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Case Report

Port site metastasis after robotic-assisted laparoscopic hysterectomy for uterine cervical cancer: A case report and literature review

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Abstract

Objective: The incidence of port site metastasis after robotic-assisted laparoscopic surgery for cervical cancer is not well known. According to recent studies of gynecological malignancies, the reported incidence is low and comparable to the results of conventional laparoscopic surgery. Here, we report the case of a patient who suffered port site metastasis after robotic-assisted laparoscopic hysterectomy for stage IB1 uterine cervical cancer.

Case report: The current case is, as we know, only the third episode of port site metastasis after robotic-assisted laparoscopic surgery for cervical cancer documented in the medical literature. Following diagnosis of the port site metastasis, the patient was treated with concurrent chemo-radiotherapy (CRT) and experienced a remarkable early response. We reviewed the patient's medical chart and imaging studies, and searched the Medline database to evaluate the incidence, prognosis and treatment outcomes of such cases of port site metastasis in uterine cervical cancer patients.

Conclusion: CRT resulted in a rapid decrease in tumor size and relief of abdominal pain in our patient. CRT might be considered as a salvage or palliative modality in patients with port site metastasis and/or locoregional recurrence.

Keywords: port site metastasis; chemo-radiotherapy; robotic-assisted laparoscopic surgery; uterine cervical cancer

Introduction

Laparoscopic surgery is widely used for the treatment of benign disease entities, and is also applied for selected cases of malignancy. Robotic-assisted laparoscopic surgery (RALS) is increasingly replacing traditional laparoscopic surgery because of its advantages such as high-resolution three-dimensional imaging and the ability to apply more physiological, wrist-like movements to the maneuvering of surgical instruments, resulting in finer control of critical movements [1]. The da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA) is increasingly being utilized in the field of gynecological oncology. Such new techniques, however, have significant learning curves and the results depend on the individual surgeon's skill. Several recent reports have shown that RALS requires longer operation times, leads to greater blood loss, and results in higher operative complication rates compared to traditional laparoscopic surgery [2].

When using minimally invasive surgical techniques such as laparoscopic surgery or RALS, trocars are placed in port sites. These port sites may become implantation hubs for tumor cells as they are manipulated during surgery. Such port site metastases are not common, but are more frequently reported after laparoscopic surgery for the treatment of gallbladder adenocarcinoma [3]. Port site metastases occur in 1–2% of

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patients with gynecological malignancies and are more commonly reported in cases of ovary, fallopian tube, or endometrial carcinomas [4,5]. For uterine cervical cancer, a study of 921 patients reported a rate of port site metastasis of 0.43%, and the incidence was lower than that of ovarian or fallopian tube carcinomas [6]. However, in small, institution-based studies of 160 and 75 patients, the rates of port site metastasis were reported as 1.25% and 1.3%, respectively [5,7]. For patients treated with RALS for uterine cervical cancer, as far we know, there have been only two reported cases of port site metastasis.

We recently encountered port site metastasis in a young patient with early stage (IB1) uterine cervical cancer after robotic-assisted laparoscopic radical hysterectomy, right salpingo-oophorectomy, and pelvic lymphadenectomy. We report here the details of this rare case accompanied by a review of prior studies of port site metastasis after minimally invasive surgery for the treatment of uterine cervical cancer.

Case report

A 35-year-old woman was referred to Samsung Medical Center due to abnormal cytological findings on a Papanicolaou smear performed for routine surveillance. On gynecological examination, a 1.5-cm pinkish mass was visualized at the two o'clock position. A punch biopsy revealed endocervical glandular atypia suggestive of endocervical adenocarcinoma. For staging work-ups, complete blood count, blood chemistry, chest X-ray, computed tomography (CT) of the abdomen and pelvis, cystoscopy, and sigmoidoscopy were performed. Pelvic magnetic resonance imaging (MRI) scanning and ^{18}F-fluorodeoxyglucse (FDG) positron emission tomography (PET/CT) were also performed. The patient was diagnosed with stage IB1 cervical cancer and sent for surgery considering her young age, and for functional preservation of the ovary.

In June 2011, the patient underwent robotic-assisted (da Vinci Surgical System) laparoscopic radical hysterectomy, right salpingo-oophorectomy, and pelvic lymphadenectomy.

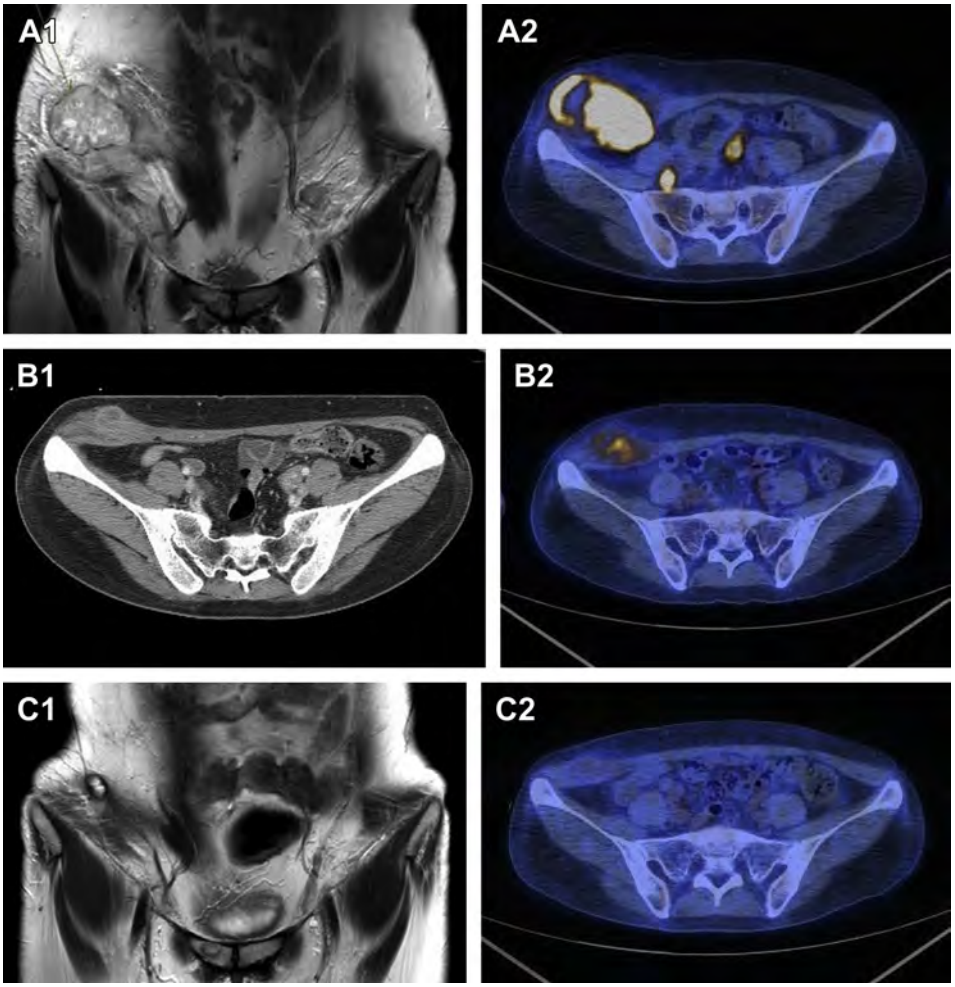

Fig. 1. (A) Before chemoradiotherapy. (A-1) A 7.2-cm abdominal wall mass was detected at the right lower quadrant trocar site on magnetic resonance imaging. (A-2) The abdominal mass showed markedly increased ^{18}F-fluorodeoxyglucose (FDG) uptake [maximum standardized uptake value (SUVmax) = 19.4]. There was also increased uptake in several pelvic lymph nodes and in the pelvic peritoneum. (B) During chemoradiotherapy (after 30.6 Gy). (B-1) The size of the abdominal wall mass decreased rapidly. (B-2) The abdominal wall mass showed markedly decreased ^{18}F-FDG uptake (SUVmax = 5.0). (C) One month after chemoradiotherapy. (C-1) There was a 1–1.5-cm fibrotic mass found on magnetic resonance imaging. There was no detectable peritoneal or pelvic disease. (C-2) The residual lesion showed markedly decreased ^{18}F-FDG uptake (SUVmax = 2.3).

The operative procedure began with a 12-mm subumbilical incision down to the abdominal wall fascia, and pneumoperitoneum was established with CO_2 gas injected through a Veress needle. The remaining four trocars were placed without difficulty in the right lower quadrant (RLQ, 8 mm), left lower quadrant (8 mm), right upper quadrant (8 mm) and mid-upper abdomen (11 mm). In the RLQ port, a trocar was inserted through the patient's prior appendectomy scar. There were no enlarged pelvic lymph nodes or ascites. Histopathological examination revealed a poorly differentiated 1 cm × 0.8 cm mucinous adenocarcinoma of the cervix with an invasion depth of 6 mm. The tumor was confined within the uterine cervix and all of the resection margins were negative. There were no involved pelvic lymph nodes. She did not receive any adjuvant therapy.

Four months after robotic surgery, the patient experienced abdominal pain. Five months after surgery, she complained of abdominal swelling. CT scans of the abdomen and pelvis and PET/CT scans revealed multiple hypermetabolic masses in the right lower abdominal wall at the RLQ port site, lower peritoneal cavities, and bilateral iliac lymph nodes (Fig. 1A1 and A2). On ultrasonography-guided core-needle biopsy, the mass in the abdominal wall showed poorly differentiated adenocarcinoma.

From January to February 2012, the patient underwent concurrent chemoradiotherapy (CCRT). The chemotherapeutic regimen consisted of five cycles of weekly cisplatin (40 mg/m^2). The initial field of irradiation covered the pelvis, including the pelvic peritoneal seeding, hypermetabolic pelvic lymph nodes, and the abdominal wall mass (Fig. 2A). A total radiation dose of 50.4 Gy was delivered using three-dimensional conformal radiotherapy in 1.8-Gy fractions. After the initial dose of 50.4 Gy, a boost dose of 10.8 Gy was delivered in six fractions to the abdominal wall mass based on the second simulation CT shown in Fig. 2B. During CCRT, the patient complained of mild nausea, vomiting, and intermittent diarrhea, but all of her adverse symptoms were manageable with oral medications. There was no interruption of CRT. During the treatment, the abdominal wall mass shrank rapidly, and at the end of CCRT, there was no palpable mass. ^{18}F-FDG PET/CT showed a marked decrease in size and metabolic activities of the abdominal and pelvic disease during CCRT (Fig. 1B1 and B2).

One month after completion of CCRT, the patient did not complain of any discomfort. On physical examination, there was no palpable mass and the only demonstrable adverse effect was skin pigmentation over the irradiated area. Pelvic MRI showed no definite mass (Fig. 1C1), and ^{18}F-FDG PET/CT scan showed no increased uptake at the previously observed sites. There was no evidence of newly developed hypermetabolic sites (Fig. 1C2). At 17 months' follow-up, there was no evidence of locoregional recurrence or distant metastasis.

Review of prior reports of port site metastases in uterine cervical cancer

We searched the PubMed database from 1990 to 2012 for other reports of port site metastasis after the minimally invasive surgery of uterine cervical cancer. We included both traditional laparoscopic surgery and robotic-assisted laparoscopic surgery in order to evaluate possible mechanisms and risk factors for port site metastasis.

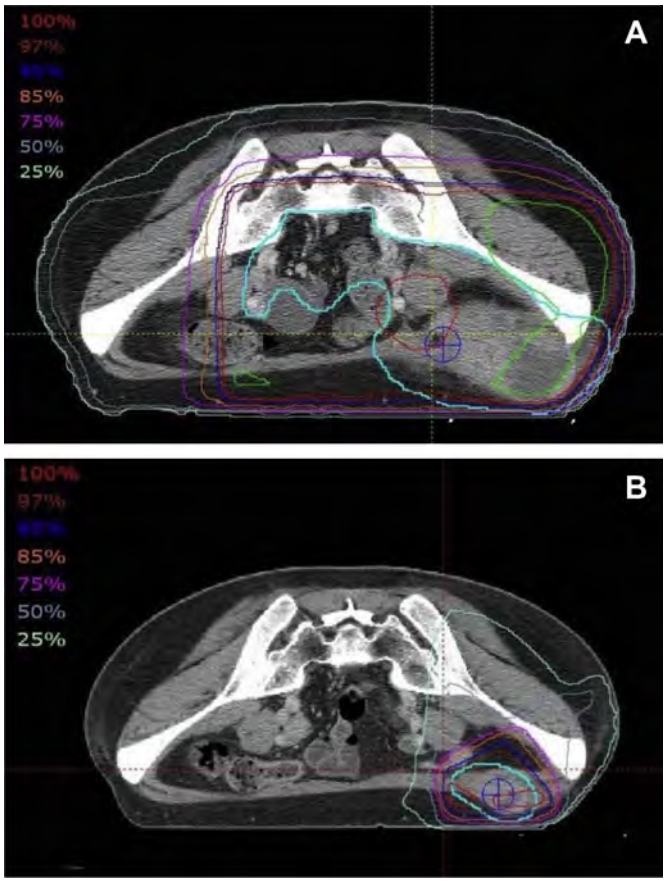

Fig. 2. Radiotherapy. Three-dimensional conformal radiotherapy was planned to cover the clinical target volume (sky blue line) by 97% isodose lines. (A) The initial radiation field included the abdominal wall mass (port site metastasis) and pelvic disease. (B) The boost volume included the residual abdominal wall mass, and mapping was generated using new computed tomography planning.

Conclusion

Port site metastasis of cervical cancer is rare. Early data suggest that most cases of port site metastasis after minimally invasive surgery for the treatment of gynecological malignancies occur in ovarian cancer patients. It is important to recognize the fact that most of the data related to the port site metastasis come from the cases of traditional laparoscopic surgery, and not from RALS. It is mainly due to the more recent application of robotic surgery in gynecological malignancies.

There have been few reports of port site metastasis in uterine cervical cancer. Our Medline search yielded 23 cases of port site metastasis after laparoscopic surgery (including diagnostic procedures) for cervical cancer published since 1990. Among these 23 cases, only six had isolated port site metastasis of cervical cancer. In the remaining 17 cases, other

recurrences in the abdomen/pelvis, peritoneal carcinomatosis, and/or distant metastases accompanied the port site metastasis (Table 1) [5–22].

In a study of 181 patients undergoing RALS for the treatment of gynecological malignancies, Ndofor et al reported a 1.1% rate of port site metastasis. Fifty patients with stage I cervical cancers were included in that study, but none suffered from port site metastasis [23]. These rates of port site metastasis after RALS for the treatment of gynecological malignancies are similar to the rates of port site metastasis after traditional laparoscopic surgery. Prior to the current study, as far as we know, there were only two reports of port site metastasis after RALS for the treatment of uterine cervical cancer. Sert reported the first case of port site metastasis after a robotic-assisted laparoscopic radical hysterectomy in a patient with stage IB1 cervical adenocarcinoma. Interestingly, the patient in that case sustained bladder damage during RALS and experienced recurrence in the bladder in addition to the port-site metastasis [24]. Including our case, all three patients with port site metastasis after RALS for the treatment of cervical cancer had early stage disease and the port site metastasis was combined with other failures such as peritoneal carcinomatosis or pelvic node metastasis (Table 2) [24,25]. Only two relevant case reports have been published in the medical literature, therefore, the incidence of port site metastasis after RALS of cervical cancer remains unknown.

Achieving a better understanding of port site metastasis is critical to prevent and predict such failures. However, the mechanism of port site metastasis has not been defined. Several possible mechanisms have been postulated, including hematogeneous spread, direct wound implantation during extraction of the malignant specimen or through a contaminated instrument, chimney effect, aerosolization of tumor cells, surgical techniques such as excessive tumor

Table 1
Port site metastasis after laparoscopic surgery for uterine cervical cancer.

Author	Surgery	Stage	LN	Removal of disease tissue	Retrieval bag	Histology	Port site mets (mo)	Location	Concomitant failure	Treatment	Outcome
Patsner [8]	Diagnostic + biopsy	IB	+	N	N	SQ	5	Umbilicus (ne)	PR	CTX	DOD 9 mo
Naumann [9]	Guide for Syed implant	IIIB	–	N	N	SQ	5	Umbilical (ne)	PC, RP LNs and liver mets	Palliative	DOD 3 wks
Wang [10]	H + PND	IB1	+	Y	N	SQ	2	Multiple	PC	CTX	DOD 5 mo
Kadar [11]	PAPND	IB2	+	Y	N	SQ	Nr	Lat (ne)	PR	Nr	DOD 24 mo
	PAND	IIIB	+	Y	N	SQ	nr	Lat (ne)	PR	nr	DOD 4 mo
Lavie [12]	H + BSO + PND	IA	–	N	N	AD, PD	9	Lat (e)	N	EXC	nr
Lane [13]	PAPND	IB1	+	Y	N	AD,SQ	10	Lat (e)	N	EXC	NED 19 mo
Carvalho [14]	PND	IB2	+	Y	nr	SQ	1.5	All ports	PC and Pelvic LNs	nr	nr
Lecuru [15]	PND	IB1	–	N	Y	SQ	48	Umbilicus (ne)	N	EXC + ERT	Lung mets 7 mo
Kohlberger [16]	Diagnostic	IB1	–	N (Biopsy)	N	SQ	19	Suprapubic (ne)	N	EXC + BRT + CCRT (ERT)	NED 49 mo
Doret [17]	LND + TOB	IIB	–	N	N	Small	6	Lat (nr)	N	EXC + ERT, CTX	NED 54 mo
Gregor [18]	PND	IIB	+	Y	N	SQ	3	Lat (e)	N	EXC	nr
Agostini [19]	PAND	IIB	+	Y	N	SQ	7	Lat (e)	PC	EXC	DOD 14 mo
Tjalma [20]	PAND	IIIB	–	N	nr	SQ	15	Umbilical (ne)	Para-arotic and liver mets	EXC + CTX	DOD 24 mo
Martinez-Palones [21]	RH + PAPND	IIIB	+	Y	Y	AD, PD	7	Umbilical	Cerivical progression	EXC	nr
Park [7]	PAPND	IIB	+	Y	Y	AD	1	Umbilical, Both lat	Liver mets	CTX	DOD
Yenen [22]	PAND	IIB	+	Y	Y	SQ	12	Lat (ne)	Vaginal recurrence	CTX + EXC	nr
Zivanovic [5]	Guide for implant	IB	–	N	Y	SQ	6.3	nr	Bladder and vaginal recurrence	nr	DOD 12 mo
	LND	IB	+	Y	Y	SQ	5.8	nr	PC	nr	DOD 9 mo
Martinez [6]	LND	IB	–	N	N	SQ	25	Umbilical (e)	Vaginal recurrence	EXC + ERT	DOD 30 mo
	PAND	IIB	+	Y	nr	SQ	6	Lat	PC	CTX	DOD 7 mo
	PAND	IIB	+	Y	nr	SQ	8	Lat	PC	CTX	DOD 26 mo
	RH + PAPND	IVA	+	Y	N	AD	8	Lat (ne)	Pelvic LNs	EXC	DOD 28 mo

AD = adenocarcinoma; BRT = brachytherapy; BSO = bilateral salpingo-oophorectomy; CCRT = concurrent chemoradiotherapy; CTX = chemotherapy; DOD = dead of disease; e = extraction port; ERT = external beam radiotherapy; EXC = excision; H = hysterectomy; Lat = lateral port; LND = lymph node dissection; mets = metastasis; N = none; ne = non-extraction port; NED = no evidence of disease; nr = not reported; PAND = para-aortic node dissection; PAPND = para-aortic and pelvic node dissection; PC = peritoneal carcinomatosis; PD = poorly differentiated; PND = pelvic node dissection; PR = pelvic recurrence; RH = radical hysterectomy; SQ = squamous; TOB = transposition of bilateral ovaries.

Table 2
Port site metastasis after robotic-assisted laparoscopic surgery for uterine cervical cancer.

Author	Age	Surgery	Stage	LN	Histology	Retrival bag	Pelvic washing	Interval from surgery	Port site	Concomittant failures	Symptoms	Treatment for recurrence
Sert [24]	60	RH + PND (bladder damage and repair)	1B1	–	AD, MD –WD	nr	nr	18 mo	Lat (Lt)	Bladder + pelvic LN	Urinary symptom	Diagnostic laparoscopy + EXC + CCRT
Bolles [25]	35	RH + BS + TOB + PND + PANS	1B2	+	SQ, PD	3 separate bags	N	5 mo	Umbilical	Pelvic LN	Abdominal pain and mass	EXC of abdominal mass + enlarged node + BSO
This study	36	RH + ROS + PND	1B1	–	AD, PD	Yes	Yes	5 mo	Lat (Rt)	Pelvic LN + PC	Abdominal pain and mass	CCRT

AD = adenocarcinoma; BS = both salpingectomy; BSO = bilateral salpingo-oophorectomy; CCRT = concurrent chemoradiotherapy; EXC = excision; Lat = lateral port; LN = lymph node; Lt = left; MD = moderately differentiated; nr = not reported; PANS = para-aortic node sampling; PC = peritoneal carcinomatosis; PD = poorly differentiated; RH = radical hysterectomy; ROS = right ovary sparing; Rt = right; SQ = squamous; TOB = transposition of bilateral ovaries; WD = well differentiated.

manipulation and a lack of surgical experience, pressure due to pneumoperitoneum, the effect of CO_2 on tumor cell biology, and impairment of local immune response after laparoscopic surgery [26]. Wilkinson et al studied an *in vivo* model of port site metastasis by comparing a laparoscopic port site with an open incision. There was no significant difference in the incidences of port site metastasis between open incision and laparoscopic video port site. Recurrences, however, occurred more frequently at the sites of laparoscopic working ports compared to the sites of open wounds or laparoscopic video ports. This result supports the possibility of direct seeding to port sites by surgical instrumentation or contamination with viable tumor cells [27], and might explain a large portion of port site metastases. Port site metastases, however, have been reported in patients who underwent diagnostic laparoscopy without manipulation of the tumor and even in patients without abdominal disease [5,6,9,12,15–17,20]. Moreover, some patients have experienced other scar site metastases independent of port sites [28]. These reports suggest that port site metastasis can occur through multiple, complex mechanisms. The reported incidence of port site metastasis varies depending on the primary tumor sites, and gallbladder adenocarcinoma is a well-known primary cancer of port site metastasis. Therefore, there may be inherent characteristics of tumor cells that make metastasis to ports or wounds more likely, especially as they relate to the patient's immune reaction after surgery.

Considering the higher probability of port site metastasis by direct tumor implantation [27], it is essential to minimize the spread of malignant cells during surgery. Several measures to prevent the spread of malignant cells during surgery have been proposed and include proper placement of trocars with minimal tissue trauma, rinsing trocars in 5% povidine–iodine before insertion, trocar fixation and prevention of gas leakage, minimal removal and reintroduction of trocars during the procedure, rinsing the tip of instruments in 5% povidine–iodine when changing instruments, minimal handling of the tumor, deflating the pneumoperitoneum with trocars in place, the use of protective bags to retrieve the tumor, removing all intra-abdominal fluid before trocar removal, irrigating the sites of the trocars with 5% povidine–iodine, and closure of 10–12-mm trocar sites [4]. In some studies, peritoneal and/or port site irrigation with cytotoxic agents was proposed to reduce port site metastasis [6].

RALS is generally considered less cost-effective, and it usually takes more time, than traditional laparoscopic or open surgery [2]. The cost-effectiveness of RALS largely depends on the status of the patient, the status of their disease, and the surgeon's skill. Longer procedures may increase the risk of port site metastasis by allowing more time for tumor cells to be shed and seed the port sites. The comparative effectiveness and safety of RALS should be verified before broader application especially in malignancies.

Port site metastasis is generally considered a poor prognostic factor. Patients with port site metastases usually have other synchronous metastases. However, there are no general recommendations for treatment of port site metastasis, perhaps

due to the heterogeneity and rarity of port site metastasis. If it is surgically resectable, excision of the port site metastasis is generally recommended. If the mass is not resectable, the patient might be treated with supportive care, chemotherapy, and/or radiotherapy. There are several reports of cervical cancer patients who suffered from port site metastasis and underwent radiotherapy (Tables 1 and 2). Brachytherapy and/or external beam radiotherapy have been attempted, but there are no reports describing the response to radiotherapy. Our patient was treated with CCRT and experienced prompt relief from pain and rapid shrinkage of tumors, as well as metabolic complete remission at short-term follow-up. She remained disease-free at 17 months' follow-up without specific complications. More follow-up is needed, but radiotherapy and/or chemotherapy might be considered as a potentially effective treatment modality for port site metastases after minimally invasive surgery, especially in cases in which recurrence is confined to the abdomen and pelvis.

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