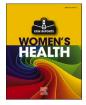


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Complicated pancreatic fistula after gynecologic surgery for left fallopian tube carcinosarcoma: A case report

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ARTICLE INFO	A B S T R A C T
Keywords: Pancreatic fistula Fallopian tube cancer Diagnostic laparoscopy Metal colonic stent Case report	Pancreatic fistulas are rare after gynecologic surgeries but are sometimes difficult to manage. A 62-year-old woman was admitted to a local hospital with acute abdominal pain. Computed tomography (CT) images showed subileus and an obstruction site in the transverse/descending colon, with invasion of peritoneal metastasis. A metal stent was placed in the bowel through colonoscopy. Suspecting advanced-stage ovarian cancer, the patient was referred to a tertiary hospital. Diagnostic laparoscopy was performed prior to neo-adjuvant chemotherapy. Due to concerns raised by gastrointestinal surgeons regarding the high risk of stent perforation during chemotherapy, an abdominal colectomy of the transverse/descending colon was performed along with the removal of the disseminated tumor and the stent. Post-surgery, the patient was histologically diagnosed with stage IVB left fallopian tube carcinosarcoma. On postoperative day 3, the patient developed a fever, and CT images showed an abscess around the pancreas/spleen, prompting the placement of a drainage tube. The amylase level in the drained fluid was 258,111 U/L, leading to a diagnosis of a pancreatic fistula. Conservative management was undertaken, with drainage, fasting, and octreotide administration. After two months, the drainage tube was removed as the volume of drained fluid had decreased. After four cycles of carboplatin/paclitaxel chemotherapy, CT images showed partial response to chemotherapy, and interval debulking surgery was performed. The necessity of metallic stent placement should be carefully considered as the subileus caused by peritoneal metastasis might be alleviated by the induction of chemotherapy for gynecologic cancer.

1. Introduction

Ovarian, fallopian tube, and primary peritoneal cancers are among the most lethal gynecologic malignancies and are often diagnosed at advanced stages, including peritoneal dissemination [1]. Debulking surgery combined with platinum-based chemotherapy remains the gold standard treatment for these diseases. As the residual tumor size after surgery is the most important prognostic factor [2], complete cytoreductive surgery, including resection of metastases, is considered ideal and is occasionally performed.

Although rare, some cases require pancreatectomy during gynecologic surgery, resulting in a complicated postoperative pancreatic fistula (POPF). POPF is a frequent complication after distal pancreatectomy (DP) [3]. It can cause abdominal abscesses, organ failure, and increased mortality [4]. This article discusses a case of complicated POPF after fallopian tube carcinosarcoma surgery without pancreatectomy or splenectomy.

2. Case Presentation

A 63-year-old Japanese woman was admitted to a local hospital with acute abdominal pain. The patient's medical history included acute appendicitis and bilateral breast cancers. Her mother and sister also had a history of breast cancer. Computed tomography (CT) showed subileus and obstructions of the transverse/descending colon with adjacent peritoneal metastases. A metal stent (Niti-S 22 \times 60 mm; Century Medical, Inc., Tokyo, Japan) was placed in the narrow bowel by the gastroenterologist through colonoscopy.

Subsequently, because ovarian cancer was suspected, the patient was referred to a tertiary hospital. Preoperative ¹⁸F-fluorodeoxyglucose

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(FDG)-positron emission tomography(PET)/CT revealed a 5 cm tumor in the left adnexa, disseminated peritoneal metastases, multiple lymph node metastases (right cardiophrenic and supradiaphragmatic lymph nodes), and the invasion of the transverse/descending colon by a 7 cm disseminated omental tumor, with the metal stent in place (Fig. 1A). The patient was preoperatively diagnosed with stage IVB (International Federation of Gynecology and Obstetrics (FIGO) 2014 system) ovarian cancer. Because complete surgical resection was considered to be challenging in this case, diagnostic/staging laparoscopy, including tumor biopsy, before neoadjuvant chemotherapy was planned. Before laparoscopic surgery, discussions with gastroenterologists concluded that removing the metal colonic stent by colonoscopy would be difficult and risky. The stent, which had been placed for more than one month, was believed to be firmly adherent to the colon.

Diagnostic/staging laparoscopy observing the overall intraperitoneal cavity was conducted, calculating a Fagotti score [5] of 8 points (2 points each for peritoneal carcinomatosis, diaphragmatic involvement, mesenteric retraction, and bowel infiltration) (Fig. 1B). Based on the preoperative CT of the thoracic lymph nodes and the laparoscopic findings, laparoscopic left salpingo-oophorectomy and biopsy for peritoneal metastases were performed, because complete cytoreduction was considered impossible. Following the suggestions of gastrointestinal surgeons regarding the high risk of intestinal perforation under chemotherapy with the stent inserted, and their strong recommendation

for the resection of the transverse/descending colon invaded by omental metastases, bowel resection and open colostomy of the transverse colon were performed (Fig. 1C). The stent insertion site in the colon was significantly narrower (Fig. 1D). The operative time was 352 min, and blood loss was 1500 mL. The surgery was suboptimal, with numerous residual abdominal diseases (including tumors of 7 cm in the omentum near the spleen, 5 cm in the Douglas fossa, 4 cm in the vesicouterine pouch, 3 cm in the omentum, and miliary lesions affecting the diaphragm and peritoneum).

Postoperative histopathology revealed a left fallopian tube carcinosarcoma (homologous type) and FIGO stage IVB. MyChoice® CDx (Myriad Genetics, Inc., Salt Lake City, UT) homologous recombination deficiency (HRD) companion diagnostic test using the left fallopian tube tumor revealed HRD positive, genomic instability score 60, and pathogenic t*BRCA2* (c.5576_5579del(p/lle1859Lysfs:3)) variant. BRACAnalysis CDx® (Myriad Genetics, Inc.) germline companion diagnostic test with the blood sample confirmed the same g*BRCA2* variant. Thus the treatment plan was for the patient to receive 3–4 cycles of triweekly paclitaxel (175 mg/m²) plus carboplatin (area under the curve 5) (TC regimen) as neoadjuvant chemotherapy before interval debulking surgery (IDS).

On postoperative day (POD) 3, the patient experienced a high fever (38.2 °C). Laboratory investigations indicated leukocytosis (19,760/ μ l) and an elevated C-reactive protein level (19.7 mg/dl). Given the clinical

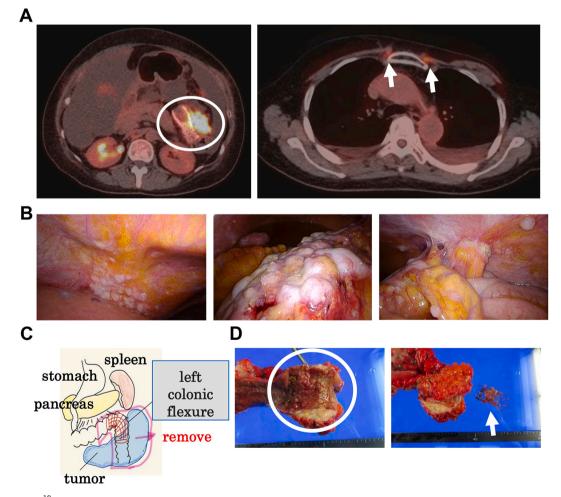
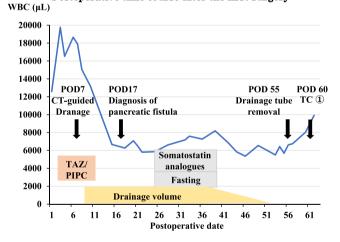


Fig. 1. A. Preoperative ¹⁸F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT. (Left) The white circle shows a metal stent in the transverse/ descending colon near the disseminated omental tumor. (Right) White arrows indicate metastasis of the parasternal lymph nodes. B. Laparoscopic findings at the primary surgery. Disseminated peritoneal carcinomatosis is seen at the left diaphragm (left), the omentum (middle), and mesentery (right). C. Schema of the abdominal colectomy of the transverse/descending colon including the disseminated tumor and the stent. The tumor at the left colonic flexure was located near the pancreas and spleen. D. Macroscopic images of the resected transverse/descending colon. The metal stent insertion site was very narrow, and the metal stent adhered to the colon wall (left, circle). The removed metal stent (right, arrow).

diagnosis of peritonitis following surgery, the administration of antibiotics (tazobactam and piperacillin hydrate) was initiated (Fig. 2). On POD 4, CT revealed suspected intra-abdominal abscesses around the spleen and pancreas (Fig. 3) and left pleural effusion. On POD 7, a repeat CT revealed enlargement of the abscess. In response, through an interventional radiology approach, a drainage tube was placed. The drained fluid appeared serous without any bacteria. Although the patient's condition and inflammation rapidly improved following initiation of drainage, the drained volume remained around 100 mL/day. On POD 17, the color of the drainage fluid changed from brown to blood-stained. The amylase level in the abscess fluid was 258,111 U/L and the patient was diagnosed with POPF. Given the persistent drainage, fasting with parenteral nutritional support was considered with subcutaneous octreotide acetate (somatostatin analog, 5 µg/kg, three times per day) on POD 26. The drainage volume reduced gradually, and enteral nutrition was resumed on POD 39. The drainage tube was clamped on POD 53 and removed on POD 55.

However, the thoracic and abdominal metastatic tumors progressed during the conservative POPF treatment. The patient received the first cycle of TC chemotherapy on POD 60, and after 4 courses showed a partial response with only the intra-abdominal tumor remaining. IDS, including abdominal total hysterectomy, right salpingo-oophorectomy, partial gastrectomy, DP, splenectomy, partial colectomy, and diaphragmatic resection of peritoneal metastasis, was achieved with complete resection. The operative time was 435 min, and blood loss was 1180 mL. The patient was discharged following IDS on POD 14 without any complications. The patient received postoperative chemotherapy (three cycles of TC combined with bevacizumab). After CT confirmed a complete response to treatment, the patient was started on maintenance therapy with olaparib and bevacizumab. Ten months after the initiation of maintenance therapy, the patient had no signs of recurrence.



Postoperative time course after the first surgery

Fig. 2. Postoperative time course after the first surgery. On postoperative day (POD) 3, the patient had a high fever, and leukocytosis (19,760 /µl) was detected. The administration of antibiotics (tazobactam; TAZ and piperacillin hydrate; PIPC) started. On POD 7, the repeated CT scan revealed the enlarged abscess, and a drainage tube was placed under CT guidance. Although the patient's condition, the inflammation, and the leukocytosis rapidly improved after the initiation of drainage, the drainage volume continued to be approximately 100 mL/day. On POD 17, the color of the drainage fluid changed from brown to blood-stained. The amylase level in the abscess fluid was 258,111 U/L and the patient was diagnosed with postoperative pancreatic fistula (POPF). As the drainage volume remained high, on POD 26 the treatment with fasting, parenteral nutrition, and somatostatin analog (subcutaneous octreotide acetate) was initiated. The drainage volume reduced gradually, and the drainage tube was removed on POD 55. After the conservative POPF treatment, the patient was finally administered the first cycle of TC chemotherapy (paclitaxel plus carboplatin) on POD 60. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)



Fig. 3. The CT image on postoperative day 7. The circle shows intra-abdominal abscess formation around the spleen and the pancreas.

3. Discussion

Although POPF rarely occurs after gynecologic surgery, it is one of the most harmful complications following pancreatic resection. In 2016, the International Study Group of Pancreatic Fistula (ISGPF) established a standard definition of pancreatic fistula as any measurable drainage from an intraoperatively or postoperatively placed drain on or after POD 3, with an amylase level three times higher than the normal serum amylase level [6]. The ISGPF grading system is defined as grades A, B, and C. Grade A, called a "biochemical leak", has no clinical impact. Grades B and C are defined as clinically relevant (CR)-POPF. Grade C involves organ failure or the need for reoperation. According to a study of 2026 patients who developed POPF after DP, 306 (15%) developed a CR-POPF [7]. It is reported that 90.8% of CR-POPF after DP are Grade B [7]. Risk factors included smoking, open DP, age, obesity, hypoalbuminemia, the absence of epidural anesthesia, neuroendocrine or nonmalignant pathology, concomitant splenectomy, and vascular resection [3,7]. CR-POPF may require fasting and pancreatic drainage for more than three weeks or repositioning of the drain tube if the drainage is inadequate. Elevated amylase levels in the drainage fluid reflected the patient's actual condition better than serum amylase levels [8]. However, the decision to remove the drainage tube depends on the decrease in the volume of drainage fluid rather than the drain amylase level [9]. Whether somatostatin analogs are effective in preventing POPF [10,11] is controversial. These conservative therapies are successful in more than 85% of patients [4]. Limited reports on POPF after gynecological surgeries are available [8,11–13]. Patients undergoing DP have a higher risk of developing POPF than those undergoing splenectomy only [13]. To the best of our knowledge, there have been no reports of POPF without undergoing DP or splenectomy during gynecological surgery, as seen in this case. Even if the spleen and pancreas are not removed, POPF can occur when the resected colon is located near the splenic flexure.

A metal stent can serve as palliative treatment for patients with colonic obstruction due to colorectal cancer. Arundhati Datye et al. reported that placement of a self-expanding metal stent is associated with perforation in 4.9% of cases [14]. Colon perforation related to metal stents has a 16% mortality rate and the risk factors include steroids, chemotherapy, and radiotherapy [14]. In Japan, Matsuzawa et al. reported that perforation events occurred in 2.1% of placements of a self-expanding metal stent [15]. Recently, colon perforation has been reported less frequently with Niti-S stents [16]. Considering that chemotherapy is usually effective for ovarian, fallopian tube, or primary peritoneal cancers, all clinicians should deliberate on the necessity of stent placement, as a subileus caused by peritoneal metastasis may heal

with the early initiation of chemotherapy.

4. Conclusion

Clinician should remain vigilant for POPF when the colectomy site is close to the splenic flexure, even without resection of the spleen and pancreas. Reevaluation of the necessity of metallic stent placement is crucial, as the subileus caused by peritoneal metastasis may be alleviated by the induction of chemotherapy for gynecologic cancer.

Contributors

Kazuna Matsutani contributed to patient care, acquiring and interpreting the data, drafting the manuscript, undertaking the literature review, and revising the article critically for important intellectual content.

Yasuto Kinose contributed to patient care, conception of the case report, acquiring and interpreting of data, drafting the manuscript, undertaking the literature review, and revising the article critically for important intellectual content.

Mayuko Kato contributed to patient care, and acquiring and interpreting the data.

Michiko Kodama participated in revising the article critically for important intellectual content.

Kenjiro Sawada participated in revising the article critically for important intellectual content.

Tadashi Kimura participated in revising the article critically for important intellectual content.

All the authors approved the final submitted manuscript.

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Patient consent

Written informed consent for publication was obtained from the patient.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

References

[1] Deborah K. Armstrong, Ronald D. Alvarez, Floor J. Backes, Jamie N. Bakkum-Gamez, Lisa Barroilhet, Kian Behbakht, et al., NCCN guidelines® insights: ovarian cancer, version 3.2022, J. Natl. Compr. Canc. Netw. 20 (9) (2022) 972–980, https://doi.org/10.6004/inccn.2022.0047.

- [2] Suk Joon Chang, Robert E. Bristow, Dennis S. Chi, William A. Cliby, Role of aggressive surgical cytoreduction in advanced ovarian cancer, J. Gynecol. Oncol. 26 (4) (2015) 336–342, https://doi.org/10.3802/jgo.2015.26.4.336.
- [3] Eric Chong, Bathiya Ratnayake, Shiela Lee, Jeremy J. French, Colin Wilson, Keith J. Roberts, et al., Systematic review and meta-analysis of risk factors of postoperative pancreatic fistula after distal pancreatectomy in the era of 2016 International Study Group pancreatic fistula definition, HPB 23 (2021) 1139–1151, https://doi.org/10.1016/j.hpb.2021.02.015.
- [4] Giovanni Butturini, Despoina Daskalaki, Enrico Molinari, Filippo Scopelliti, Andrea Casarotto, Claudio Bassi, Pancreatic fistula: definition and current problems, J. Hepato-Biliary-Pancreat. Surg. 15 (3) (2008) 247–251, https://doi. org/10.1007/s00534-007-1301-y.
- [5] A. Fagoti, G. Ferrandina, F. Fanfani, A. Ercoli, D. Lorusso, Marco Rossi, et al., A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study, Ann. Surg. Oncol. 13 (8) (2006) 1156–1161, https://doi.org/10.1245/ASO.2006.08.021.
- [6] Claudio Bassi, Giovanni Marchegiani, Christos Dervenis, Micheal Sarr, Mohammad Abu Hilal, Mustapha Adham, et al., The 2016 update of the international study group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after, Surgery 161 (3) (2017) 584–591, https://doi.org/10.1016/j. surge 2016 11 014
- [7] Brett L. Ecker, Matthew T. McMillan, Valentina Allegrini, Claudio Bassi, Joal D. Beane, Ross M. Beckman, et al., Risk factors and mitigation strategies for pancreatic fistula after distal pancreatectomy: analysis of 2026 resections from the international, multi-institutional distal pancreatectomy study group, Ann. Surg. 269 (1) (2019) 143–149, https://doi.org/10.1097/SLA.00000000002491.
- [8] Kazuyoshi Kato, Shinichi Tate, Kyoko Nishikimi, Makio Shozu, Management of pancreatic fistulas after a splenectomy as part of cytoreductive surgery for ovarian cancer, Int. J. Gynecol. Cancer 23 (8) (2013) 1506–1511, https://doi.org/10.1097/ IGC.0b013e3182a0fa66.
- [9] Violante Di Donato, Erlisa Bardhi, Luca Tramontano, Filippo Maria Capomacchia, Innocenza Palaia, Giorgia Perniola, et al., Management of morbidity associated with pancreatic resection during cytoreductive surgery for epithelial ovarian cancer: a systematic review, Eur. J. Surg. Oncol. 46 (4 Pt A) (2020) 694–702, https://doi.org/10.1016/j.ejso.2019.11.516.
- [10] Katarzyna Mech, Łukasz Wysocki, Tomasz Guzel, Marcin Makiewicz, Paweł Nyckowski, Maciej Słodkowski, et al., A review of methods for preventing pancreatic fistula after distal pancreatectomy, Pol. Przegl. Chir. 90 (2) (2018) 33–39, https://doi.org/10.5604/01.3001.0011.7491.
- [11] Siobhan M. Kehoe, Eric L. Eisenhauer, Nadeem R. Abu-Rustum, Yukio Sonoda, Michael D'Angelica, William R. Jarnagin, et al., Incidence and management of pancreatic leaks after splenectomy with distal pancreatectomy performed during primary cytoreductive surgery for advanced ovarian, peritoneal and fallopian tube cancer, Gynecol. Oncol. 112 (3) (2009) 496–500, https://doi.org/10.1016/j. vgvno.2008.10.011.
- [12] Kyoko Nishikimi, Shinichi Tate, Ayumu Matsuoka, Satoyo Otsuka, Makio Shozu, Predictors of postoperative pancreatic fistula after splenectomy with or without distal pancreatectomy performed as a component of cytoreductive surgery for advanced ovarian cancer, J. Gynecol. Oncol. 33 (3) (2022) e30, https://doi.org/ 10.3802/jgo.2022.33.e30.
- [13] Nicolò Bizzarri, Porfyrios Korompelis, Valentina Ghirardi, Rachel Louise O'Donnell, Stuart Rundle, Raj Naik, Post-operative pancreatic fistula following splenectomy with or without distal pancreatectomy at cytoreductive surgery in advanced ovarian cancer, Int. J. Gynecol. Cancer 30 (7) (2020) 1043–1051, https://doi.org/10.1136/ijgc-2020-001312.
- [14] Arundhati Datye, Jeff Hersh, Colonic perforation after stent placement for malignant colorectal obstruction - causes and contributing factors, Minim. Invasive Ther. Allied Technol. 20 (3) (2011) 133–140, https://doi.org/10.3109/ 13645706.2010.518787.
- [15] Takeaki Matsuzawa, Hideyuki Ishida, Shuntaro Yoshida, Hiroyuki Isayama, Toshio Kuwai, Iruru Maetani, et al., A Japanese prospective multicenter study of self-expandable metal stent placement for malignant colorectal obstruction: shortterm safety and efficacy within 7 days of stent procedure in 513 cases, Gastrointest. Endosc. 82 (4) (2015) 697–707.e1, https://doi.org/10.1016/j.gie.2015.03.1978.
- [16] Yuki Miyasako, Toshio Kuwai, Sauid Ishaq, Kanae Tao, Hirona Kohisi, Ryoichi Miura, et al., Newly developed self-expandable Niti-S MD colonic metal stent for malignant colonic obstruction, World J. Gastrointest. Surg. 12 (4) (2020) 138–148, https://doi.org/10.4240/wjgs.v12.i4.138.