

Endometrial carcinoma complicated by malignant pericardial effusion

A case report on the therapeutic regimen

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Abstract

Rationale: High-stage endometrial carcinoma is an aggressive tumor with a high propensity for distant spread. However, metastases to the pericardium are rare in gynecological cancer, and are usually fatal.

Patient concerns: A 69-year-old woman was diagnosed with endometrial carcinoma with pericardium metastasis. The symptoms at presentation were panic and shortness of breath.

Diagnoses: The cytologic examination of pericardial fluid obtained by pericardiocentesis confirmed metastasis.

Interventions: In addition to cisplatin instilled into the pericardial space, for systemic chemotherapy, we chose that gemcitabine and lobaplatin regimen be preferred.

Outcomes: The patient has been participating in telephone follow-up for 8 months and has generally remained in a good condition.

Lessons: Endometrial carcinoma can have pericardial metastases. When this happens, we recommend ultrasound-guided pericardial puncture and the pericardial injection of cisplatin, in combination with systemic chemotherapy that consists of gemcitabine and lobaplatin.

Abbreviation: MRI = magnetic resonance imaging.

Keywords: endometrial carcinoma, pericardial metastasis, treatment

1. Introduction

Endometrial carcinoma is the most common gynecological cancer in developed countries. More than 90% of cases of endometrial cancer occur in women >50 years of age, with a median age at diagnosis of 63 years.^[1] Multiple risk factors for endometrial cancer have been identified: the early onset of menstruation,

obesity, nulliparity, late menopause, diabetes mellitus, hypertension, infertility, unopposed estrogen exposure tamoxifen, and genetic syndromes.^[2] Endometrial carcinoma metastasis is common, particularly at high surgical stages and grades, and the more frequent metastatic sites include lymph nodes, omentum, lungs, and liver.^[3] However, pericardium metastasis for endometrial cancer is very rare. Here we report a case of endometrial adenocarcinoma cardiac metastasis that presented as malignant pericardial effusion with cardiac tamponade. The patient has remained in good condition throughout the treatment.

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2. Case report

A 69-year-old woman, gravida 4, para 3, was admitted to the hospital for curettage because of vaginal bleeding in January 2017. The histologic examination of the endometrial specimen revealed a poorly differentiated (grade 3) endometrioid-type endometrial adenocarcinoma (Fig. 1A). Immunohistochemical staining showed diffuse positivity of the neoplastic cells for cytokeratin, vimentin, carcinoembryonic antigen, p16, estrogen receptor alpha, progesterone receptor, and p53. Magnetic resonance imaging (MRI) revealed direct invasion of the rectal mucosa, and she was staged as IVA (Fig. 2). Systemic chemotherapy (paclitaxel and carboplatin) was given for 4 courses, with 28-day intervals, until May 2017. On June 25, 2017, she was admitted to our hospital due to panic and shortness of breath, which became heavier after activity, adopting the supine position. The physical examination revealed bilateral jugular vein dilatation and increased heart rate, on both sides. The echocardiogram confirmed the presence of a large

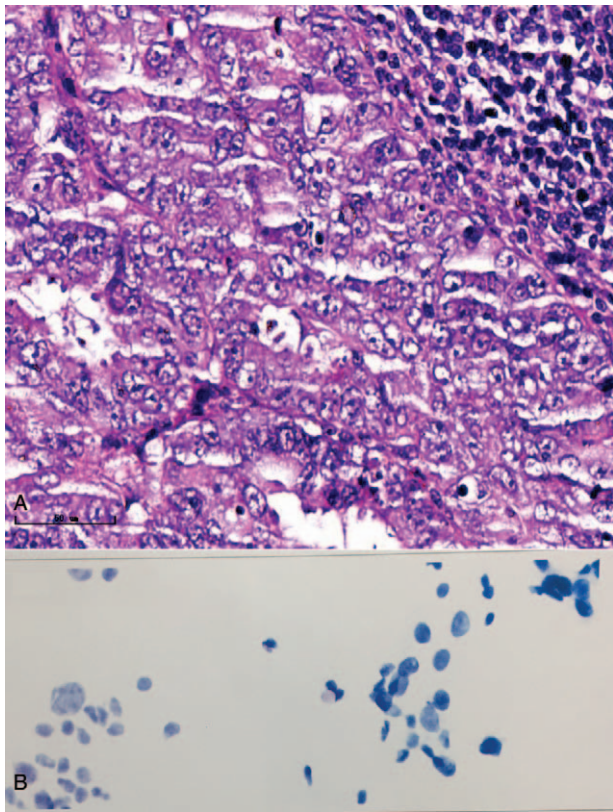


Figure 1. (A) Histologic examination of the endometrial specimen reveals a poorly differentiated endometrial adenocarcinoma. (B) The cytologic examination of pericardial fluid identifies tumor cells.

amount of pericardial fluid (Fig. 3A), and the chest X-ray revealed a prominent cardiomegaly, with evidence of pericardial effusion (Fig. 3B). Thoracocentesis was performed, a pericardial catheter was placed, and 900 mL of fluid was drained. The cytologic

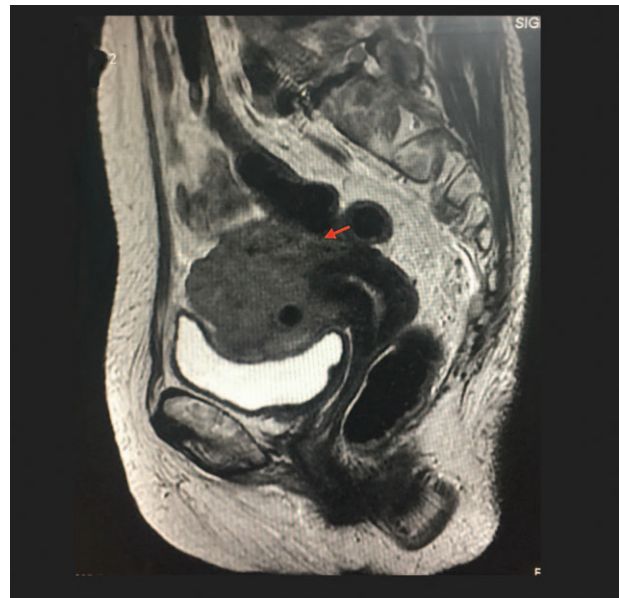


Figure 2. MRI reveals direct invasion of the rectal mucosa.

examination of the pericardial fluid identified the presence of tumor cells (Fig. 1B). The patient was diagnosed with endometrial cancer after chemotherapy, with pericardial metastases.

Then, cisplatin was instilled into the pericardial space on July 1 (20 mg), July 4 (40 mg), and July 9 (20 mg), and systemic chemotherapy that consisted of cyclophosphamide and carboplatin was given over 2 courses, until September 20, 2017. However, 6 weeks later, she was admitted to our hospital for the same symptoms that were previously observed. The echocardiogram confirmed the presence of a large pericardial effusion (Fig. 4A), and the chest X-ray revealed an increase in heart shadow (Fig. 4B). We performed a thoracocentesis, placed the catheter, and drained 700 mL of fluid. These findings indicated

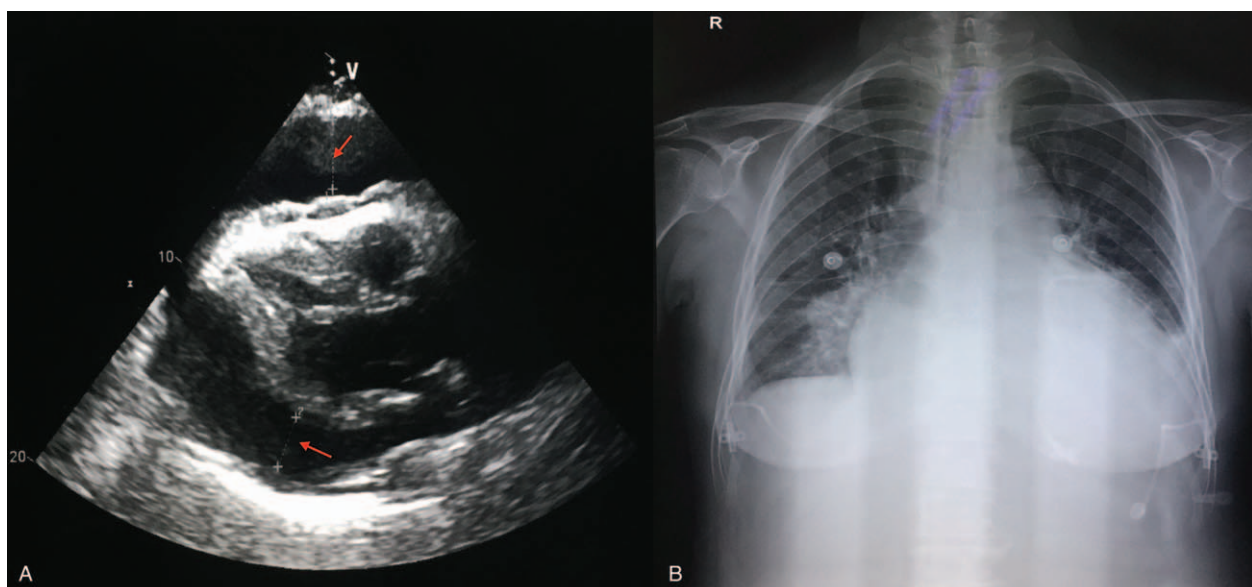


Figure 3. (A) Echocardiogram shows a large amount of pericardial effusion. (B) The chest X-ray reveals prominent cardiomegaly, with evidence of pericardial effusion.

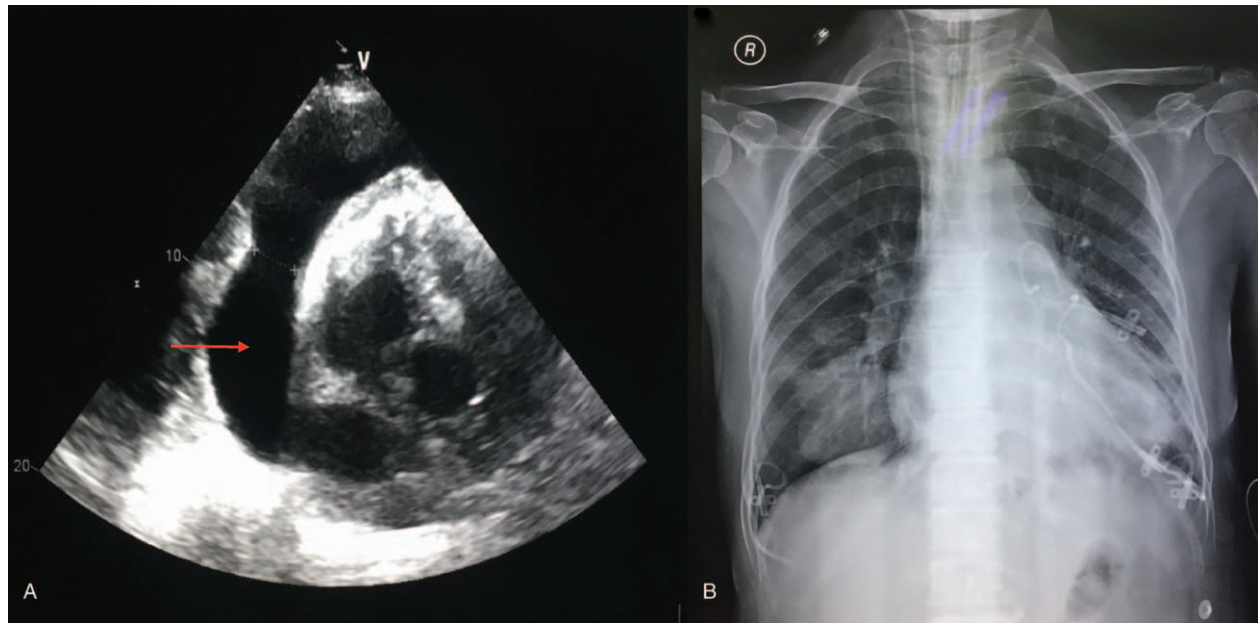


Figure 4. (A) Echocardiogram confirms the presence of a large pericardial effusion. (B) The chest X-ray reveals an increase in heart shadow.

that the last treatment did not control the pericardial effusion (according to RECIST v1.1 criteria).^[4] Therefore, we again instilled cisplatin with a dose of 20, 40, and 20mg into the pericardial space on November 4, 7, and 11, respectively. Furthermore, systemic chemotherapy with gemcitabine (1.2g, d1 and d8) and lobaplatin (30 mg, d1) was given over 4 courses, with 28-day intervals, until March 10, 2018. No obvious adverse reactions occurred during the chemotherapy, and the patient was continuously followed up by telephone for 8 months and had generally remained in a good health condition (<http://ctep.cancer.gov/forms/CTCAEv3.pdf>).

This study complied with the Declaration of Helsinki and was approved by the Human Ethics and Research Ethics Committees of the Fourth Hospital of Hebei Medical University. Informed written consent was obtained from the patient for publication of this case report and accompanying images.

3. Discussion

Malignancy is the most common cause of pericardial effusion.^[5] Hematopoietic malignancies are the most frequent cause of malignant effusion, followed by lung cancer, breast cancer, and malignant melanoma.^[6] Under the physiological state, there

is 25 to 50 mL liquid in the pericardium, which can be detected by ultrasound when >50 mL. However, normal compliance pericardium may be able to slowly collect up to 2 L of fluid without obvious symptoms before signs of tamponade appear.^[7] When symptoms occur, they include shortness of breath, dyspnea (exertional), orthopnea, chest discomfort or chest pain, cough, malaise, weakness, fatigue, peripheral edema, palpitations, hemoptysis, nausea, and vomiting. The most common body findings are pulsus paradoxus, tachycardia, peripheral edema, elevated jugular pressure, hypotension, pericardial rub, and decreased heart sounds.^[8] When patients develop these symptoms or signs, doctor should consider pericardial effusion. Confirmation of the diagnosis is primarily made through echocardiography, which allows full assessment of the hemodynamic effects of the effusion and also allows serial monitoring of the effusion before/after treatment.^[9] When the volume of malignant pericardial effusion exceeds 60 mL,^[6] pericardial puncture and exfoliation should be performed in time to detect the exfoliation of the drainage and determine whether cancer cells are present.

Mukai K et al evaluated 2177 patients with endometrial carcinoma between 2006 and 2016 and found that locoregional relapse included recurrences in the regional pelvic lymph nodes

Table 1

Review of the previously reported cases of endometrial carcinoma with pericardial metastasis.

Age, y	Stage (according to FIGO)	Radiotherapy	Treatment of pericardial effusion	Control of effusion	Survival, d	References
62	III	No	Pericardiocentesis Cisplatin instillation	No	87	[11]
59	IVB	No	Pericardiocentesis Cyclophosphamide and carboplatin chemotherapy	No	173	[12]
57	IIIA	No	Pericardial window Tamoxifen orally	Yes	Not stated	[13]
64	Not stated	Yes	Pericardial window Paclitaxel chemotherapy	No	19 d after the first chemotherapy	[14]
62	IC	Yes	Not stated	No	17	[15]

(1.0%) and the vaginal vault (4.5%), whereas distant recurrences included lung (including pleura and lymphangitic carcinomatosis) (3.4%), peritoneal (1.6%), liver (1.4%), distant lymph node metastases (beyond the regional lymph nodes) (1.2%), bone (including bone marrow) (1.1%), and brain (0.8%).^[10] This study did not report pericardial metastasis. We reviewed previous literature and found that only 5 cases of endometrial carcinoma with pericardial metastasis have been reported (Table 1). Overall, the prognosis of these patients was very poor after diagnosis of pericardium metastasis (survival of 17–173 days). However, our patient has lived >240 days after proper treatment. Reports demonstrated that gemcitabine may reverse the resistance mechanism of cisplatin in endometrial cancer by regulating the expression of glutathione (GSH)/glutathione-S-transferase (GST) and phosphorylation of p53, increasing cytotoxic activity.^[16,17] In addition, Tanaka et al treated 30 patients with advanced or recurrent endometrial cancer with gemcitabine, levofloxacin, irinotecan, and 5-fluorouracil (5-FU) (GLIF). The response and disease control rate were 7.1% and 39.3%, respectively, and the median survival was 3 months.^[18] Moreover, some similar studies showed that gemcitabine and cisplatin in patients with advanced endometrial cancer had a disease response rate of 50%.^[19,20] Furthermore, it is notable that most of the single-center small-scale studies of clinical trials on gemcitabine lack scientific rigor, the data seem to be less stringent, and sometimes controversial conclusions can be found.^[21]

Currently, there is no very effective treatment for patients with advanced endometrial carcinoma. Prognosis remains poor for those patients, despite receiving chemotherapy.^[22] However, if cardiac tamponade symptoms occur, ultrasound-guided pericardial puncture is currently the simplest and most effective method.^[23] On the basis of our experience in treating this patient, we recommend the pericardial injection of cisplatin, in combination with systemic chemotherapy that consists of gemcitabine and lobaplatin (second-line chemotherapy^[18]) instead of cyclophosphamide and carboplatin (first-line chemotherapy).

Author contributions

Conceptualization: Ning Zhang, Jinli Zhang.

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Formal analysis: Ze Li.

Software: Ze Li, Ning Zhang.

Writing – original draft: Guang Liu.

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