelita Medical, Eberbach, Germany) and we review the literature to better define the purpose and limits of OC as a hemostatic agent.

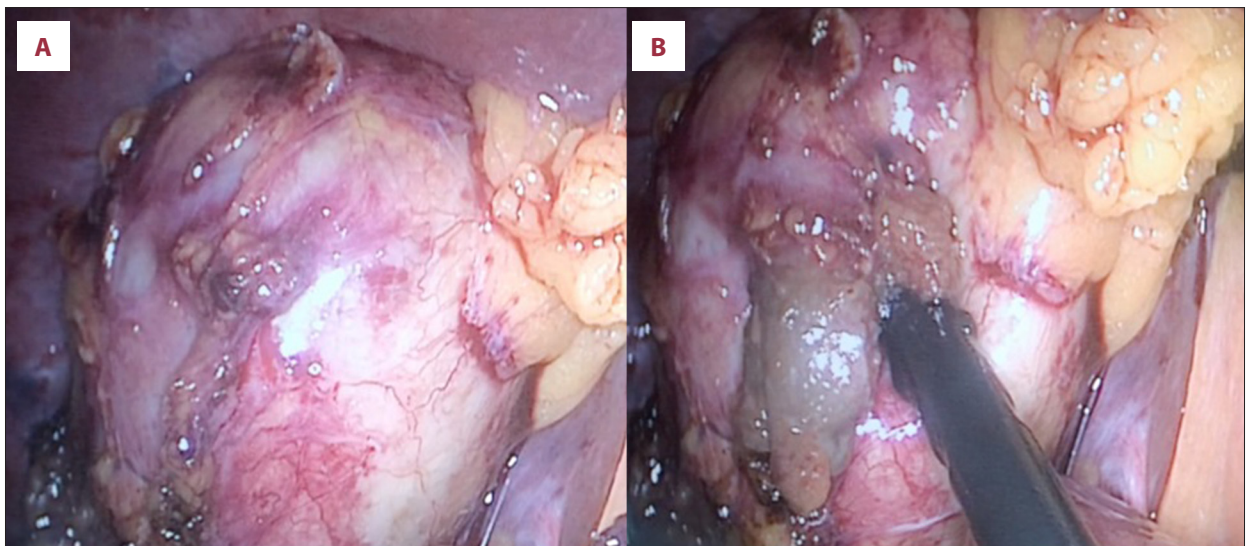
## Case Report

A 51-year-old male patient presented in our emergency department with acute abdominal pain, nausea, and vomiting. Laboratory test results were normal with no evidence of inflammation markers (white blood cells:  $8.03 \times 10^3/\mu\text{l}$ ; neutrophils: 68.2%; C reactive protein: 3 mg/l). He had been admitted to our department for laparoscopic cholecystectomy for acute cholecystitis 25 months previously. The patient complained of moderate abdominal pain since his first operation; therefore, he had abdominal CT scan at 6 months, showing evidence of



**Figure 1.** Cystic lesion with homogeneous fluid content close to surgical clips resembling a “neo-gallbladder” (white arrow).

a circular mass (39×34 mm) with fluid content (density 35–45 HU). In addition, an abdominal US at 24 months showed a non-vascularized mass in the liver bed that was suspected to be a granuloma. The patient was admitted for an abdominal CT scan and the results confirmed a circular cystic mass with homogeneous fluid content, close to the surgical clips of the previous surgery, resembling a “neo-gallbladder” (Figure 1). Although the patient had no signs of inflammation or infection, a hepatic abscess was suspected based on imaging results and previous surgical history. To better define the patient’s unclear clinical condition, we chose to perform a surgical drainage instead of a percutaneous (US- or CT-guided). Therefore, the patient underwent laparoscopic abdominal exploration, incision of the hepatic bed mass, and drainage of amorphous, brown, dense material (Figure 2). A drain was left in the liver bed and



**Figure 2.** (A) Intraoperative image of “neo-gallbladder”; (B) drainage of amorphous material.

**Table 1.** Imaging features of OC retention.

Technique	Main characteristics
US	<ul style="list-style-type: none"> <li>– Complex mass</li> <li>– Well-encapsulated hypoisoechoic lesion</li> <li>– Circumscribed margins</li> <li>– Internal hyperechoic nodules (“ile-flottante”)</li> <li>– Perilesional vascularization (Doppler)</li> </ul>
CT scan	<ul style="list-style-type: none"> <li>– Mixed-/low-attenuation mass</li> <li>– Focal central collection of gas</li> <li>– Absence of air-fluid levels</li> <li>– Peripheral faint enhancement</li> <li>– Proximity to the surgical site</li> </ul>
MRI	<ul style="list-style-type: none"> <li>– Nonspecific</li> <li>– Hypointense stripes inside cystic-like cavity on T2</li> </ul>
PET/CT	<ul style="list-style-type: none"> <li>– Image with high glucose uptake</li> <li>– False-positive</li> </ul>

was removed on the 2<sup>st</sup> postoperative day. Histological examination reported protein-based amorphous material with rare lymphocytes and macrophages. Culturing was negative for bacterial growth. After antibiotic prophylaxis with extended spectrum B-lactam, the patient was discharged without symptoms on the 4<sup>th</sup> postoperative day. The primary surgical report was evaluated for evidence of use of Gelita-Cel<sup>®</sup> Standard for hemostatic purposes. The 12-month follow-up was uneventful.

## Discussion

Bleeding can be a major intraoperative complication during surgical procedures. When conventional methods such as ligature and diathermocoagulation are ineffective for bleeding management, hemostatic agents (HA) can be used. In 1909, fibrin was described as an effective HA [1] and since then numerous hemostatic devices have been used such as topical thrombin, porcine collagen, and OC [5]. OC was first used for medical purposes in 1945 [2,3], and since then it has been widely used in surgery, with several forms available. OC is easy to use and has good biocompatibility and bactericidal properties [4]. OC is made of cellulose, which is a homopolysaccharide of glucopyranose polymerized through  $\beta$ -glucosidic bonds [6,7]. Cellulose can be either regenerated to form organized fibers or non-regenerated with unorganized fibers prior to oxidation. When cellulose fibres are oxidized, conversion of hydroxyl groups to carboxylic acid groups occurs, yielding polyuronic acid [6,7]. The low pH of the carboxylic acid groups is responsible for several actions: primary local hemostyptic action, secondary platelet activation to form a temporary platelet plug [6,7], and hostile acidic environmental conditions for bacterial survival [8]. Moreover, the knit structure and thickness of the gauge is responsible for bactericidal properties, with thinner loose-knit

patterns being less effective than thicker tight-knit patterns against antibiotic-resistant microorganisms [9].

Oxidized regenerated cellulose (ROC) is a re-absorbable material that can be intentionally left in the surgical field. *In vivo* studies on rats were performed to analyze the tissue reaction to locally implanted hemostatic agents [10]. ROC absorption starts after 24–48 h; at day 7 the gauze is surrounded by inflammatory granulation tissue, and complete degradation occurs between 4–8 weeks [6,10,11]. However, absorption is not always complete, with consequent gauze retention as first described by Vanderhoof et al. [12]. Therefore, it is common for ROC to appear as a mass during the immediate postoperative period, mimicking a postoperative abscess [13], tumor [14], or hematoma [15], posing a serious challenge in differential diagnosis [16].

On CT scan, a retained OC may appear as a mixed- or low-attenuation mass containing a focal central collection of gas, located inside or near the operative site, with a faint enhancement at the mass periphery and absence of air-fluid levels [13,17,18] (Table 1). Over time, the central collection of air is completely replaced by soft tissue, leading to the formation of a foreign-body granuloma [13].

MRI findings are nonspecific, but the presence of hypointense stripes inside a cystic-like cavity on T2-weighted images is considered to be a characteristic sign of ROC-associated granuloma [19].

PET/CT images may produce false-positive results in case of foreign body granuloma as a consequence of localized inflammation, mimicking malignant tissue glucose uptake [20–22].

Retained OC is frequently found in ultrasound imaging (US) as a complex mass or well-encapsulated hypo-isoechoic lesion with circumscribed margins and internal hyperechoic nodules at the surgical site [23]. The presence of hyper-isoechoic nodules within a complex cystic mass can be explained as typical granulomatous foreign body reaction induced by the presence of ROC and was described by Giuliani et al. as “ile-flottante” [23,24]. Moreover, the use of color/power Doppler should be considered as part of the ultrasound procedure. A perilesional vascularization is probably indicative of compression exerted by OC on neighboring tissues or connected to the presence of granulation tissue around the surgical site [25,26]. Nevertheless, imaging can be useful and clinical evaluation is fundamental in confirming diagnostic suspicion.

We reviewed the literature and retrieved a total of 28 papers comprising 38 cases of OC retention. The details of cases are shown in Table 2. Surgical sites included: brain (6), cervical spine (1), thoracic spine (1), thorax (10), abdomen (12), and

**Table 2.** Reported cases of OC retaining complications in the literature.

Author	Year	Age	Sex	Device	Surgical Site	Primary diagnosis	Primary surgery	Time (days)	Symptoms	Suspect	Removal
Dutton et al. [32]	1983	35	M	Surgicel	Brain	Head injury	Frontotemporal skull and lacerated left frontal lobe repair	2,5 h	Vision impairment	Hematoma	Yes
Perez-Guerra et al. [31]	1984	59	F	Surgicel	Thorax	Squamous cell carcinoma	Left pneumonectomy	2 h	Paraplegia	Cord compression	Yes
Ito et al. [39]	1989	n.a.	n.a.	OC	Brain	Intracranial meningioma	Intracranial meningioma removal	390	Incidental	Large granuloma	Yes
Ito et al. [39]	1989	n.a.	n.a.	OC	Brain	Intracranial meningioma	Intracranial meningioma removal	630	Incidental	Large granuloma	Yes
Ito et al. [39]	1989	n.a.	n.a.	OC	Brain	Anterior communicating artery aneurysm	Vascular treatment	n.a.	Incidental	Large granuloma	Yes
Short [28]	1990	72	F	OC	Thorax	Bronchogenic carcinoma	Right upper/middle lobectomy	few days	Paraplegia	Cord compression	Yes
Short [28]	1990	49	M	OC	Thorax	Lung adenocarcinoma	Right upper lobectomy	2	Paraplegia	Cord compression	Yes
Short [28]	1990	59	M	OC	Thorax	Bronchogenic carcinoma	Right lower lobectomy	3,5 h	Paraplegia	Cord compression	Yes
Bradley et al. [40]	1991	58	M	Oxycel	Abdomen	Cholecystitis	Cholecystectomy	120	Incidental	Abscess/Hematoma	No
Deger et al. [41]	1995	71	F	Surgicel	Abdomen	Ovary serous adenocarcinoma	Ovariectomy	150	Abdominal discomfort	Tumor recurrence	Yes
Sandhu et al. [42]	1996	n.a.	n.a.	Surgicel	Brain	Intracranial meningioma	Intracranial meningioma removal	60	Incidental	Tumor recurrence	Yes
Sandhu et al. [42]	1996	n.a.	n.a.	Surgicel	Brain	Intracranial meningioma	Intracranial meningioma removal	360	Incidental	Tumor recurrence	Yes
Iwabuchi et al. [43]	1997	46	F	Surgicel	Thorax	n.a.	Right lower lobectomy	1	Paraplegia	n.a.	Yes
Concha et al. [37]	1997	41	F	Surgicel	Abdomen	Kidney failure	Kidney transplant	570	Fever, abdominal pain, renal function impairment	Granuloma/neoplasia	Yes, allograft extirpation
Banerjee et al. [44]	1998	28	M	Surgicel	Spinal	Disk degeneration, spinal stenosis	Spinal decompression	2	Cauda equina syndrome	Cord compression	Yes
Lovstad et al. [29]	1999	56	F	Surgicel	Thorax	Lung tumor	Left lower lobectomy	2,5 h	Paraplegia	Cord compression	Yes
Azmy [35]	2001	2	M	Surgicel	Abdomen	Neuroblastoma	Right adenectomy	4	Incidental	Tumor recurrence	Yes
Ibrahim et al. [45]	2002	53	F	Surgicel	Thorax	Aortic root aneurysm	Aortic root replacement	42	Incidental	Abscess	Yes
Gao et al. [46]	2002	37	F	Surgicel	Pelvic	Hemoperitoneum, ruptured corpus luteum	Hysterectomy, right salpingo-oophorectomy	30	Abdominal pain, vaginal discharge	Granuloma	Yes
Brodbelt et al. [27]	2002	37	F	Surgicel	Thorax	Metastatic sarcoma	Lung lobectomy	1	Paraplegia	Extradural mass	No

**Table 2 continued.** Reported cases of OC retaining complications in the literature.

Author	Year	Age	Sex	Device	Surgical Site	Primary diagnosis	Primary surgery	Time (days)	Symptoms	Suspect	Removal
Brodbelt et al. [27]	2002	50	M	Surgicel	Thorax	Thoracic trauma	Thoracic surgery	3	Weakness/ numbness right leg	Extradural mass	Yes
Brodbelt et al. [27]	2002	15 (m)	M	Surgicel	Thorax	n.a.	Cardiac surgery	2	Flaccid paraparesis, extradural mass	Extradural mass	Yes
Farina Perez et al. [47]	2004	63	F	Surgicel	Abdomen	Renal cell carcinoma	Laparoscopic partial necrectomy	8	Incidental	Gas collection	No
Somani et al. [34]	2005	62	F	Surgicel	Abdomen	Myelofibrosis	Splenectomy	540	Renal tumor suspect	Kidney tumor	Yes, necrectomy
Arnold et al. [38]	2007	55	M	Surgicel	Abdomen	n.a.	Cholecystectomy	4	Abdominal pain	Postoperative abscess	No
Salmo et al. [48]	2009	n.a.	M	Oxycel	Abdomen	Rectal cancer	Colon resection	90	Incidental	Tumor recurrence	Yes
Agarwal et al. [49]	2010	47	M	Surgicel	Abdomen	Renal cyst	Laparoscopic nephron-sparing surgery	90	Incidental	Kidney mass	No
Royds et al. [36]	2012	56	F	Surgicel	Cervical	Multinodular goiter	Total thyroidectomy	30	Wound swelling	Suture abscess	Yes
Tefik et al. [50]	2012	50	F	Surgicel	Abdomen	Cystic papillary renal cell carcinoma	Laparoscopic nephron-sparing surgery	180	Incidental	Heterogeneous mass	Yes
Wang et al. [51]	2013	83	M	Surgicel	Abdomen	GIST	Recurrent GIST	120	GIST recurrence	Heterogeneous mass	Yes
Behbehani et al. [52]	2013	47	F	Surgicel	Pelvic	Uterine leiomyoma	Laparoscopic total hysterectomy, bilateral salpingo-oophorectomy	21	Pelvic pain, fever	Postoperative abscess	No
Behbehani et al. [52]	2013	46	F	Surgicel	Pelvic	Uterine leiomyoma and adenomyosis	Laparoscopic total hysterectomy	10	Abdominal pain, fever	Postoperative abscess	Yes
Tam et al. [53]	2014	50	F	Surgicel	Pelvic	Endometriosis	Laparoscopic hysterectomy	6	Pelvic pain	Gas collection	No
Tam et al. [53]	2014	45	F	Surgicel	Pelvic	Endometriosis	Robotic-assisted laparoscopic hysterectomy, left salpingo-oophorectomy, right salpingectomy, appendectomy	10	Abdominal pain, vaginal discharge	Abscess	No
Tam et al. [53]	2014	43	F	Surgicel	Pelvic	Endometriosis	Laparoscopic hysterectomy, left oophorectomy, bilateral salpingectomy	4	Malaise	Abscess	No
Zhang et al. [54]	2015	21	F	Surgicel	Pelvic	Symptomatic ovarian cyst	Ovarian cystectomy	7	Pelvic pain	Heterogeneous mass	No
Cormio et al. [55]	2016	67	F	Surgicel	Pelvic	Cystocele, anterior genital prolapse	Pubovaginal sling, cystocele repair	180	Irritative voiding symptoms	Ovarian cancer	Yes
Singh et al. [56]	2016	71	M	Surgiflo	Abdomen	Clear cell carcinoma	Left robotic partial nephrectomy	30	Nodular lesion	Recurrence/residual tumor	No

pelvis (8). Twenty-nine patients received Surgicel®, 2 received Oxycel®, 1 received Surgiflo® (Johnson and Johnson, Somerville, NJ, USA), and 6 received non-specified OC (Table 2). Here, we report the first case of complications due to Gelita-Cel® retention.

The preoperative diagnosis and surgical procedure are described in Table 2. The times from primary surgery to detection of retained OC ranged between 2 hours and 630 days. Twelve cases were incidental and the others were symptomatic. Various symptoms were described, ranging from malaise and fever to paraplegia, cauda equina syndrome, and vision impairment. Diagnostic suspicion was tumor recurrence (6), abscess (7), cord compression (6), granuloma (4), extradural mass (3), heterogeneous mass (3), gas collection (2), kidney tumor (2), ovarian cancer (1), hematoma (1), abscess/hematoma (1), granuloma/neoplasm (1), and non-specified lesion (1). Gauze removal was performed in 27 cases. In 2 patients, removal of the gauze required a major procedure: 1 patient underwent nephrectomy and another had allograft extirpation that resulted in need for dialysis.

Despite the fundamental importance of OC as an essential hemostatic agent in surgery, some precautions are needed to avoid future complications. Although 38 cases, in addition to our reported case, are very few compared to all surgical procedures performed with OC use with no associated complication, complications may also be severe and associated with risky surgical procedures.

Our review of the literature found that 8 patients experienced paraplegia, which occurred between 2 hours and 2 days after thoracic surgery [27–29]; cord compression was suspected and urgent laminectomy was performed, revealing a mass of Surgicel® in the extradural space. A surgical report showed the use of OC to control difficult bleeding from the posterior angle of the thoracotomy incision. The posterior end of the rib adjacent to the gaping thoracostomy is usually a bleeding site that is hard to manage. During thoracostomy closure, the rib approximation may produce a compressive force on the OC, forcing it to migrate into the adjacent foramen. The established negative pressure of the intravertebral subdural space can enhance this pressure gradient and cause OC herniation with consequent symptomatology [26]. Product information warns against leaving OC *in situ* next to foramina after hemostasis due to swelling, which can result in nerve damage due to pressure in a bony confined area [30]. However, there is no report regarding the potential of material migration. Five out of 6 patients presented with total motor and sensory deficit, with extension according to the cord compression site [27–29]: one had spastic monoplegia involving the right leg [28], one patient has to use a cane to walk [27], and one has walking impairment requiring leg braces and obligatory catheterization [27].

In circumstances requiring extensive dissection in the costovertebral angle, precise technique is imperative. Uncontrolled or poorly controlled bleeding in an intervertebral foramen should be an indication for consultation of a neurological surgeon.

Dutton et al. [32] reported a case of compressive optic neuropathy after OC migration from the anterior cranial fossa into the orbital apex through an orbital roof fracture. Banerjee et al. [33] reported a case of cauda equina syndrome treated with OC removal and consequent severe impairment of quality of life. To avoid major complications, particular attention must be paid to hemostatic control in rigid inextensible anatomical structures such as the skull and spinal cord.

In 9 cases, tumor mass or neoplasm recurrence was suspected, with consequent resective treatment. Somani et al. [34] reported a case of clinically/radiologically suspected renal cell carcinoma in a patient who previously underwent splenectomy for myelofibrosis, evidenced as a heterogenous kidney mass formation on abdominal CT scan with paraortic lymphadenopathy. Nephrectomy was performed, but histology did not show a neoplasm and instead found a foreign-material granuloma. This is an important case of retained OC mimicking a neoplasm. Azmy et al. [35] reported a case of OC removal in a patient suspected to have a recurrence of neuroblastoma.

Royds et al. [36] documented the first case of local tissue reaction associated with Surgicel® in head and neck surgery, with removal and resolution confirming its cause. Concha et al. [37] reported a case of xanthogranulomatous pyelonephritis caused by OC retention in a renal allograft, with consequent extirpation of the allograft and return to dialysis in a 41-year-old patient. Arnold et al. [38] documented an abscess mimicking a mass following cholecystectomy and liver biopsy.

Among all 38 cases described, plus our reported case, 11 patients were treated conservatively due to suspicion of an OC-retaining lesion after surgical history evaluation and multidisciplinary analysis by surgeons and radiologists. Although retained OC has been described by many authors [27–29,31,32,34–56], we believe it is important to focus on the cases in which there were severe complications in order to form some conclusions and recommendations

The manufacturers recommend OC removal after hemostasis is obtained. If the surgeon decides to leave an OC gauze *in situ*, it should be used sparingly, as many problems have been attributed to excessive use [45]. If OC is left *in situ*, the surgical report and the discharge document should state it in order to correctly inform the patient in detail about this condition.

In surgical procedures in rigid inextensible anatomical structures as the skull, spinal cord, and pleural cavity (in proximity

**Table 3.** Practical suggestions for safe use of OC.

Practical suggestion
– Remove OC after hemostasis
– If left <i>in situ</i> , use it sparingly
– Report the use of OC in the surgical report
– Inform the patient about OC retention
– Use extreme care in rigid non-extensive anatomical structures (eventual neurosurgical aid)
– Accurate surgical history evaluation

to the spine), OC should be used with extreme care and, if possible, neurosurgical support should be used for better and safer hemostasis [32] (Table 3).

Moreover, when a mass is observed, accurate imaging evaluation and surgical history are required to assess a possible retained granulomatous lesion and to provide the best medical/surgical treatment.

Further studies are needed to determine if layer versus coiled disposal of oxidized cellulose may have a role in complications and to assess whether fibrillar oxidized cellulose is safer than the gauze form. Our surgical case report is fully compliant with the SCARE criteria [57].

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## Conclusions

Bleeding is a major intraoperative complication during surgical procedures. OC is an effective aid in hemostasis when ligature and diathermocoagulation are ineffective. Despite biocompatibility and reabsorption, cases of retained OC complications have been described in the literature. OC should be removed when hemostasis is obtained. If necessary, only a small quantity of OC should be placed *in situ* and it should be documented in the surgical report and the discharge document in order to correctly inform the patient. Accurate surgical history evaluation should always be performed, and multidisciplinary case evaluation between surgeons and radiologists should be done to achieve a more accurate diagnosis and prevent unnecessary revision surgery or further medical and/or surgical interventions. In case of surgical procedures with hemostatic control in rigid inextensible anatomical structures such as the skull and spinal cord, OC should be used with extreme care in order to avoid major complications and, if possible, neurosurgical support should be used for better and safer hemostasis. We also presented the first case of a complication following Gelita-Cel® retention in a case of “neo-gallbladder”. Our aim here is not to criticize the use of OC as hemostatic agent – it has well-documented effectiveness in surgery – but rather to provide some practical suggestions on how to avoid the severe complications reported in the literature.

## Conflicts of interest

None.

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