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Right Ventricular Metastasis From Cervical Cancer Treated With Pembrolizumab-Containing Chemotherapy: A Case Report and Literature Review

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Manuscript Preparation E
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Patient: Female, 51-year-old
Final Diagnosis: Cervical cancer
Symptoms: Heart failure
Clinical Procedure: —
Specialty: Obstetrics and Gynecology
Objective: Unusual clinical course

Background: Cardiac metastasis from cervical cancer is extremely rare and associated with a poor prognosis. Given its rarity and the critical anatomical location of the lesion, optimal treatment strategies have not been established. We report a case of right ventricular metastasis from cervical squamous cell carcinoma that was treated with pembrolizumab-containing chemotherapy.

Case Report: A 51-year-old woman with stage IB2 cervical squamous cell carcinoma underwent radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. Three years and 7 months after initial treatment, she developed heart failure due to cardiac tamponade. Echocardiography and computed tomography revealed a mass in the anterior wall of the right ventricle. Histopathological examination confirmed metastatic squamous cell carcinoma consistent with cervical cancer. Surgical resection was considered inappropriate given the risk of worsening heart failure and right ventricular dysfunction; radiotherapy was avoided because of potential cardiac toxicity. The patient received paclitaxel, carboplatin, and pembrolizumab every 3 weeks without bevacizumab due to the potential risk of cardiac perforation. After 6 cycles, the tumor diameter decreased from 57.3 mm to 28.7 mm. Cancer antigen 125 (CA125) decreased from 473 to 20 U/mL, and B-type natriuretic peptide decreased from 24.8 to 7.2 pg/mL. No adverse events were observed, and the patient was subsequently transitioned to maintenance pembrolizumab.

Conclusions: Pembrolizumab-containing chemotherapy may be a feasible treatment option for selected patients with cardiac metastasis from cervical cancer when surgery or radiotherapy is not appropriate. Further accumulation of cases is needed.

Keywords: cardiac metastasis • cervical cancer • pembrolizumab
Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/952931

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Introduction

Cardiac tumors are rare. Approximately 25% of cardiac tumors are malignant, most of which are metastatic; only 0.3% originate as primary cardiac tumors. Cardiac tumors are uncommon for 2 main reasons: the myocardium is highly differentiated and does not undergo cell division, and the heart has poorly developed afferent lymphatic vessels. Lung cancer, hematologic malignancies, and breast cancer are the most common primary sources of cardiac metastases, whereas cardiac metastasis originating from the uterus is rare [1].

Here, we present the case of a 51-year-old woman diagnosed with right ventricular metastasis from cervical cancer 3 years and 7 months after resection of the primary lesion. Cardiac metastasis from cervical cancer presents unique diagnostic and therapeutic challenges. Due to its rarity, optimal treatment strategies have not been established. The objective of this report is to describe a rare case of isolated right ventricular metastasis and discuss the associated therapeutic decision-making.

Case Report

A 51-year-old woman was previously diagnosed with cervical cancer at another hospital. Her only prior medical history was 2 cesarean sections. The patient underwent radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. The pathological diagnosis was squamous cell carcinoma (SCC) (pT1b2N0M0, stage IB2) (**Figure 1**). Given the intermediate risk of recurrence, no postoperative adjuvant therapy was administered. Eight months after surgery, bone metastasis was detected in the left sciatic region. Radiation therapy (54 Gy/18 fractions) was administered for the sciatic metastasis, resulting in a complete response.

Three years and 7 months after the initial treatment, the patient was admitted to another hospital because of heart failure due to cardiac tamponade. Echocardiography revealed pericardial effusion, mild-to-moderate tricuspid regurgitation, and mitral regurgitation. The ejection fraction was 68%, and a 55-mm mass was identified in the anterior wall of the right ventricle. The estimated right ventricular systolic pressure was 23 mm Hg. A 9-mm pericardial effusion was noted on the right side, along with trivial mitral regurgitation and mild-to-moderate tricuspid regurgitation. Pericardial drainage yielded bloody pericardial fluid. Minimally invasive cardiac surgical biopsy was performed, revealing SCC histologically similar to the cervical specimen, which confirmed that the cardiac tumor represented metastatic cervical cancer (**Figure 1**). The patient was subsequently referred to our hospital for further evaluation.

A computed tomography (CT) scan of the chest (**Figure 2**) showed a 57.3-mm mass (slight variation in size due to use of different imaging modality) in the anterior wall of the right ventricle, without evidence of metastasis to other organs. The carbohydrate antigen 19-9 (CA19-9) and cancer antigen 125 (CA125) levels were elevated to 35 and 473 U/mL, respectively (institutional reference ranges: CA19-9 < 37 U/mL; CA125 < 35 U/mL). SCC antigen was also measured throughout the clinical course; however, it remained within the normal range and did not reflect disease activity. In contrast, CA19-9 and CA125 levels were elevated upon diagnosis of the cardiac metastasis and decreased after treatment. Therefore, CA19-9 and CA125 were used as auxiliary markers of treatment response in this case.

The possibility of surgery was discussed with the cardiovascular surgery department at our hospital, and surgical treatment was deemed inadvisable given the risk of worsening heart failure resulting from involvement of the left anterior descending artery and right ventricular dysfunction. Radiation therapy was also considered, but this option was excluded given the risk of radiation-induced heart disease. After reviewing the available treatment options, chemotherapy was selected; a combination of paclitaxel, carboplatin, and pembrolizumab (TC + Pem) was administered. The regimen consisted of pembrolizumab 200 mg, paclitaxel 175 mg/m² (300 mg), and carboplatin at an area under the curve of 5 (610 mg), administered every 3 weeks. Although paclitaxel, carboplatin, bevacizumab, and pembrolizumab is typically the preferred regimen for recurrent cervical cancer, bevacizumab was omitted in this case due to the risk of cardiac perforation [2]. Before initiation of TC + Pem, a baseline cardiopulmonary assessment was performed. The B-type natriuretic peptide level was 24.8 pg/mL. Electrocardiography showed QT prolongation, negative T waves in leads II, aVF, V3, and V4, and flattened T waves in leads V5 and V6.

Tumor response was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. The cardiac tumor was measured on chest CT using the longest lesion diameter. After 6 cycles of TC + Pem, chest CT showed a reduction in tumor diameter to 28.7 mm (**Figure 2**). The CA19-9 and CA125 levels decreased to 29 U/mL and 20 U/mL, respectively, indicating reductions in tumor size and tumor marker levels. The B-type natriuretic peptide level also decreased to 7.2 pg/mL. The patient was subsequently transitioned to maintenance therapy. Four additional cycles of pembrolizumab were administered, during which a partial response was maintained. The total follow-up period after initiation of chemotherapy was 10 months.

Discussion

Few cases of cardiac metastasis from cervical cancer have been reported; therefore, no standard treatment strategy has been

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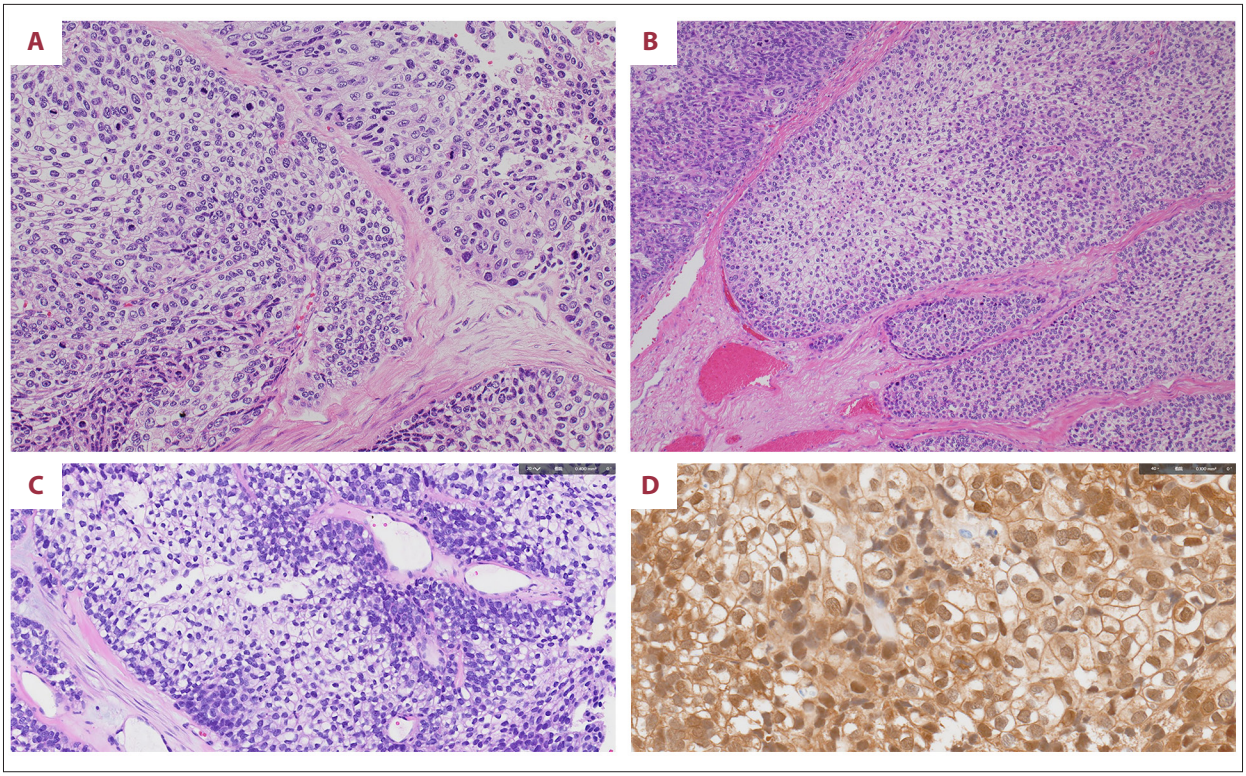

Figure 1. Histopathological images of the cervical and cardiac tumors. (**A**) Cervical tumor, hematoxylin and eosin (H&E) staining, ×200. (**B**) Cervical tumor, H&E staining, ×100. (**C**) Cardiac tumor, H&E staining, ×200. (**D**) Cardiac tumor, p16 immunohistochemical staining, ×400.

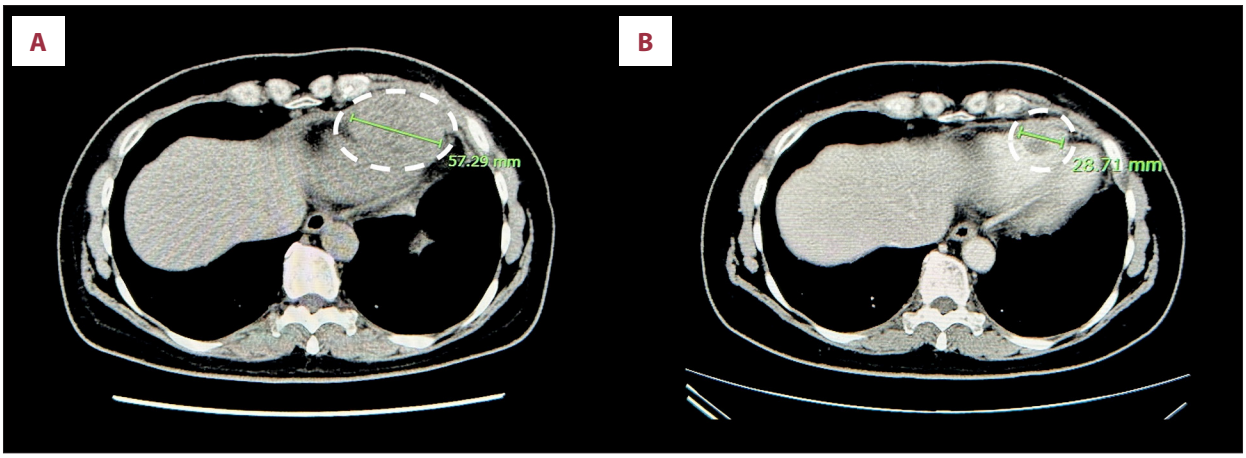

Figure 2. (**A**) Chest computed tomography scan before treatment. The area outlined by the dotted line indicates the tumor, which measured 57.3 mm in diameter. (**B**) Chest computed tomography scan after chemotherapy. The area outlined by the dotted line indicates the tumor, which measured 28.7 mm in diameter. Tumor size was assessed using the longest lesion diameter, and treatment response was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. The reduction in tumor size corresponded to a partial response.

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Table 1. Reported cases of cervical cancer with cardiac metastasis (n = 33).

Case [Ref]	Age	Stage	Primary treatment	Other metastatic sites	Time to cardiac metastasis (months)	Secondary treatment	Regimen	Time to death from cardiac metastasis (months)
1 [4]	64	IB	Op, CCRT	Longitudinal, abdominal wall	7	CCRT	Gemcitabine + carboplatin	2
2 [4]	32	IIA	Op, CCRT	–	15	Op, CTx	Carboplatin + paclitaxel	13
3 [4]	28	IIB	Op, RT	–	10	NA	–	3
4 [4]	28	NA	Op, CCRT	Mediastinal lymph node	16	CTx	Cisplatin	1
5 [4]	32	IIB	CTx	Pleura	4	Op	–	NA
6 [4]	36	IB	Op, CTx	Lung, periaortic lymph nodes	33	CTx	Cisplatin + mitomycin C + vincristine	NA
7 [4]	37	IIIB	CCRT	–	3	RT	–	> 8
8 [4]	41	IIB	Op, RT	–	12	CTx	Cisplatin + mitomycin C + vincristine	5
9 [4]	42	IVB	RT	–	6	Op	–	NA
10 [4]	43	IIB	RT	–	5	CTx	NA	NA
11 [4]	49	IIIB	RT	–	6	CCRT	5-fluorouracil + cisplatin	7
12 [4]	53	IB	RT, Op	Lung	14	CCRT	5-fluorouracil + cisplatin	1
13 [4]	49	IVB	CCRT	Abdominal lymph node	0	CCRT	NA	2.5
14 [4]	57	IIIB	CCRT	Periaortic lymph node	10	Op	–	2
15 [4]	58	IB	Op, CTx	Periaortic lymph node	43	Op	–	4
16 [4]	63	NA	Op, CCRT	–	33	Op	–	> 5
17 [4]	64	IIIB	RT	–	7	BSC	–	0.3
18 [4]	68	IIIB	RT	–	10	Op, CTx	NA	5
19 [4]	78	IIIB	RT	–	5	BSC	–	1
20 [3]	32	IIA2	Op, CCRT	–	15	Op, CTx	Carboplatin + paclitaxel	13
21 [3]	39	IIA	Op, CTx	Left obturator lymph nodes	21	RT	–	13
22 [3]	22	IVB	CCRT	–	12	Op, CCRT	NA	> 6
23 [3]	NA	IB2	CCRT	Small intestine	48	Op, CCRT	NA	8
24 [3]	64	IB	Op, CCRT	Abdominal muscle	6	CCRT	NA	10
25 [3]	42	–	NA	–	6	Op	–	NA
26 [3]	63	–	Op, CCRT	–	396	Op	–	> 5
27 [3]	81	–	Op, RT	–	60	BSC	–	0.1
28 [3]	57	IIIB	CCRT	–	10	Op	–	2
29 [3]	68	IIIB	NA	–	24	Op, CTx	NA	5

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Table 1 continued. Reported cases of cervical cancer with cardiac metastasis (n = 33).

Case [Ref]	Age	Stage	Primary treatment	Other metastatic sites	Time to cardiac metastasis (months)	Secondary treatment	Regimen	Time to death from cardiac metastasis (months)
30 [3]	37	IIIB	–	–	0	RT	–	> 8
31	51	IB2	Op	Ischium	43	CTx	Carboplatin + paclitaxel + pembrolizumab	–
32 [6]	NA	IVB	CTx	Mediastinal lymph node, bilateral pleura	–	CCRT	Cisplatin + paclitaxel + atezolizumab	16
33 [5]	55	IVB	CCRT	Spine	3	Op, CTx	Pembrolizumab	NA

Abbreviations: Op, operation; CCRT, concurrent chemoradiotherapy; RT, radiation therapy; CTx, chemotherapy; NA, not available; BSC, best supportive care. Note: Case 31 represents the present case.

established. Several review articles have summarized cases of cardiac metastasis from cervical cancer. Among 33 reported cases, the mean age was 49.6 years, the mean interval from the initial diagnosis to detection of cardiac metastasis was 28 months, and the mean survival time after diagnosis of cardiac metastasis was 4.9 months (excluding cases with unknown durations). These findings indicate that cardiac metastasis is associated with a poor prognosis (**Table 1**) [3-6]. Among the 33 cases, 54.5% received treatment that included chemotherapy, 45.5% underwent surgery, and 27.2% received radiotherapy. Of the 7 cases treated with chemotherapy alone, 3 received paclitaxel-carboplatin (TC) plus an immune checkpoint inhibitor (ICI); therapeutic efficacy was observed in all 3 cases. Programmed death-ligand 1 (PD-L1), mismatch repair immunohistochemistry, microsatellite instability testing, and tumor mutational burden analysis were not performed in the present case. In Japan, pembrolizumab-containing chemotherapy can be used to manage recurrent or advanced cervical cancer regardless of PD-L1, mismatch repair, microsatellite instability, or tumor mutational burden status; these biomarker tests are not mandatory for treatment selection in routine clinical practice. Thus, TC + Pem was selected without additional biomarker testing.

All reported cases with surgical treatment involved metastases to the right side of the heart, and tumor resection may have helped to prevent pulmonary tumor embolization. Surgical resection is generally considered the treatment of choice for cardiac metastases when tumor removal may prevent sudden death. In the present case, however, the tumor was located in the apical region of the right ventricle, and surgical resection was considered high risk given the potential for worsening cardiac function. Radiation therapy has been associated with cardiotoxic effects, including constrictive cardiomyopathy, arrhythmias, and valvular heart disease [7]; therefore, it was not selected in our case.

We also reviewed reports of bevacizumab and ICIs for cardiac metastases from other carcinomas, given the limited number of reported cases of cervical cancer with cardiac metastasis and the increasing use of ICIs in this setting. To our knowledge, there have been no previous reports of bevacizumab use for cardiac metastases from cervical cancer; however, 2 cases have been reported in other carcinomas. In the first case, a 70-year-old woman was diagnosed with a right ventricular metastasis from sigmoid colon cancer 5 years after initial treatment. The cardiac metastasis was controlled for more than 2 years with capecitabine plus bevacizumab [8]. In the second case, a 24-year-old man with multiple metastases from sigmoid colon cancer developed a right ventricular cardiac metastasis. Bevacizumab was added during the seventh cycle of FOLFOX chemotherapy, resulting in tumor reduction; however, disease progression occurred 9 months later, and the patient was subsequently referred for palliative care [9]. Conversely, a case of ventricular free-wall perforation was reported in a 62-year-old patient with non-small cell lung cancer who developed ischemic myocardial infarction while receiving bevacizumab, highlighting the need for caution when administering this agent [10]. In the present case, bevacizumab was avoided due to the potential risk of cardiac perforation related to the tumor's location within the ventricular wall.

Several cases of cervical cancer with cardiac metastasis treated with ICIs have also been reported. For instance, a 55-year-old woman with cervical SCC developed a right ventricular mass causing functional pulmonic stenosis and an increased pulmonary arterial thrombus burden. Surgical resection of the right ventricular mass was performed, and pathological examination confirmed metastatic SCC. Postoperatively, the patient received maintenance pembrolizumab and systemic anticoagulation. At 32 months after surgery, she remained alive without disease progression or new metastases [5]. In contrast, an adult woman exhibiting advanced cervical cancer presented

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with right ventricular metastasis, pulmonary embolism, and immune thrombocytopenia. Despite treatment comprising anticoagulation, chemotherapy, immunotherapy (atezolizumab), and palliative radiotherapy, her condition showed only partial improvement and subsequently deteriorated due to delayed platelet recovery and worsening dyspnea. She ultimately died of circulatory failure, highlighting the challenges associated with managing advanced cervical cancer complicated by immune thrombocytopenia and cardiac metastasis [6].

ICIs may be advantageous because they avoid mechanical stress on cardiac structures while providing systemic disease control. However, careful monitoring for immune-related adverse events is essential. Pembrolizumab is known to induce a broad spectrum of immune-related adverse events affecting multiple organ systems. For example, autoimmune hemolytic anemia has been identified as a rare but potentially life-threatening complication, even after a single treatment cycle [11]. Additionally, pembrolizumab-associated lung injury can present with diverse radiological findings and may require histopathological confirmation for accurate diagnosis [12]. Immune-mediated dermatomyositis has also been described, reflecting systemic immune activation and the need for prompt immunosuppressive therapy in severe cases [13]. These reports underscore the importance of vigilant monitoring for immune-related adverse events during ICI treatment, particularly in patients with critical organ involvement such as cardiac metastasis.

In summary, although cases of cardiac perforation associated with bevacizumab have been reported, the overall incidence of bevacizumab-related cardiotoxicity is low. Symptomatic cardiac dysfunction or heart failure associated with cancer treatment is termed cancer therapy-related cardiac dysfunction, and its reported incidence with bevacizumab is only 1.6% to 4% [14]. Therefore, bevacizumab may be a reasonable treatment option depending on the location of the cardiac metastasis, including lesions that involve the right ventricle (with modification according to perforation risk), as described in the present and previous reports. Furthermore, ICI-containing chemotherapy has shown potential efficacy in the treatment of cardiac metastatic tumors. Our findings in this case suggest that ICI-containing chemotherapy can represent a feasible treatment option for selected patients with cardiac metastasis from cervical cancer when local therapies are not appropriate. However, this report is limited by its short follow-up period and single-case design.

Conclusions

Cardiac metastasis from cervical cancer is extremely rare and associated with a poor prognosis; optimal management strategies have not been established. In this report, we described a patient with isolated right ventricular metastasis from cervical SCC who was treated with pembrolizumab-containing chemotherapy after surgical and radiotherapeutic approaches had been deemed inappropriate. Although the observation period was limited, radiologic and biochemical responses were achieved, suggesting that ICI-containing chemotherapy can represent a feasible treatment option for carefully selected patients with cardiac metastasis from cervical cancer. Further accumulation of cases is required to clarify its role and long-term outcomes. This approach may be particularly useful for patients with high surgical risk and contraindications to radiotherapy.

Department and Institution Where Work Was Done

Saitama Prefectural Cancer Center, Juntendo University Hospital, Japan.

Patient Consent

Written informed consent was obtained from the patient for publication of this report.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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