



Unusual Peritoneal Metastasis of Late Recurrent Uterine Cervical Cancer: A Case Report and Literature Review

후기 재발성 자궁 경부암의 비전형적인 복막 전이:
증례 보고 및 문헌 고찰

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Uterine cervical cancer is one of the most common malignancies of the female genital tract. Most recurrent cases of uterine cervical cancer are diagnosed within two years after primary treatment, and late recurrence after a disease-free interval of more than five years is rare. In addition, peritoneal metastases usually present as multifocal discrete nodules in the peritoneal cavity with nodular or diffuse peritoneal thickening. Herein, we report an extremely rare case of late recurrent cervical cancer peritoneal metastasis with an unusual manifestation of a large, solitary necrotic mass in the right subphrenic space on contrast-enhanced CT.

Index terms Neoplasm Metastasis; Uterine Cervical Neoplasms; Recurrence; Multidetector Computed Tomography; Positron-Emission Tomography

INTRODUCTION

Uterine cervical cancer is one of the most common malignancies of the female genital tract. Squamous cell carcinomas account for approximately 80% of malignant tumors of the uterine cervix (1). Most recurrent cervical cancers are diagnosed within 2 years after primary treatment and late recurrence after a disease-free interval of more than 5 years is rare. There have been a few case reports of recurrent cervical cancer with peritoneal metastasis (2). In this report, we describe a very rare case of unusual peritoneal metastasis of late recurrent cervical cancer.

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CASE REPORT

A 68-year-old female presented to the cardiothoracic surgery department because of right lower chest wall pain. The symptom started 1 year ago and worsened 1 week ago. She had undergone total abdominal hysterectomy for uterine cervical cancer at an outside hospital 32 years ago. Previous medical records associated with the histologic type and staging of the uterine cervical cancer and adjuvant therapy could not be identified, because she received primary treatment at an outside hospital long time ago. She was evaluated 1 year ago with no evidence of recurrent disease on abdomen and chest CT, and no significant genitourinary symptom suggesting recurrence had been noticed. Her C-reactive protein level was elevated at 4.91 mg/dL. There were no significant abnormalities detected on plain radiography.

Multidetector CT was performed to acquire pre- and three-phase contrast-enhanced CT scans with iodinated non-ionic contrast media. Contrast-enhanced CT detected a necrotic mass measuring approximately 6.2 cm, with an irregularly thick enhancing wall in the right subphrenic space on the portal venous and equilibrium phases (Fig. 1A). The mass invaded the right intercostal muscles and right hemidiaphragm, and several enlarged left cardiophrenic lymph nodes were observed (Fig. 1B). There were no other tumors in the peritoneal and pelvic cavity including the solid organs and vaginal stump. Neither peritoneal nodule nor ascites was present. In addition, there were no enlarged lymph nodes in the retroperitoneal space, para-aortic and bilateral iliac chain areas. Based on radiological findings, the mass in the right subphrenic space was suspected to be a tuberculous abscess or primary peritoneal tumor, such as peritoneal malignant mesothelioma and desmoplastic small round cell tumor.

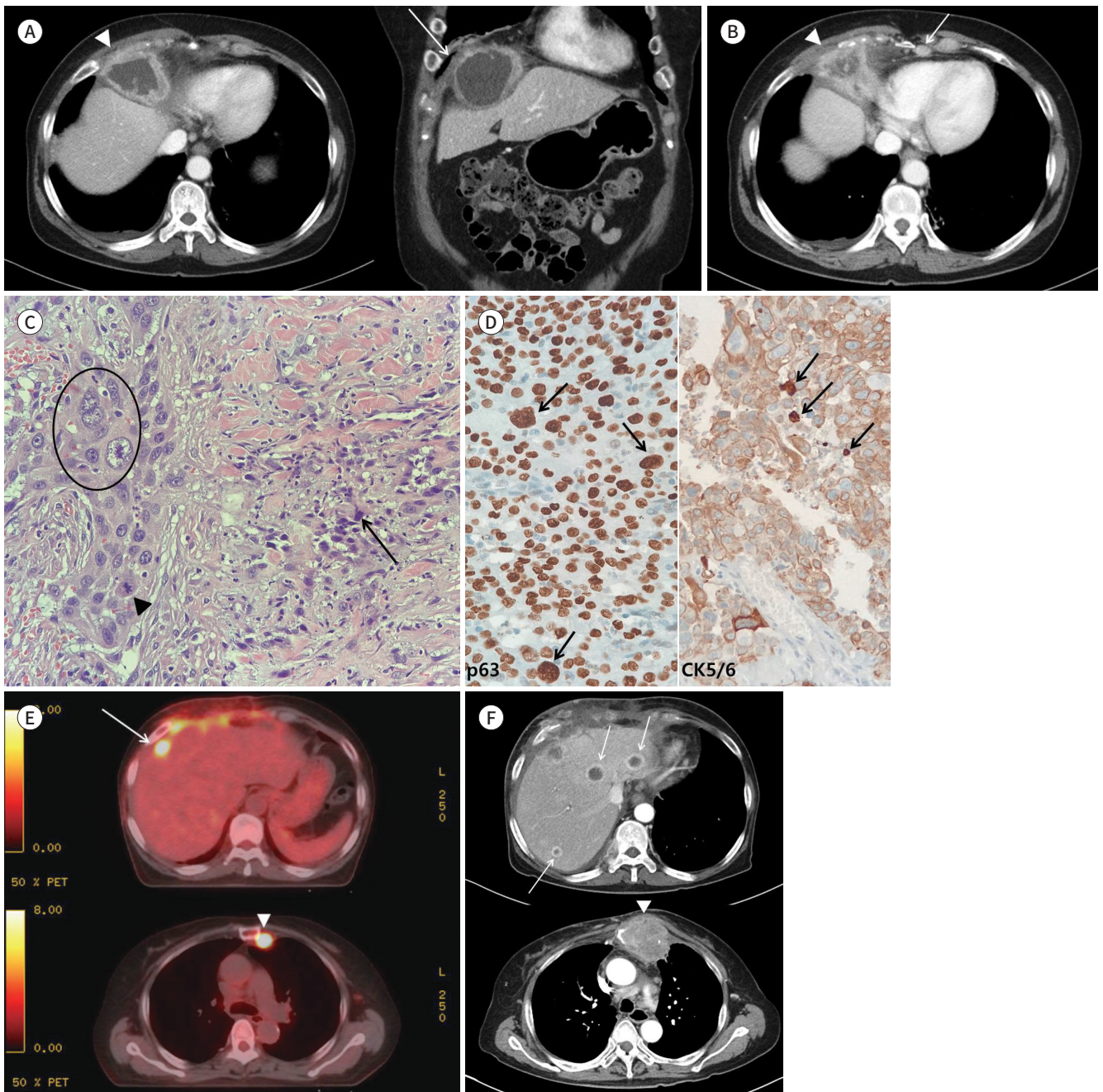
Percutaneous drainage of the necrotic mass and cytological examination of the aspirated fluid were performed. There were no malignant cells in the aspirated fluid, and a polymerase chain reaction assay was negative for tuberculosis. Resection of the mass in the right subphrenic space was performed to diagnose and treat the mass. During the surgery, the mass was located in the right subphrenic space and showed transmural invasion to the diaphragm, parietal peritoneum and intercostal muscles. The mass was pathologically confirmed to be squamous cell carcinoma (Fig. 1C) and suggested to be a metastatic tumor within the background of previous uterine cervical cancer. In immunohistochemical staining, the tumor cells showed a positive reaction on p63 and CK5/6 (Fig. 1D), and showed a negative reaction on thyroid transcription factor 1 (TTF-1), napsin-A and calretinin. It was pathologically consistent with squamous cell carcinoma.

1 month after surgery, ¹⁸F-fluorodeoxyglucose (FDG) PET/CT was performed to plan radiotherapy. The ¹⁸F-FDG PET/CT scan showed a hypermetabolic nodule in fourth segment of the liver and a hypermetabolic lymph node in the left internal mammary chain (Fig. 1E). These were suggested to be distant metastases. Tumor marker such as squamous cell carcinoma antigen was not checked.

The patient received the adjuvant radiotherapy and chemotherapy. 3 months later, the patient developed multiple metastatic nodules in the liver and metastatic lymphadenopathy in the left internal mammary chain was enlarged on follow-up CT (Fig. 1F).

This case report was approved by our Institutional Review Board, and the requirement for informed consent was waived (IRB No. EMC 2021-07-014).

Fig. 1. A 68-year-old female with an unusual peritoneal metastasis of late recurrent uterine cervical cancer in the right subphrenic space.
A. Axial and coronal images of contrast-enhanced CT show a large necrotic mass (arrowhead) with an irregularly thick enhancing wall and contiguous invasion of the right hemidiaphragm (arrow) in the right subphrenic space.
B. Axial image of contrast-enhanced CT shows the necrotic mass with invasion of the right intercostal muscles (arrowhead) and two enlarged left cardiophrenic lymph nodes (arrow).
C. The specimen from the mass in the right subphrenic space shows atypical squamous cells with abundant cytoplasm (circle), hyperchromatic nuclei (arrow), and abnormal mitosis (arrowhead) that were compatible with squamous cell carcinoma ($\times 400$; hematoxylin and eosin stain).
D. On immunohistochemical stain, multiple tumor cells (arrows) are positive for p63 and CK5/6 ($\times 400$).
E. ^{18}F -fluorodeoxyglucose PET/CT shows a hypermetabolic nodule (arrow) in the fourth segment of the liver and a hypermetabolic lymph node (arrowhead) in the left internal mammary chain.
F. Axial images of contrast-enhanced CT obtained three months after chemoradiotherapy show multiple low attenuating nodules with rim enhancement (arrows) in both lobes of the liver, suggesting multiple hepatic metastases, and a bulky enlarged left internal mammary lymph node (arrowhead) with invasion of the sternum.



DISCUSSION

The prevalence of late recurrence at 5 years or more after treatment in patients with uterine cervical cancer is 0.4%–7.5% (3). Furthermore, very late recurrence after 10 years is rarer still and was reported in less than 0.4% of the cervical cancer patients (3). In our case, late recurrence was detected approximately 30 years after primary treatment, which is extremely rare. Late recurrence of uterine cervical cancer was frequently observed in patients receiving primary treatment, including radiotherapy, which is considered a risk factor for recurrence, because many of these patients already had pelvic lymph node metastasis at initial treatment (3). Also, late recurrence was significantly less frequently observed in patients who underwent a primary operation than in those who did not undergo a primary operation, because it was suggested that lymphadenectomy could reduce lymph node recurrence (3).

The typical manifestations of recurrent cervical cancer are pelvic masses and lymphadenopathies. According to previous study (4), pelvic masses can involve the uterus, parametria, bladder, ureters, rectum and ovaries. Lymphadenopathies can present as enlarged pelvic and retroperitoneal lymph nodes.

Moreover, atypical manifestations including solid organ metastases can occur. The liver is the most commonly involved intraabdominal solid organ. Hepatic metastases were reported in approximately 30% of patients with recurrent cervical cancer (4). Hepatic metastases from recurrent cervical cancer usually appear as multiple focal lesions with variable enhancement patterns on CT.

Peritoneal metastases of cervical cancer are rare. Approximately 1% of patients with cervical cancer have peritoneal metastases (5). The typical CT findings of peritoneal metastases are multifocal discrete nodules in the peritoneal cavity, omental haziness, ascites, and peritoneal thickening, nodularity and enhancement (6). In addition, peritoneal involvement of recurrent cervical cancer may present as implants, which result in scalloping of the liver contour, peritoneal nodularity and serosal soft-tissue masses that cause extrinsic compression of the bowel (4). There has been no report on peritoneal metastasis of recurrent cervical cancer whose manifestation was a large single necrotic mass like our case.

Although possible pathway for tumor spread in our case is uncertain, the following hypothesis may allow us to explain. It has been reported that lymphogenous recurrence was more frequent in late recurrence of cervical cancer compared to hematogenous metastasis (3). Peritoneal lymphatic stomata are channels connecting the peritoneal cavity with lymphatics in the peritoneum. According to previous study (7), peritoneal lymphatic stomata may be the main pathway for draining from the peritoneal cavity and the diaphragmatic peritoneum has the strongest absorption in all parts of the peritoneum. Therefore, the tumor cells might be absorbed into peritoneal lymphatic stomata of the diaphragm.

In our patient, CT scans showed a large single necrotic mass with an irregularly thick enhancing wall in the right subphrenic space. The mass invaded the adjacent structures including right hemidiaphragm and right intercostal muscles, suggesting tuberculous abscess or primary peritoneal tumor. Our initial differential diagnoses included tuberculous abscess, peritoneal malignant mesothelioma and desmoplastic small round cell tumor. In our case, tuberculous abscess was considered because tuberculosis can present as abscess formation

in the perihepatic space with lymphadenopathy and it extend to the adjacent structures such as abdominal wall muscles (8). Although it is difficult to distinguish tuberculous abscess from malignant necrotic tumor, tuberculous abscesses usually have evenly thin wall with mild enhancement and several internal septa on CT (8). Peritoneal malignant mesothelioma is malignant neoplasm that arises from mesothelial cells or multipotential subserosal mesenchymal cells of the peritoneum. Localized peritoneal malignant mesothelioma appears as a heterogeneous, solid intraperitoneal mass and the invasion of adjacent visceral structures may occur (9). Desmoplastic small round cell tumor is a rare and highly aggressive primary peritoneal malignancy. The tumor presents as a large and bulky intraperitoneal mass and it has characteristically heterogeneous attenuation on CT or has centrally located low-attenuation region, which reflects intratumoral necrosis or hemorrhage (9).

The prognosis of patients with cervical cancer after the development of metastasis is usually poor. Patients with recurrence in lymph nodes had a median survival of 24 weeks, whereas those with recurrence in other organs had a median survival of only 12 weeks (10). Treatment options include all modalities of cancer treatment. Surgery followed by palliative chemotherapy and local radiotherapy are the general treatments offered to patients.

Our case report has a few limitations, because the medical record associated with histologic type of the uterine cervical cancer was not identified. First, there is another histologic type of the uterine cervical cancer, such as adenocarcinoma and adenosquamous cell carcinoma less commonly, although squamous cell carcinoma is the most common histologic type. Second, cancer of unknown primary site could not be completely excluded. However, no other primary cancer which could develop squamous cell carcinoma was detected on abdomen and chest CT and PET/CT. Moreover, squamous cell carcinoma originating from the subphrenic bronchogenic cyst was also possible. However, bronchogenic cyst or ciliated pseudostratified columnar epithelial cell was not found in the specimen pathologically.

In conclusion, although late recurrence of uterine cervical cancer is rare, very late recurrence, which is detected more than 30 years after primary treatment, may also occur. When there is a large single necrotic mass in the right subphrenic space and the patient has a history of uterine cervical cancer, unusual manifestation of peritoneal metastasis can be considered as a differential diagnosis.

Author Contributions

Conceptualization, K.H.J.; data curation, P.S.; supervision, K.H.J.; writing—original draft, P.S.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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후기 재발성 자궁 경부암의 비전형적인 복막 전이: 증례 보고 및 문헌 고찰

박상민 · 김희진*

자궁 경부암은 여성 비뇨 생식기계에서 가장 흔한 악성 종양이다. 대부분의 재발성 자궁 경부암은 초기 치료 후 2년 이내에 진단되고 무병 기간이 5년 이상인 후기 재발은 매우 드물다. 또한 복막 전이는 보통 복강 내 뚜렷한 다발성 결절 그리고 결절성 또는 미만성 복막 비후의 형태로 나타난다. 여기서 우리는 조영증강 컴퓨터단층촬영에서 우측 횡격막하 공간에 큰 단일 괴사성 종괴로 보인 후기 재발성 자궁 경부암의 비전형적인 복막 전이라는 매우 드문 증례를 보고하고자 한다.

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