Case Report

The Case Report of Malignant Pericardial Effusion in Recurrent Endometrial Cancer: An Emergency Treatable Condition

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Malignant-related pericardial effusion from endometrial cancer is a considerably rare condition. Massive fluid accumulation can cause a cardiac tamponade, which could lead to a life threatening condition. Here, the author presented a case of 45-year-old woman diagnosed of stage IIIC2 endometrial cancer, with para-aortic lymph nodes metastases. Fourteen months after completion of systemic chemotherapy and adjuvant sequential radiotherapy, she had been suffering from acute shortness of breath, tachypnea, tachycardia, and hemodynamic instability. Massive pericardial effusion was confirmed by echocardiogram. Malignant tumor cells were found on the cytological analysis. Beside pericardial effusion, computed tomography scan also demonstrated pleural effusion and multiple enlarged para-aortic lymph nodes. Pericardial window was done on the second day of admission after the diagnosis was confirmed by pericardiocentesis. Six courses of systemic chemotherapy, carboplatin and paclitaxel, were administered, followed by hormonal therapy. The patient was scheduled for follow up, every month, for 10 consecutive times. Her physical performance was in good condition without any clinical potential recurrence. Pericardial window is a palliative surgical treatment in emergency circumstance and systemic chemotherapy should be considered with clinical response result.

Keywords: Malignant pericardial effusion, Endometrial cancer, Treatment

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Endometrial cancer is the most common gynecological cancer in developed countries. The estimated age-standardized incidence rates (ASR) are 20.1 per 100,000 women in the U.S. compared to the rate of 6.2 in Thailand[1]. More than 90% of cases of endometrial cancer occur in women 50-years-old and older. The median age of diagnosis was 63 years[2]. Endometrial cancer is more common in post-menopause than pre-menopause. Many risk factors have been positively correlated with older age, early menarche, late menopause, obesity, diabetes mellitus, hypertension, unopposed estrogen, tamoxifen exposure, and genetic syndromes[3]. Most cases of endometrial cancer are diagnosed in early stage, with 80% in stage I, and the five years survival rates is over 95%. Conversely, the survival rates are decreasing when the patients have regional spreading or distant metastases with survival rates of 68% and 17%, respectively[4]. Pericardial metastasis is a rare site of disease recurrence. Catastrophic condition can be caused by cardiac tamponade from the pericardial effusion.

The author presented a case of complicated malignant pericardial effusion originating from the endometrial cancer treated with pericardiocentesis followed by pericardial window. The patient maintained a good condition for 10 months after completion of six cycles, four weekly carboplatin and paclitaxel (TC) regimen. Prolonged overall survival of this case comparing to previous similar case report would be explained by the high response rate of TC and favorable toxicities when compared to other regimens.

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Case Report

A 45-year-old woman, gravid 1, para1, had been referred to the author's hospital due to prolonged abnormal uterine bleeding since December 2017. She underwent fractional and uterine curettage. Histologic examination of surgical specimens revealed a well differentiated adenocarcinoma with positive CK7 and negative vimentin in immuno-histochemical staining.

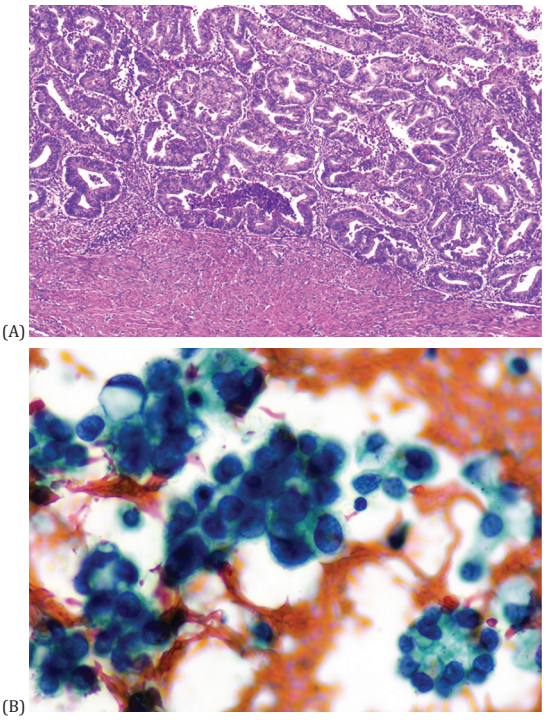

Figure 1. (A) Histologic examination of endometrial tissue depicts confluent glands line be stratified columnar epithelium. (Hematoxylin and eosin, x100). (B) Cytologic examination of pericardial fluid demonstrated groups of neoplastic cell with cytoplasmic vacuolization. (Hematoxylin and eosin, x400).

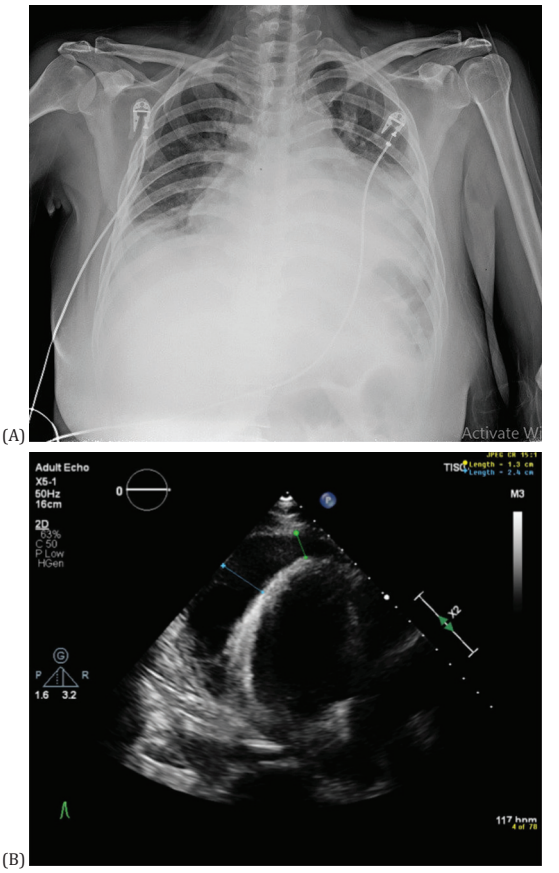

Figure 2. (A) The chest X-RAY revealed cardiomegaly with bilateral pleural effusion. (B) Echocardiogram confirmed accumulated pericardial effusion, measuring about 2.6 cm at posterior wall.

Surgical staging was performed subsequently. The final pathologic report demonstrated endometrial adenocarcinoma, grade 2 endometrioid type (Figure 1A) with para-aortic lymph node metastasis of 5/13 nodes. The patient had unexpectedly suffered from acute pulmonary embolism after the surgical procedure and was treated with low molecular weight heparin. Finally, she was diagnosed with endometrial cancer stage IIIC2 from revised FIGO staging (2009). After completion of six cycles of systemic chemotherapy of carboplatin AUC5 plus paclitaxel 175 mg/m², with 28-days intervals between March 2018 and July 2018, she proceeded to adjuvant radiotherapy (RT) 5.04 Gy divided in 28 fractions plus and 0.5 Gy of 3 HDR (high dose rate). However, she did not receive extended field radiation at para-aortic lymph nodes region. After completion of the sequential radiochemotherapy (RT), the computed tomography (CT) scan did not demonstrate residual disease. Therefore, the patient's condition was classified as clinical complete remission (CR). Nine months after completion of radiotherapy (April 2019), her CA-125 level had been rising to 100 unit/mL (12 unit/mL) compared with 1,155 unit/mL at pretreatment state. She also remained in good condition without clinical potential recurrence. There was no demonstrated lesion from the CT scan. She was prescribed with aromatase inhibitor (letrozole 2.5 mg per day) for systemic disease control.

Five months later (September 2019), she was admitted to the hospital due to dyspnea or shortness of breath, orthopnea, and epigastrium pain. Her physical examination revealed bilateral jugular veins engorged, tachypnea, and tachycardia. Marked cardiomegaly was demonstrated from chest X-ray. The pericardial effusion was suspected as shown in Figure 2A. The echocardiogram confirmed the pericardial effusion at the posterior wall, size measuring 26 mm in thickness (Figure 2B). Moreover, CT scan also demonstrated bilateral pleural effusion and multiple bilateral enlarged para-aortic lymph nodes. Pericardiocentesis was performed and 50 mL of serosanguinous pericardial fluid was submitted for cytological analysis. The cytological report confirmed

malignant cells in pericardial fluid (Figure 1B). Eventually, recurrence endometrial cancer with complicated malignant-pericardial effusion was diagnosed. Subxiphoid pericardial window was done with a small upper midline incision. The pericardium was accessed anteriorly over the right ventricle. Jackson-Pratt drain was introduced to the pericardium sac and directed it posteriorly. An amount of 750 mL of pericardial fluid was drained, and the tube was retained for a week. She had a good recovery from surgery and was discharged two weeks later. Regarding the poor patient's performance status, the sclerosing agent instillation was not employed. Re-induction of the same regimen of chemotherapy, which was carboplatin and paclitaxel, proceeded for six cycles after surgery. Delayed treatment of chemotherapy from severe bone marrow suppression occurred in two cycles. An echocardiogram was done three months after surgery and did not demonstrate any evidence of re-accumulated pericardial effusion. Para-aortic lymph node enlargement and pleural effusion from CT scan disappeared six months later (April 2020). Subsequently, a prescription of 180 mg per day of megestol acetate was done to stabilize and control the disease.

Ten months after the palliative surgical treatment, which was the pericardial window, the patient remained in good medical condition assessed by Eastern Cooperative Oncology Group (ECOG) performance score.

Discussion

Malignancy is among the most common cause of pericardial effusion[5]. In the previous large case series reported, one third of all originated from hematopoietic malignancies followed with squamous cell carcinoma, adenocarcinoma from lung, and breast cancer[6]. Malignant pericardial effusion resulted from deposit of tumor cells within the pericardium either by direct extension, lymphatic, or hematogenous routes[7]. The pericardial sac normally contain 50 mL of a plasma ultrafiltrate. Therefore, an amount of 150 mL to 200 mL of accumulating effusion would cause cardiac tamponade[8]. Symptoms reported by patients include dyspnea, chest pain, cough, palpitation, and orthopnea. Clinical suggestive malignancy, such as unintentional weight loss, night sweats, fever, and fatigue had been reported as well. Under physical examination, some cases had tachycardia, arrhythmias, and sign of low cardiac output, hypotension, and hypoperfusion. Distant heart sounds, jugular venous distension, narrowed pulse pressure, pericardial rub, and a pulsus paradoxus would be demonstrated simultaneously[9].

In severe cases, cardiac silhouette sign, round and flask-like could be found on chest X-ray. Chest X-ray had low sensitivity and specificity to detect pericardial effusion. Therefore, the echocardiography was recommended in suspected pericardial effusion cases with nearly 100% accuracy[10]. Echocardiography can be used to classify the effusion size. Distance space greater than 25 mm was defined as very large. Because of single dimension can misrepresent the volume, the specific size and location should be interrogated and reported[11].

Despite that pericardiocentesis had some diagnostic and therapeutic value, it was virtually not considered a definitive treatment. Only one-third of the cases were under-controlled, while 90% of the cases recurred within 90 days[12]. Subxiphoid pericardial window, providing a conduit to another reabsorptive cavity such as the pleural cavity or the peritoneum, is considered a safe and effective procedure in the management of pericardial effusion[13]. Currently, there is no randomized trial to confirm its effect. However, pericardial window is generally more effective than performing repeated pericardiocentesis because the malignant pericardial effusion trends to recur[14]. Gornik et al reported in 2005 that pericardial effusion with either abnormal cytology or cancer related had poor outcomes and short survival[15].

Various sclerosing agents promoting adhesion and obliteration of the cavity have been studied. The study from Martinoni et al reported no recurrences at 30 days in about 70% to 80% of the patients receiving intrapericardial instillation of sclerosing agents[16]. In one retrospective study reported by Di Liso et al, it was shown that the overall survival of neoplastic pericardial effusion was only 3.9 months. Beside older age, extrapericardial disease, and poor performance status, the patients treated with loco-regional therapy alone had poor survival outcome[17]. In addition to sclerosing agents, the instillation of various chemotherapeutic agents has been widely used after pericardial effusions' evacuation. Platinum-based chemotherapy were mostly employed, particularly cisplatin. It had high responsiveness in various types of tumor[9].

Liu et al reported a case of malignant pericardial effusion from recurrent endometrial cancer in 2019. The patient underwent pericardial window with catheter retaining. Intrapericardial space was instilled by cisplatin concurrent with systemic chemotherapy.

Gemcitabine and lobaplatin were prescribed as systemic chemotherapy. They reported the longest survival time, which was more than eight months. The five cases reviewed in this literature reported overall survival from 17 to 173 days. The longest survival time was found in a patient receiving carboplatin and cyclophosphamide chemotherapy after pericardiocentesis[18].

Endometrial cancer has a low rate of disease recurrence. Data from retrospective studies show a recurrence rate of only 12.4%. Distant metastases were the highest site of recurrence (46.2%), followed with vagina (42.3%), and pelvic (26.9%), respectively. The median disease specific survival after recurrence was 11 months and overall survival of eight months[19].

Multimodality approach should be considered in different instances of recurrent endometrial cancer. Surgery could be employed in cases macroscopic residual disease can be achieved from cytoreduction, and palliative surgery can be performed to alleviate symptoms such as bleeding or bowel obstruction. RT with curative intent is indicated in isolated vaginal relapse after surgery as well as palliative symptoms such as bleeding, bone metastases, and painful retroperitoneal lymph node recurrence. However, most patients would be candidate for systemic treatment including hormonal therapy and chemotherapy. Hormonal therapy such as megestol acetate is the front-line systemic therapy for patients with hormone receptor-positive grade 1 or 2 tumors without rapidly progressive disease, due to an excellent benefit over risk ratio and less toxicity profile[2]. The patients who are not considered to likely respond to hormonal therapy will be treated with chemotherapy. Endometrial cancer is a relatively chemo-sensitive disease. Doublet regimens with anthracyclines based such as doxorubicin and cyclophosphamide (AC) and doxorubicin and cisplatin (AP) demonstrated higher response rate at 33% to 43% when compared to single-agent doxorubicin, which are at 17% to 25%, but there was no benefit in overall survival. A triplet regimen of paclitaxel and doxorubicin and cisplatin (TAP) compared with AP had been studied. Response rate and overall survival were significantly higher in the TAP group. Unfortunately, TAP regimens required granulocyte-colony stimulating factor support and peripheral neuropathy was significantly increased[20]. Finally, GOG 209 was a randomized, non-inferiority trial that compared TAP with TC regimens and revealed comparable response rate at 51.3% versus 51.2%, with a median progression-free survival of 14 months in both arms, and an overall survival of 38 months versus 32 months, but TC had more favorable toxicity profile than TAP[21]. Regarding to the National Comprehensive Cancer Network (NCCN) 2020 guideline, multiagent chemotherapy regimens should be provided in cancer cases with condition of metastatic or recurrent if tolerated. Carboplatin and paclitaxel are the preferred regimen due to less toxicity and favorable tolerability. The response rate and overall survival range from 40% to 62% and 13 to 29 months, respectively[22].

The limitation of the present case was lack of loco-regional control such as sclerosing agent or chemotherapy instillation, due to poor patient's performance status and toxicity concerns. Interestingly, using a sequential combination of paclitaxel and carboplatin followed with hormonal therapy gave a survival time of more than 10 months. Systemic chemotherapy (TC) would be standard of care after palliative surgery.

Conclusion

Pericardial metastasis from endometrial cancer is considerably rare. Cardiac tamponade from accumulated fluid in the pericardial space is a catastrophic event. Cardiogenic shock and respiratory failure were rapidly developed and needed prompt rescue. Prognosis of recurrent endometrial cancer was poor and there was no effective treatment. Systemic chemotherapy should be emphasized to control pericardial effusion, future symptoms, and to prolong the overall survival time.

What is already known on this topic?

Pericardial effusion from endometrial cancer is a rare event. A serious adverse effect is the cardiovascular collapsed from cardiac tamponade. Subxiphoid pericardiotomy is the treatment of choice. It can rapidly relieve symptoms and decrease repeated pericardiocentesis procedure.

What this study adds?

Subxiphoid pericardiotomy was the emergency lifesaving procedure. Prolonged survival time could be achieved by intensively effective cytotoxic chemotherapy. The additional loco-regional treatment as chemotherapy instillation, might not improve survival outcome.

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Ethic approval and consent to participate and consent for publication

Written informed consent was obtained from the patient and the present case report was approved by the Human Ethics and Research Ethics Committee of Saraburi General Hospital, Thailand, and complied with the declaration of Helsinki.

Conflicts of interest

The author declares no conflict of interest.

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