

Case report

Laparoscopic spacer placement for bulky lymph node metastasis of cervical cancer: A case report

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1. Introduction

Irradiation for pelvic tumors can cause various acute and late complications of the gastrointestinal (GI) tract, bladder, skin, bone, and gynecologic system. Radiation enteritis is quite common after pelvic irradiation and causes diarrhea, obstruction, hemorrhage, and fistula, occasionally requiring surgical intervention. Its incidence accounted for 50 % of irradiated patients whose quality of life (QOL) was significantly impaired (Stacey and Green, 2014; Olopade et al., 2005). To prevent and minimize these late complications, the improvement of radiation technique could reduce radiation exposure to surrounding organs at risk, as well as a surgical procedure to insert 'spacers' distancing normal surrounding tissues from the target (Tang et al., 2018). Spacer usage for prostate cancer has been intensively researched, and the SpaceOARTM Hydrogel injection method was already established (Miller et al., 2020; Ismael et al., 2016). On the other hand, other materials used as spacers have been only sporadically reported, including allografts, tissue expanders, silicone balloons, and Gore-Tex sheets for pediatric, gynecologic, and other abdominal and retroperitoneal tumors (Tang et al., 2018; Sezeur et al., 1999; Lee et al., 2021). The method of inserting these materials varies from endoscopic injections (Feng et al., 2021) to surgical procedures such as open or minimally invasive (Tang et al., 2018). Spacer usage for malignancies except prostate cancer requiring multidisciplinary management, including radiotherapy beyond standard

treatment, has not been standardized.

Here, we present a case requiring multidisciplinary treatment of a metastatic pelvic lymph node with a rare iliac venous variation, for which the laparoscopic placement of a spacer promptly initiated high-dose radiation therapy.

2. Case report

A 64-years-old woman was referred to our hospital for edema of the right lower leg. Pelvic examination revealed no gross lesion in the cervix, no parametrium invasion, and no bleeding. Laboratory examination showed that CA125 was at 46 U/ml, SCC at 36.7 ng/ml, and D-dimer at 2.24 µg/m. The histological finding of the cervix was HSIL/CIN3. However, the exam of the endometrium was impossible due to cervical stenosis. Computed tomography (CT) and magnetic resonance imaging (MRI) showed a 69 × 49 mm sized mass located in the right-half side of uterine myometrium from the cervix to mainly fundus and para-aortic and pelvic lymphadenopathy, complete obstruction of right external iliac vein due to the enlarged 57 × 49 × 67 mm right obturator lymph node, and type 4 iliac venous variation, which bilateral internal iliac veins form the common trunk and then flow into the left external iliac vein (Fig. 1).

(Left) Horizontal view of uterus on computed tomography. Mass is mainly located on the right-half side of uterine myometrium from cervix

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to fundus. (Middle) 3D constructed image of iliac vein, in which bilateral internal iliac veins form common trunk and flow into the left external iliac vein. (Right) Coronal view of bulky right obturator lymph node on magnetic resonance imaging.

Ultrasonography of veins on lower extremities detected the thrombus formation at the obstructed right external iliac vein, for which edoxaban 30 mg per day was initiated.

Based on these findings, the pretreatment diagnosis was squamous cell carcinoma of the cervix, FIGO2018 IIC2r, although the tumor mainly developed in the uterine corpus. Since bulky lymph node and tumor in the uterine corpus were considered uncontrollable by irradiation, we decided to initiate chemotherapy first. Combination therapy of paclitaxel and carboplatin (TC) three times every-three weeks improved the leg edema. Partial response was confirmed as follows; the primary uterine tumor had shrunk to 56 × 31 mm, and the para-aortic and pelvic lymphadenopathy had disappeared except for a 30 × 33 × 47 mm right obturator lymph node. SCC was decreased to 7.0 ng/ml. The multidisciplinary conference determined that laparoscopic hysterectomy, spacer placement on the right obturator lymph node, and postoperative high-dose radiation to the node were the best choices. It was because the uterine mass, still mainly located in the corpus, was too large to be cured with radiotherapy; however, the uterus could be removed with margin negative resection. Lymphadenectomy was not planned because it required vein grafting, of which long-term patency was uncertain in malignant disease following radiotherapy, and might cause tumor cell dissemination.

Laparoscopic hysterectomy plus bilateral adnexectomy and spacer placement were performed. The tumor could be observed through the serosa at the fundus of the uterus but was barely exposed. Lymphadenopathy extremely distended the right retroperitoneum, and the ureter was displaced inward. To avoid tumor dissemination, the retroperitoneal cavity was opened as little as possible. Three GORE-TEX® Soft Tissue Patch (W.L. Gore & Associates, USA) 15 × 20 × 2 mm were folded, joined together to create a thickness of at least 1 cm to cover the right distended retroperitoneum region, and inserted via umbilical port (Fig. 2). The sheet was fixed to the peritoneum in six places with non-absorbable sutures.

(Upper left) Tumor was located beneath the serosa near to intramural part of right fallopian tube. White arrows showed the tumor. (Upper right) The bulky lymph node is widely distended retroperitoneum. Black arrows showed right ureter. (Lower left) GoreTex soft tissue patch was placed onto the right obturator lymph node. (Lower right) Macroscopic findings revealed that major portion of tumor was located in the uterine corpus. White arrows indicated tumor location.

An omentum flap mobilized to the pelvic further covered the spacer. The operative time was 247 min, and the bleeding was 0 ml. Postoperative histopathological findings showed non-keratinizing squamous cell carcinoma of the cervix expanding to right fundus of uterus, ypT1b1NxMx, with lymphatic and vascular invasion but with a negative resection margin (Fig. 2). Radiotherapy planning CT confirmed that a spacer could provide a distance of 1 cm between the GI tract and lymph node, which has not been exacerbated compared to preoperative

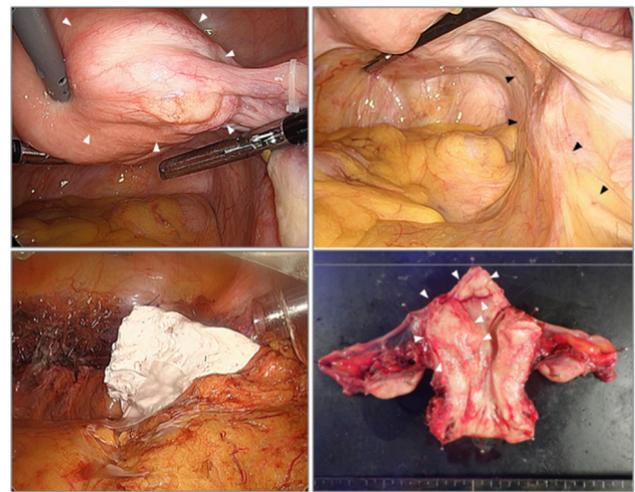


Fig. 2. Intraoperative findings.

findings (Fig. 3).

(Left) Spacer was fixed on the lymph node and distanced the bowel. White arrows showed spacer location, and yellow dotted lines surrounded the tumor. (Right) Radiation planning CT scan for right obturator lymph node.

Intensity-modulated radiation therapy began on postoperative day 10, with 20 Gray (Gy) /5 fr for the right enlarged pelvic lymph node, followed by 45 Gy /25 fr for whole pelvis, including enlarged node, and para-aorta nodes, completed without acute complications. Two months later, partial response was confirmed based on decreased SCC value to 0.5 ng/ml, shrunk right obturator lymph node to 21 × 16 mm in CT. The size and location of the spacer were unchanged; however, right hydronephrosis and hydroureter and fluid retention on the spacer appeared, suggesting infection. Abdominal pain and partial vaginal dehiscence also appeared. Laparotomy was performed to remove the spacer, with partial resection of the small intestine adherence to the spacer, anastomosis, suture of vagina vault, omentum flap mobilization, and placement of a DJ catheter in the right ureter. Based on the stony hard tissue-like degeneration of the right retroperitoneum, the hydronephrosis and hydroureter may be due to the fibrotic effects of radiation therapy. On postoperative day 9, the vaginal discharge turned dark green in color, and laboratory examination showed a high AMY level of 90,408 U/l of the fluid, suggesting micro-perforation of the small intestine. Antibiotic treatment with 3 g meropenem per day and total parenteral nutrition therapy were effective, vaginal discharge disappeared, and the patient was discharged 37 days after surgery. The size of right obturator node has been stable during the course. Unfortunately, 16 months after primary diagnosis and ten months after completion of radiotherapy, CT showed lymphadenopathy in the common iliac, para-aortic, and new obturator lymph nodes, except for the lymph node irradiated at a high dose. The patient has been currently treated again with TC regimen. Throughout the course, the patient did not develop radiation enteritis.

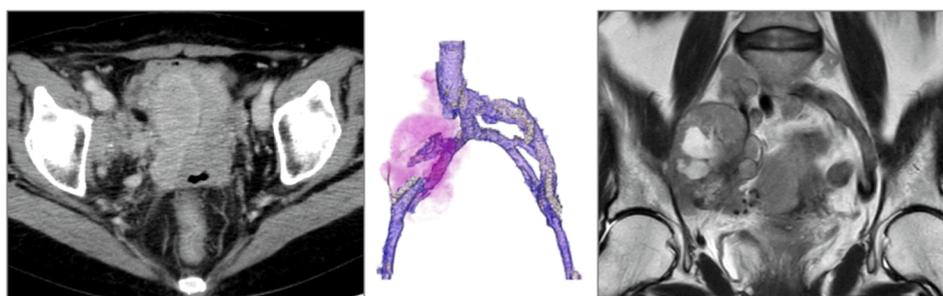


Fig. 1. Pretreatment imaging examination.

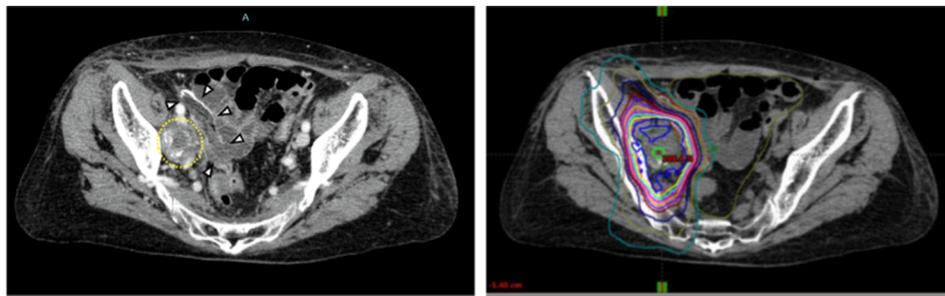


Fig. 3. Postoperative imaging.

3. Discussion

In pelvic radiotherapy for gynecological cancer, enteritis, cystitis, fistula of GI tract, and vaginal stenosis occur as late complications. Gynecological and GI tumors suffer more from radiation enteritis than urological tumors (Olopade et al., 2005). Chronic radiation enteritis generally develops between 3 months and 20 years after the therapy and remains at the rate of 10–20 % of patients even ten years after the irradiation (Loge et al., 2020). Almost half of the irradiated patients impair the QOL, with moderate to severe symptoms in 20–30 % (Stacey and Green, 2014; Loge et al., 2020). The pathogenesis of chronic radiation enteritis is irreversible mucosal atrophy, fibrosis of the intestinal wall, and prominent microvascular sclerosis, which alter intestinal transit, nutrient malabsorption, and gut dysmotility (Hauer-Jensen et al., 2014). Clinically, diarrhea with or without pain is the most common symptom, and others include obstruction, and hemorrhage, occasionally requiring endoscopic treatment such as laser ablation or surgical intervention if the symptoms do not respond to conservative management. Tolerability of GI tract to irradiation varies with irradiated tumor volume, concurrent anticancer and molecular targeting drug, history of pelvic inflammatory disease and previous surgery, and poor nutritional status. The small intestine was most sensitive to irradiation; on the other hand, the esophagus was the least. TD5/5 Gy and TD 50/5 Gy were 50 and 60 if one-third of the normal small intestine was irradiated and 45 and 55 for the rectum (Emami et al., 1991). Severe chronic enteritis requires complex surgical intervention, of which morbidity and mortality are varied between reports, generally less than 5 % and ranging from 22 to 75 %, respectively. Poor healing of the anastomosis and recurrence of the symptoms due to incomplete resection of the damaged segment are common complications, and short bowel syndrome also impairs patients' QOL (Boland et al., 2010).

To reduce the adverse impact on adjacent normal organs, radiation techniques, such as 3-dimensional conformal radiotherapy, intensity-modulated radiotherapy, and stereotactic body radiotherapy, have been employed. As with other approaches to holding the lesion away from the surrounding organs, there is the surgical method to insert a tool called a “spacer.” The materials of the spacer vary depending on the targets. Blood patch, human collagen, acellular human dermis (Ismael et al., 2016; Dalwadi et al., 2019), hyaluronic acid, and polyethylene-glycol hydrogel have been used, mainly via injection for prostate cancer (Tang et al., 2018; Ismael et al., 2016; Feng et al., 2021). Since the first report of the clinical use of spacers in 1984 (Dürig et al., 1984), several placement methods and materials of spacers have been reported in head and neck cancer (Shibuya, 2009) and abdominal pelvic tumors (Sezeur et al., 1999), liver (Ismael et al., 2016), retroperitoneal tumor, and pancreatic cancer (Feng et al., 2021), and researched very intensively in prostate cancer (Tang et al., 2018). Recently, a meta-analysis confirmed the benefit of percutaneous SpaceOAR™ Hydrogel injection for prostate cancer temporarily distances the rectum from the prostate. This method is recommended by the National Comprehensive Cancer Network and National Institute of Health and Care Excellence guidelines (Miller et al., 2020).

On the other hand, as one of the methods not yet established, GoreTex sheets have been used as spacers. GoreTex soft tissue patch, easily sized and precisely placed at the required site, is a biomaterial for repairing the abdominal and inguinal hernia and fascia defects; therefore, it does not necessarily require removal after use as a spacer (Lee et al., 2021). In addition to GoreTex sheets, silicon balloons, tissue expanders, and saline-filled spacers have been used as surgical spacers for various anatomical sites (Tang et al., 2018; Sezeur et al., 1999; Lee et al., 2021). Methods of “spacer” placement also vary with the target location. Non-surgical techniques such as transrectal ultrasound-guided infusion of hydrogel for prostate cancer are ideal and effective methods, but these methods are limited to accessible organs from the body surface. Instead, for organs that can only be reached surgically, minimally invasive procedures such as endoscopic and laparoscopic procedures are considered advantageous over open surgery because of their benefits, such as earlier initiation of treatment and less potential for infection. In this case, the patient recovered quickly without complications after laparoscopic surgery and promptly followed with radiotherapy. However, few reports describing the insertion of surgical spacers via minimally invasive surgery have been published yet (Ismael et al., 2016; Dalwadi et al., 2019).

Meanwhile, using non-absorbable biocompatible materials as spacers should be considered with caution. Non-absorbable materials may cause several complications and issues, including organ damage, bleeding, foreign body reactions, infection, adhesions, entrapment in other organs, and fistula formation, in contrast to absorbable materials. In the present case, unfortunately, the spacer became infected and had to be removed, probably due to the hysterectomy being a clean-contamination procedure. Even with a clean approach such as GoreTex sheet insertion for pancreatic cancer without GI tract resection, one patient caused a spacer infection four months after radiation (Lee et al., 2021). Early removal might be considered when inserting a non-absorbable spacer concurrent with a procedure that may result in entrapment. It is desired that absorbable materials could be used as spacers in the future. Although the opportunities for spacer use have decreased due to improved radiation techniques that minimize radiation exposure to adjacent organs, spacers may still be necessary for malignant tumors, such as recurrent cases that require multidisciplinary treatment, including radiation therapy beyond the standard treatment. Experiences should be accumulated to evaluate the benefits and safety of surgical spacers.

In summary, multidisciplinary treatment was performed for the cervical cancer patient with bulky lymph node and a rare type of iliac venous variation and achieved a favorable response. With laparoscopic spacer placement, high-dose radiotherapy was initiated promptly after surgery to control the tumor. However, given that infection was unavoidable in our case, if a non-absorbable material is placed as a spacer, even biocompatible material, in a concomitant procedure with the potential for contamination, it should be removed. In the future, ideal absorbable surgical spacers should be available for the multidisciplinary treatment of gynecological cancers.

Informed Consent

Written informed consent was obtained from the patient to publish

this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author Contributions

Kuruma A reviewed the case and wrote manuscript, Kodama M treated the patient and edited manuscript, Miyoshi A, Isohashi F, Toda A, Nakagawa S, Kinose Y, Takiuchi T, Kobayashi E, Hashimoto K, Ueda Y, and Sawada K treated the case, and Kimura T supervised and edited manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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