

## Rare metastases of recurrent cervical cancer to the pericardium and abdominal muscle

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**Abstract** Pericardial metastasis from recurrent cervical cancer is very rare. There have been few case reports of such cases in which antemortem diagnoses were established. Cases of additional abdominal muscular metastasis have not been reported previously, although a small number of cases of additional skin metastasis have been reported. A 64-year-old woman with intermittent vaginal bleeding was referred under the clinical impression of cervical cancer. Further investigation revealed a cervical cancer (FIGO stage Ib), and she underwent a radical hysterectomy followed by adjuvant concurrent chemoradiation. During the post-operative follow-up period of 6 months, pericardial and abdominal muscular metastases were developed along with the symptoms of dry cough and dyspnea. We recommended a palliative pericardial window, but the patient rejected it. Although palliative radiation therapy and chemotherapy were performed for the control of the metastases, she expired due to cardiac failure 16 months after the operation. The prognosis of patients with pericardial and abdominal wall metastases from recurrent cervical cancer is usually poor because of the systemic dissemination of the disease. Aggressive local and systemic treatments may provide significant palliation of associated symptoms.

**Keywords** Pericardial · Abdominal muscular · Metastasis · Recurrent · Cervical cancer

### Introduction

Cardiac metastases from neoplastic diseases such as melanoma, lymphoma and lung and breast cancers are found in approximately 10–15% of such cases, but they were rarely metastasized from gynecologic cancer. A cardiac metastasis at autopsy is rare with a frequency ranging from 1.6 to 8.0% in patients with cervical cancer. The most common site of cardiac involvement has been reported to be as pericardium (approximately 62–81%), whereas myocardial or endocardial involvements are very rare [1].

Pericardial metastasis from primary cancer including cervical cancer is often not diagnosed until autopsy because related symptoms usually manifest at the late stage of the clinical course [2]. Moreover, it is very difficult to standardize the management of patients with pericardial metastasis from recurrent cervical cancer because the prognosis of them is generally poor and its incidence is very low. In addition, there have been few reports about muscular metastasis without the extension of recurrent cervical cancer to the subcutaneous tissue or skin although the citation of metastasis to skin seems redundant.

Herein, we present a case of pericardial and abdominal muscular metastases from recurrent cervical cancer which terminated fatally from cardiac failure.

### Case report

A 64-year-old woman with intermittent vaginal bleeding was referred to our clinic with the suspicion of cervical

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**Fig. 1** Whole body FDG–PET shows recurrent lesions in the pelvic cavity and metastases in the anterior mediastinum and abdominal wall (white arrows)

intraepithelial neoplasm (CIN) III on Papanicolaou smear. Gynecological examination revealed no abnormal findings except an approximately 0.4 × 0.2 cm central erosion of the cervix with the acetowhite epithelium by colposcopy. Colposcopically directed punch biopsy showed histopathological findings compatible with invasive squamous cell carcinoma. Squamous cell carcinoma antigen (SCCA) increased to 2.6 ng/ml (normal range, 0–2 ng/ml). Computed tomography (CT) of the pelvis with intravenous contrast revealed an approximately 5 cm diameter cervical mass that extended to the upper vagina with parametrial invasion. Sigmoidoscopy, cystoscopy, and intravenous pyelography showed no abnormal findings.

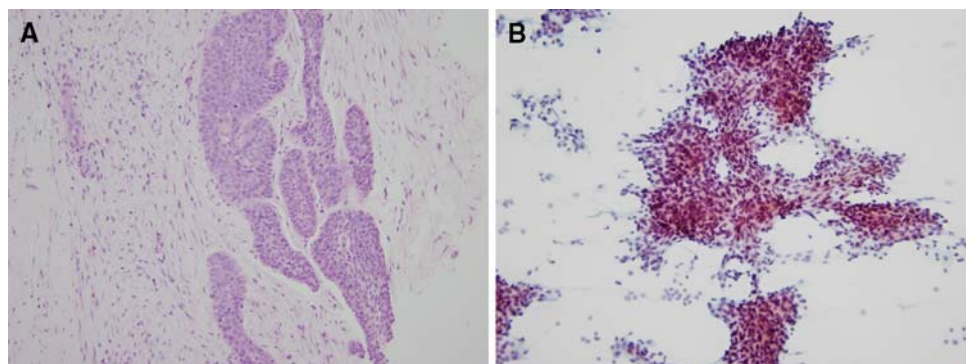
To avoid the complications of primary concomitant chemoradiation treatment, a radical hysterectomy along with bilateral salpingo-oophorectomy, and pelvic and para-

aortic lymph node dissection was performed under the diagnosis of International Federation of Gynecology and Obstetrics (FIGO) stage Ib because the complete resection of tumor and surrounding tissues with tumor invasion was considered to be possible. Histologically, the surgical specimen revealed invasive squamous cell carcinoma involving the endometrium, myometrium, and parametrium. The upper vagina and lymph nodes were not involved histologically. Concurrent chemoradiation with two cycles of paclitaxel (135 mg/m<sup>2</sup>)/carboplatin (AUC 5, Calvert formula) and adjuvant chemotherapy with four cycles of the same regimen were performed after surgical treatment.

Two months after the completion of adjuvant treatment, abdomen CT with intravenous contrast revealed a metastatic lesion in the abdominal muscle in the right lower quadrant area. Additionally, chest CT with intravenous contrast revealed a peripheral rim-enhanced lesion in the medial aspect of the pulmonary artery and a pericardial effusion. Whole body fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) showed a recurrence in the pelvic cavity with metastases on the anterior mediastinum and abdominal wall (Fig. 1). SCCA increased to 4.6 ng/ml. Based on the aforementioned results, she was diagnosed with pericardial and abdominal muscular metastases from recurrent cervical cancer, and thus fine needle aspiration biopsy (FNAB) of the abdominal metastatic lesion was percutaneously performed. Since histopathology showed metastatic squamous cell carcinoma (Fig. 2a), four cycles of gemcitabine (750 mg/m<sup>2</sup>) on day 1, 8 and 15 with carboplatin (AUC 5, Calvert formula) on day one were administered as second-line chemotherapy.

Five months after the completion of adjuvant treatment, she complained of dry cough and dyspnea. Echocardiography and transesophageal echocardiography (TEE) were performed for further evaluation. They showed a moderate pericardial effusion and an invasion of a suspicious soft tissue mass from the right atrium and AV groove to the aortic root. She was followed-up with chest CT with intravenous contrast, which showed a soft tissue mass in the pericardial space and a pericardial thickening with extension to the aortic root.

**Fig. 2** Histopathology demonstrates metastases from recurrent cervical cancer **a** squamous cell carcinoma of the abdominal muscle metastasized lesion from recurrent cervical cancer obtained by fine needle aspiration biopsy (FNAB) and **b** malignant cell clusters on cytological examination of pericardial effusion obtained by pericardiocentesis (H&E, ×200)



Ten months after the completion of adjuvant treatment, abdomen and chest CT scans with intravenous contrast were performed due to aggravation of the symptoms. The abdominal metastatic lesion was enlarged (Fig. 3a), and the pericardial effusion and mass increased compared to that of the last follow-up studies (Fig. 3b). Cytological examination of the fluid obtained by pericardiocentesis showed malignant cell clusters (Fig. 2b). We recommended a palliative pericardial window using thoracoscopy for the control of symptoms, but the patient rejected it. Although palliative chemotherapy with one cycle of 5-fluorouracil (1,000 mg/m<sup>2</sup>)/cisplatin (60 mg/m<sup>2</sup>) and radiation therapy for abdominal and pericardial metastases were performed, she expired due to cardiac failure 12 months after the completion of adjuvant treatment.

## Discussion

The common sites of extrapelvic metastasis of recurrent cervical cancer include lung, liver, bone, and lymph nodes. Nevertheless, cardiac metastasis of cervical cancer is observed less commonly. The factors that possibly contribute to the lower incidence of cardiac metastasis are suggested as follows: the strong kneading action of the myocardium, the metabolic peculiarities of the striated muscle, the rapid flow of blood through the heart, and the lymph flow normally moving away from the heart [1].

The common clinical manifestations of pericardial metastasis are cough, dyspnea, arrhythmia, and tachycardia. Approximately 30% of the patients with pericardial metastasis are symptomatic and 16% of them develop cardiac tamponade which is a life-threatening complication [3]. However, many metastatic cardiac lesions are clinically silent and found only at autopsy because the proliferation rate of metastatic tumors appears to be slow and the valves and tissues of the cardiac conduction system are relatively resistant to tumor invasion.

On the other hand, abdominal muscular metastasis without extension to the subcutaneous tissue or skin, which

occurred in our case, has not yet been reported to the best of our knowledge. Furthermore, it has not yet developed at post-operative drain sites or abdominal wall incision sites in this patient.

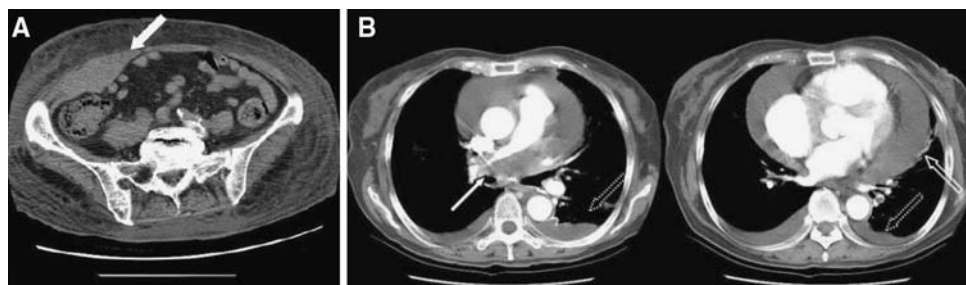
Treatment modalities for the control of pericardial metastasis from recurrent cervical cancer are as follows: pericardiocentesis [3], pericardial instillation of sclerosing agents [4], pericardial window [5], pericardiectomy [6], radiotherapy, and chemotherapy [7].

Although pericardiocentesis is the choice for the control of symptoms and the immediate relief of cardiac tamponade, it is ineffective because of re-accumulation of pericardial fluid [3].

Pericardial instillation of sclerosing agents is an effective treatment method for controlling malignant pericardial effusion. The recurrence rate was reported to be 57% of the patients undergoing pericardiocentesis versus 11% of the patients undergoing pericardial instillation of sclerosing agents. Tetracycline is the most frequently used sclerosing agent and other drugs such as bleomycin, mechlorethamine, quinacrine, thiotepa, 5-fluorouracil, and alkylating agents are also used. However, adverse effects such as severe local pain, bone marrow suppression, arrhythmia, ventricular laceration, sepsis, and death were reported in rare cases [4].

The creation of a pericardial window through a subxiphoid approach provides the control of pericardial effusion in 85–90% of the patients. It allows direct examination of the pericardium and biopsy for the confirmation of metastatic disease [5]. Moreover, it is the preferred approach over a pericardiectomy because of significantly lower morbidity and mortality [6]. Nevertheless, local treatments including pericardiocentesis and pericardial window may provide only the palliation of symptoms by relieving cardiac tamponade without the improvement of prognosis [8].

Thus, systemic treatments such as chemotherapy and radiation therapy are important for the control of recurrent cervical cancer. In particular, cisplatin-based chemotherapy may be recommended and patients with isolated recurrence has been reported to have longer survival than those with multiple metastases [7].



**Fig. 3** Abdomen and chest CT scans show metastatic lesions from recurrent cervical cancer 10 months after the completion of adjuvant treatment **a** metastatic lesion in the abdominal muscle at the right lower

quadrant area (*white arrows*) and **b** pericardiac mass (*white arrows*), pericardial effusions with thickening (*blank arrows*) and pleural effusion (*dotted arrows*)

Although a pericardial effusion is ominous, the disease-free interval prior to its occurrence may be predictive of the prognosis. Nelson et al. [9] found that patients with late development of pericardial effusion of longer than 20 months from the initial diagnosis lived for 9–10 months while patients who had a pericardial effusion at the initial diagnosis of cervical cancer had a particularly low survival rate. In addition, the prognosis of patients with abdominal wall metastasis from recurrent cervical cancer is poor because it is associated with the systemic dissemination of the disease. Therefore, the mainstay of treatment for such patients remains palliation with radiation, chemotherapy, and surgery alone or these treatments in combinations [2].

In the present case study, a palliative pericardial window for the control of pericardial metastasis was not performed because the patient rejected it. However, her prognosis was poor because palliative radiation and chemotherapy were not effective and the local treatment for the control of pericardial metastasis could provide only the control of symptoms. For improving the prognosis, new modalities such as molecular targeted therapy should develop in the future.

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