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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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.

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...
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 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 thoracentesis, placed the catheter, and drained 700 mL of fluid. These findings indicated
that the last treatment did not control the pericardial effusion (according to RECIST v1.1 criteria). Therefore, we again instilled cisplatin with a dose of 20, 40, and 20 mg into the pericardial space on November 4, 7, and 11, respectively. Furthermore, systemic chemotherapy with gemcitabine (1.2 g, 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. Hematopoietic malignancies are the most frequent cause of malignant effusion, followed by lung cancer, breast cancer, and malignant melanoma. Under the physiological state, there is 2.5 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. 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. 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. When the volume of malignant pericardial effusion exceeds 60 mL, 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

| 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%). 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 lopabatin (second-line chemotherapy)[18], instead of cyclophosphamide and carboplatin (first-line chemotherapy).

**Author contributions**

Conceptualization: Ning Zhang, Jinli Zhang.

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