Undifferentiated Carcinoma After Laparoscopic Surgery for a Cystic Ovarian Tumour: A Case Study

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Abstract. Background: Laparoscopic surgery for malignant tumours occasionally results in recurrence at the trocar insertion site or port-site metastasis (PSM). We report on a patient requiring emergency laparoscopic surgery for an ovarian tumour with a review of the relevant literature. Case Report: A 42-year-old woman developed sudden abdominal pain and underwent laparoscopic right adnexectomy because of a suspected ovarian cystic tumour rupture. The postoperative histological diagnosis was a mucinous borderline ovarian tumour; however, an undifferentiated carcinoma was detected at the port site eight months after the initial surgery. The histopathological diagnosis of the abdominal wall tumour at the port site differed from intraoperative pathological findings, which was contradictory to PSM definition. Postoperatively, she received three systemic chemotherapy courses but died consequent to tumour metastasis. Conclusion: This is an atypical PSM case with histopathological differences from the initial tumour. Careful preoperative diagnosis and intraoperative attention are essential in such cases.

Port-site metastasis (PSM) occurs in the abdominal wall at the trocar insertion site after laparoscopic surgery, which is performed for abdominal malignancies, including gastrointestinal or gynaecological cancers. The pathological and histological signs are the same as those of primary tumours. Borderline ovarian tumours are rare, especially those with low malignant potential, while the incidence rate of malignant ovarian tumours ranges from 2% to 40%, depending on the progression stage (1-3). With the increasing popularity of laparoscopic surgery for malignant tumours, PSM has become a growing concern. Various theories have been reported regarding the onset of PSM, including damage by collection bags, implantation of exfoliated tumour cells at the trocar insertion site, and exposure to carbon dioxide gas (4-7). Risk factors for PSM in ovarian cancer include progressive ovarian cancer and malignant ascites (8). PSM is considerably rare in borderline ovarian tumours, with only a few reported cases (9). This case report is about a patient with a lesion believed to be PSM that was discovered after an emergency laparoscopic surgery for a ruptured ovarian mucinous borderline tumour. The reported case is discussed with a review of the relevant literature.

Case Report

A 42-year-old woman (gravida 8, para 6) had hypertension and no notable familial history. She developed sudden upper abdominal pain and was taken to her former physician. Abdominal computed tomography (CT) revealed a large quantity of fluid extending to the upper abdomen (Figure 1A) and an 8-cm floating cystic lesion lacking tension in the pelvis (Figure 1B). Thus, the patient was transferred to our hospital with a suspected rupture of the ovarian cystic tumour. Emergency surgery was performed due to a suspected rupture of the ovarian cystic tumour.
We performed laparoscopic right adnexectomy because the tumour was assumed to be benign. A 5-mm port was inserted using the optical method from the umbilical area, and a scope was inserted from the same site for intraperitoneal observation. We confirmed a rupture of the wall in the right ovarian tumour with mucinous ascites. There were no abnormal findings in the left adnexa or the rest of the abdominal cavity. Port sites were established in the lateral one-third of the line joining the bilateral iliac crests and umbilical area. We inserted 5- and 12-mm trocars in the lower left and right abdomen, respectively (Figure 2). An ultrasonic coagulation scalpel (Harmonic ACE7+; Ethicon, Somerville, NJ, USA) was used to resect the right uterine adnexa. A wound protector was placed around the 12-mm port, and the resected specimen was placed into a retriever bag (Endopouch, Ethicon) and removed. The collection bag was sealed during removal and no spread of tumour tissue inside the abdominal cavity was noted. The surgery was completed in 56 min with minimal blood loss. The total volume of ascites and liquid tumour content was 1,900 ml. The postoperative histopathological diagnosis was a mucinous borderline tumour (Figure 3). Additional laparotomy was performed two months after the first surgery. No abnormal findings were observed in the abdominal cavity, uterus, or left adnexa. A small volume of ascites was noted (peritoneal washing cytology: class II). The surgery was concluded with left salpingo-oophorectomy and partial omentectomy. The surgery was completed in 87 min with minimal blood loss. The postoperative histopathological findings showed no malignant tissue in the resected left adnexa or omentum. The patient was diagnosed with a stage I C3 (FIGO 2014) ovarian mucinous borderline tumour.

Six months after the first surgery, the patient noticed a mass near the lower right abdominal port insertion site. Contrast-enhanced CT revealed no notable findings, but a mass was suspected. Thus, abdominal contrast-enhanced magnetic resonance imaging (MRI) and whole-body fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT were performed eight months after the first surgery. Abdominal contrast-enhanced MRI revealed a mass...
lesion with poorly defined margins exhibiting a non-uniform contrast effect (inside the mass) in the abdominal wall of the lower right abdomen (Figure 4), with high FDG accumulation on FDG-PET/CT. Furthermore, FDG-PET/CT showed no other lesions suspected of distant metastasis. The lesion localization matched the insertion site of the lower right abdominal port from the first surgery. Hence, PSM was suspected, and an exploratory laparotomy was planned.

Intraoperative findings showed that the right abdominal wall tumour had extensively invaded into the rectus abdominis muscle without any invasive extensions beyond the peritoneum into the abdominal cavity. There was no accumulation of ascites (peritoneal washing cytology: class V). Since the tumour invaded the rectus abdominis muscle, complete resection was impossible, permitting only the performance of an abdominal wall mass biopsy. The surgery was completed in 87 min with minimal blood loss. Histopathological findings of the excised specimen showed dense proliferation of large, atypical cells with irregularly shaped, richly polymorphic nuclei. An evident adenocarcinoma component and some large, atypical cells were positive for cytokeratin AE (CKAE1/AE3). Although some CKAE1/AE3-negative cells were present, they were vimentin positive. All atypical cells were negative for oestrogen receptor, α-smooth muscle actin, and S-100 immunostaining. The differential diagnoses included undifferentiated carcinoma and carcinosarcoma. Since we morphologically observed a transition between the adenocarcinoma components with strong differentiating tendencies and atypical cells with individual cell characteristics believed to be mesenchymal cells, we diagnosed the tumour as an undifferentiated carcinoma with epithelial–mesenchymal transition (EMT) (Figure 5 and Figure 6).

Because preoperative imaging did not reveal any other potential primary lesions and the lesion location corresponded to the port site of the first surgery, we inferred that the malignant transformation of the borderline ovarian tumour cells left at the port site resulted in epithelial ovarian cancer and that the EMT had resulted in an undifferentiated carcinoma. After surgery, the patient received three systemic chemotherapy courses involving paclitaxel and carboplatin; however, tumour metastasis resulted in death of the patient 13 months after the first surgery.

Discussion

There has been a recent tendency to select laparoscopic surgery for ovarian tumours with no malignant findings on preoperative imaging; this tendency also applies to emergency surgeries for ruptured ovarian cysts or ovarian torsion. In clinical practice, 0.4-2.5% of cases involve surgeries performed on the assumption of a benign ovarian tumour before surgery but result later in a discovery of ovarian borderline malignant tumour or ovarian cancer based on postoperative pathological diagnosis (10).

Thus, laparoscopic surgeries performed for ovarian tumours assumed to be benign require utmost caution to prevent intra-abdominal spread. Since laparotomy is generally preferred for suspected ovarian cancer, most patients in whom PSM occurs after ovarian cancer or borderline ovarian tumour treatment, may be eligible for laparoscopic surgery on the assumption of a benign tumour (with a few exceptions), as seen in our case.

More facilities are also performing diagnostic laparoscopy for cases with suspected progressive ovarian cancer, thus necessitating caution.
Factors leading to PSM include the intraperitoneal spread of tumour cells during surgery, breach of specimen collection bags, implantation of tumour cells at the trocar insertion site, or wound exposure to carbon dioxide gas (4). Carbon dioxide gas used for creating pneumoperitoneum could promote the proliferation of tumour cells that have been implanted in the peritoneum (5-7, 11). Countermeasures against PSM development include using a wound protector at the trocar insertion site, preventing carbon dioxide gas leakage or avoiding rapid removal of gas, and ample washing of the abdominal cavity and instruments used before trocar removal. Other reported countermeasures include debridement of the trocar insertion wound or preventative irradiation of the port site. However, the effectiveness of these various countermeasures remains unclear (12-16). In our case, a wound protector was used at the trocar insertion site and a collection bag was used to collect the specimen (with no apparent breach in the bag). Before completing the surgery, a thorough cleaning of the abdominal cavity interior and trocar insertion sites was performed. However, PSM occurred despite employing conceivable countermeasures. As it is currently difficult to completely prevent PSM, cases of malignancy after laparoscopic surgery require ample precaution against recurrence inside the abdominal cavity and at the trocar insertion site.

In PSM, tumours occurring at the port site have the same histological features as the primary tumours. In our case, the primary tumour was a mucinous borderline tumour, yet the tumour occurring at the port site was an undifferentiated carcinoma. This is an atypical PSM case, indicating that the borderline tumour had likely undergone malignant transformation caused by EMT. Among borderline ovarian tumour patients, approximately 20% of recurrence cases reportedly lead to invasive ovarian cancer owing to malignant transformation (2).

However, normally, low-grade carcinomas undergo malignant transformations. Although no studies have reported the recurrence rate of malignant transformation, borderline tumour recurrence rates are generally 4-20% (17). Therefore, the early recurrence of this case as a high-grade carcinoma is atypical (2, 4, 17, 18).

The mean period until PSM extraction in ovarian cancer is seven months (3), but our case involved a borderline tumour. Therefore, if we assume that malignant transformation occurred in this borderline tumour followed by EMT, it is evident that the period until recurrence was relatively short.

There is little evidence to prove that laparoscopic surgery for ovarian cancer is superior to laparotomy for preventing complications or improving prognosis (19). Approximately 10-47% of patients who undergo laparoscopic surgery for advanced ovarian cancer develop PSM (1, 8, 20-22). Thus,

Figure 4. Imaging findings at the onset of port-site metastasis. Contrast-enhanced magnetic resonance imaging (MRI) reveals a mass with an irregular margin of approximately 6 cm on the right abdominal wall and a non-uniform contrast-enhancing effect inside (white arrow). A high fluorodeoxyglucose concentration, similar to that observed in the lower right abdomen mass, is noted on both positron emission tomography-computed tomography and MRI (white arrow). The image shows no other abnormal findings suggestive of other distant metastases.
Figure 5. Pathology at the time of port-site metastasis surgery (haematoxylin and eosin staining). Histopathology of the right abdominal wall mass biopsy (haematoxylin and eosin (H&E) staining). A) ×2 H&E staining. The circled part is enlarged. B) ×4 H&E staining. The circled part is enlarged. Some adenocarcinoma components are observed but most are poorly differentiated, large, atypical cells (circled part). C) Dense solid growth of large, atypical cells; however, the muscle tissue is unclear. A glandular component appears to be present in certain parts (arrow). Signs of transition together with poorly differentiated, large, atypical cells are observed between the adenocarcinoma components (arrow) with a strong tendency for morphological differentiation. The smaller atypical cells (arrowhead) are thought to be of mesenchymal origin.

Figure 6. Pathology at the time of port-site metastasis surgery (immunostaining). Histopathology of the right abdominal wall mass biopsy (immunostaining). A, B) An evident adenocarcinoma component with some large, atypical cells that are positive for cytokeratin AE (CKAE)1-3 (arrow). However, only a few negatively stained cells are present (black arrow), some of which are vimentin positive (arrowhead). C-F) All atypical cells are negative for estrogen receptor (ER), α-smooth muscle actin (α-SMA), desmin, and S-100 in immunostaining (arrow).
even with an increase in the number of favourable indications for laparoscopic surgery in gynaecological malignancies, it should be limited to cases of early ovarian cancer or where laparoscopic observation indicates that complete resection would be feasible.

Moreover, the PSM mechanism remains poorly understood, and its elucidation in future studies could be considerably important for expanding indications for laparoscopic surgery for gynaecological malignancies.

In conclusion, in our case, an atypical PSM developed early after laparoscopic surgery performed for managing a borderline ovarian tumour rupture. PSM has attracted attention as a new recurrence form associated with the increasing use of laparoscopic surgery. However, in some ovarian tumour patients, in whom laparoscopic surgery is often performed, malignancy is diagnosed after surgery. Therefore, preoperative diagnosis should be meticulously performed, and intraoperative precautions should be taken.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors’ Contributions

SK wrote the article and obtained consent from the patient; SK, TU, TA, SM, and TN revised the article; SK and JT performed the pathological examination. Final permission to write the paper was obtained by TY.

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