Vaginal Mucosal Implantation After Total Laparoscopic Hysterectomy for an Early Stage Endometrial Cancer

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Abstract

We present an extremely rare case of vaginal implantation of endometrial cancer, which is presumed to have been caused by transvaginal uterine removal during laparoscopic hysterectomy. A 48-year-old woman, nulligravida, had undergone a bilateral salpingo-oophorectomy due to benign mature cystic teratoma at 46 years old. She presented abnormal genital bleeding and had a total laparoscopic hysterectomy, due to stage Ia endometrial cancer. Postoperative pathology revealed an endometrioid adenocarcinoma G1, showing myometrial invasion, not exceeding the half of the muscular layer. The vascular space invasion and lymphatic space invasion were markedly recognized. Three cycles of combination chemotherapy with paclitaxel and carboplatin, with an interval of 3 weeks, have been postoperatively executed. Four months after the completion of adjuvant chemotherapy, a gross tumor of 6 mm in diameter was found at left vaginal mucosa near hymen. Vaginal biopsy of the lesion revealed a serous adenocarcinoma, and review of the primary endometrial tumor concluded that the primary endometrial carcinoma is corrected to a diagnosis of serous adenocarcinoma. It is considered that the vaginal lesion has been implanted through transvaginal uterine removal during the laparoscopic surgery. The vaginal lesion was surgically resected, however, during the follow-up examination, the other undifferentiated sarcoma was detected at right lung and the treatment was focused on the sarcoma. And the patient died of the sarcoma, without the further recurrence of endometrial cancer.

Keywords: Vaginal implantation; Endometrial cancer; Laparoscopic hysterectomy

Introduction

Laparoscopic surgery has been widely spread in gynecology for both benign and malignant disease, because of its minimal invasiveness. In Japan, laparoscopic surgery for early stage endometrial cancer was approved as the coverage of medical insurance at April 2014, and routinely implemented nationwide afterward [1]. Endometrial cancer is the most common gynecological malignancy and approximately 70% of the disease is diagnosed as stage I [2]. And most frequent recurrent endometrial cancer occurs as local invasion within 2 or 3 years from surgery [3]. The vaginal implantation of endometrial cancer is quite rare and we would present a case of vaginal implantation of endometrial cancer, which is presumed to be caused through transvaginal uterine removal during laparoscopic hysterectomy. Documented informed consent has been obtained from the patient.

Case Report

A 48-year-old woman, nulligravida, had undergone a bilateral salpingo-oophorectomy due to benign mature cystic teratomas at 46 years old. Bilateral ovarian tumors did not show any pathological malignancy. She had not had a history of hormone replacement therapy after the oophorectomy. At 48 years old, she presented abnormal genital bleeding, and was diagnosed as endometrioid adenocarcinoma G1, with endometrial biopsy. She consulted to our hospital for the treatment of endometrial cancer. At the consultation, bimanual examination revealed an atrophic uterus and the bilateral adnexa were free. Pelvic magnetic resonance imaging (MRI) showed a low signal endometrial mass of 19 mm in diameter on T2-weighted sagittal section. The endometrial mass was enhanced in contrast study (Fig. 1). Myometrial invasion or uterine cervical invasion of the mass was not proven in MRI. No observable metastatic lesion was detected in positron emission tomography-computed tomography (PET-CT). The serum tumor markers were CA 125: 6 U/mL, CA 19-9: 8 U/mL, and CEA: 1.8 ng/mL, and they were below the cut-off value. Estimated preoperative diagnosis of the endometrial cancer was endometrioid adenocarcinoma G1, clinical stage Ia. For the primary treatment of early stage endometrial cancer, we operated total laparoscopic hysterectomy (TLH). In surgical procedure, a 12 mm trocar was inserted through the umbilicus and via the trocar the abdominal cavity was explored. Other three trocars of 5 mm were inserted into lower abdomen with diamond style [4, 5]. In the abdominal cavity, a slight adhesion was observed between the abdominal wall and the omentum. There was no ascites or dis-
Semination in the peritoneal cavity. Uterine manipulator was used for uterine support and a vaginal pipe was used at vaginal incision. After the vaginal incision, the resected uterus was transvaginally removed, without intraabdominal division and without a use of specimen retrieval bag. The total operation time was 173 min, and the blood loss in the hysterectomy was 50 mL. Postoperative diagnosis was endometrial adenocarcinoma grade 1, pT1aN0M0, peritoneal washing cytology was negative, and the tumor had invaded into the myometrium, but remained within half of the muscular layer. There were findings of vascular space invasion and lymphatic vascular space invasion (Fig. 2). The primary endometrial cancer was considered as to be intermediate risk group [6, 7], and we administered three cycles of adjuvant combination chemotherapy with paclitaxel and carboplatin, with 3-week interval [6-8].

Four months after the completion of chemotherapy (8 months after initial surgery), a symptom of genital bleeding occurred and internal examination have found a protruding lesion on the left wall of vaginal mucosa near hymen. The biopsy of the vaginal tumor proved a serous adenocarcinoma. The atypical cancer cells were proliferating with papillary appearance, with forming multiple layers. At H&E staining appearance, the findings of vaginal tumor was not similar with the primary endometrioid adenocarcinoma, which had not formed papillary proliferation.

For the investigation of the vaginal tumor, the vaginal tumor was surgically resected. And for the investigation of other lesions, thoracic CT scan revealed a nodular mass of 6 mm in diameter at right lung S3, which was also suspected as metastatic lesion.

Histological finding of the resected vaginal tumor revealed the same serous adenocarcinoma as that found in former vaginal biopsy. And immunostaining results of the vaginal tumor were positive for p53, strongly positive for p16, and negative for ER (Fig. 3). And additionally, exactly same immunostaining results were obtained from the primary endometrial cancer, which was diagnosed as endometrioid adenocarcinoma (Figures not shown). The histological and immunostaining results indicated that the origin of the primary endometrial cancer and the vaginal serous adenocarcinoma were same, and immunohistochemistry assumed that the both cancers are serous adenocarcinoma. We concluded the vaginal tumor as a vaginal recurrence of primary serous adenocarcinoma of endometrium, pTa1N0M0. It is considered that the vaginal lesion has been implanted through transvaginal uterine removal during the laparoscopic surgery.

Adjuvant chemotherapy for the vaginal recurrence of serous adenocarcinoma had been planned; however, the right lung nodule found at CT scan was subsequently resected with thorascopic resection and was histologically probed to be other undifferentiated sarcoma. Histological examination did not clarify the similarity between the sarcoma and the endometrial cancer; and review of the uterine/vaginal cancer lesions does not prove a sarcomatous component. At the follow-up

**Figure 1.** Pelvic MRI, sagittal section at the first consultation. (a) There is a low signal endometrial mass of 19 mm in diameter on T2-weighted sagittal section (arrow). (b) The endometrial mass was enhanced in contrast study (arrow). Myometrial invasion or uterine cervical invasion of the mass was not proven in MRI.

**Figure 2.** Histological findings of the endometrial tumor of surgically resected uterus (H&E stain; the original magnification is × 40). (a-b) Atypical glands are proliferating with tubular and cribriform pattern. There is no finding of papillary proliferation. The tumor had invaded into the myometrium within half of the muscular layer. There were findings of vascular space invasion and lymphatic vascular space invasion (b), (arrows). Postoperative diagnosis was endometrial adenocarcinoma grade 1, pT1aN0M0.

Thoracic/abdominal CT after 1 month from lung surgery, new lesion was found at the upper lobe of right lung and the treatment for the patient was focused for the sarcoma after that. However, the recurrent sarcoma further progressed and the patient died of sarcoma at 15 months from the right lung nodule resection, without further recurrence of endometrial cancer.

Discussion

Laparoscopic surgery for malignant diseases requires not only minimally invasiveness and tolerability, but also achievement of oncologic outcomes equivalent to laparotomy. In a RCT of the Gynecologic Oncology Group (GOG) LAP 2, laparoscopic surgery for endometrial cancer showed the hazard ratio for recurrence of 1.14 (95% CI: 0.92 - 1.46), comparing to laparotomy, and the RCT resulted that there was no difference in the estimated 5-year survival between laparoscopy and laparotomy. In literature, there are also several reports that showed laparoscopic surgery is superior on intraoperative complications, blood loss during the surgery, shorter term of hospitalization, and post-operative psychosomatic and social recovery [9, 10]. So the adaptation of laparoscopic surgery will be expected to expand in the future.

On the other hand, there are some recurrence patterns peculiar to laparoscopic surgery, such as port site recurrence [11-13] and as cancer dissemination with using uterine manipulator [14-16]. According to the use of the uterine manipulator, the laparoscopic surgery with uterine manipulator does not increase the possibility of atypical cytology of peritoneal cavity [17, 18], and does not affect the risk of recurrence [19, 20]. The present case was after the removal of both adnexa, so the bilateral fallopian tube had already been closed. We estimated there was low risk of peritoneal dissemination of cancer, and the use of the uterine manipulator was considered to have been safe. The intraperitoneal cytology was negative, whereas the recurrence occurred after surgery on the vaginal mucosa. We have not used the sample collection bag at the removal of the resected uterus. The report on the vaginal implantation after laparoscopic surgery of endometrial cancer is extremely limited [12]; and there is no report on the relationship between the use of sample collection bag and vaginal implantation of endometrial cancer. However, it is suggested that use of a bag during removal of the uterus through the vagina can limit seeding of malignant cells. Abdullah et al reported the vulvar recurrence of endometrial cancer at 8 months after the robotic surgery; and it is said that such cases are iatrogenic recurrence, which can be avoided by using sample collection bag [21].

Another diagnostic issue of the present case is the histological aggressiveness of the cancer. Serous adenocarcinoma of the uterine endometrium is known as aggressive type of histology and is responsible for 40% of deaths of endometrial cancer [22]. Pathological feature of serous adenocarcinoma is a predominant papillary growth, which is also found in some subtypes of endometriod adenocarcinoma. Distinction is usually easy when attention is paid to the presence of papillary architecture, however, serous adenocarcinoma may also present a pseudoglandular pattern, and in such cases, differential diagnosis may be problematic with endometrioid adenocarcinoma [22]. The primary uterine lesion of the present case was first diagnosed as endometrioid adenocarcinoma with lack of papil-
lary structure. Immunohistochemistry of p53, p16, IMP2 and IMP3 are reported to be useful for the specific in serous adenocarcinomas [22, 23] and we reached the diagnosis of serous adenocarcinoma after the investigation of vaginal lesion. The vaginal implantation of the present case was highly due to aggressive feature of serous adenocarcinoma, although, the primary lesion of endometrium has showed relatively low-grade endometrioid histology. In the adaptation of laparoscopic surgery for endometrial cancer, as well as laparotomy, we should take care for the diagnostic problem on the pathology of endometrial cancer. If we had recognized the serous pathology at the primary surgery, we should have done more extended surgery including lymphadenectomy and have done more thorough adjuvant therapy.

Conclusions

We experienced a quite rare case of vaginal implantation of endometrial cancer, which is caused by transvaginal uterine removal during laparoscopic hysterectomy. And there also seems to be difficulty in the pathological diagnosis of endometrial cancer. With the coverage of medical insurance, it is expected that increasing number of institutions conduct laparoscopic surgery for endometrial cancer in Japan. In order to achieve oncologic outcomes comparable to laparotomy, it is important to carefully establish the safe procedures preventing from anticipated surgical complications and from cancer recurrence.

Conflict of Interest

The authors declare no conflict of interest regarding this paper.

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References


