

## A Case of Metastatic Uterine Cervical Squamous Cell Carcinoma in the Right Atrium

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**Introduction:** Metastasis of uterine cervical carcinoma to the heart is uncommon and cases with metastasis to the right atrium are especially rare. This type of metastasis occurs in the epicardium and the myocardium in over 90% of cases with a heart metastatic tumor. Most cases of a metastatic tumor in the heart are found by chance during autopsy.

**Case report:** We present the case of a patient with stage IIa uterine cervical carcinoma who visited our hospital with a chief complaint of arrhythmia 1.9 years after surgical treatment of carcinoma. CT and MRI showed that recurrent metastatic uterine cervical carcinoma had grown from the inferior vena cava upward into the right atrium.

**Conclusion:** Although gynecological malignant tumors rarely metastasize to the heart, it is important to consider this possibility in patients with chest symptoms, and to make an early definite diagnosis and give appropriate treatment.

**Key words:** cervical cancer, paraaortic lymph node metastasis, intraatrial metastasis, cardiovascular angiography

### INTRODUCTION

Based on autopsy cases of patients with a malignant tumor, the rate of tumor metastasis into the heart is 1.5 to 20.6% (an average of about 6%) [1–4]. A retrospective study of over 12,000 autopsy cases showed that the rates of metastasis to the heart of pulmonary carcinoma, esophageal carcinoma, malignant lymphoma, hepatic carcinoma, leukemia, and gastric carcinoma were 31.7%, 28.7%, 11.9%, 6.9%, 4.0%, and 4.0%, respectively in male patients; and the equivalent rates for pulmonary carcinoma, malignant lymphoma, breast carcinoma, and pancreatic cancer were 35.9%, 17.0%, 7.5%, and 7.5%, respectively, in female patients [3]. The metastatic sites in the heart include the epicardium (59.8%), myocardium (30.4%), and endocardium (6.8%), as well as formation of an intraventricular tumor (3.0%) [5, 6]. Commonly observed sites for spread of uterine cervical carcinoma include the lung, bones, cervical region, and supraclavicular lymph nodes [7], but metastasis into the heart only develops rarely and most of cases are diagnosed by autopsy [1–4]. Here, we report the case of a patient with a right intraatrial metastasis detected 1.9 years after surgical treatment of uterine cervical carcinoma. A diagnosis of metastatic uterine cervical squamous cell carcinoma was made by biopsy performed under cardiovascular angiography.

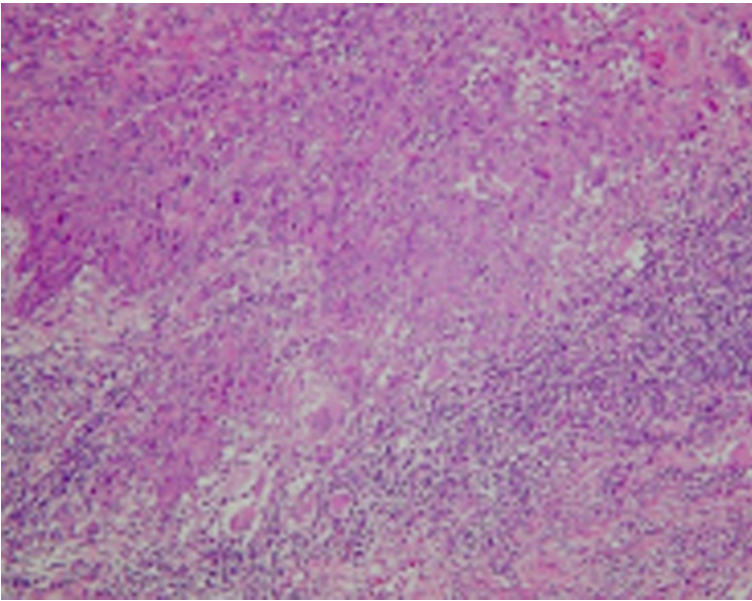
### CASE REPORT

The patient was a 39-year-old Japanese female. Prior to visiting our hospital, she had been diagnosed

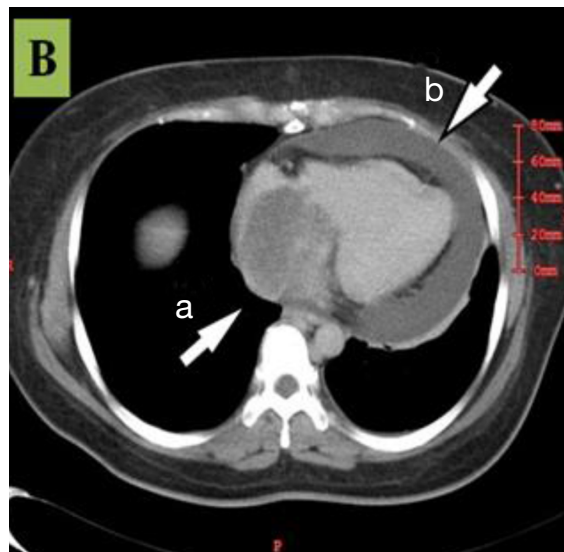
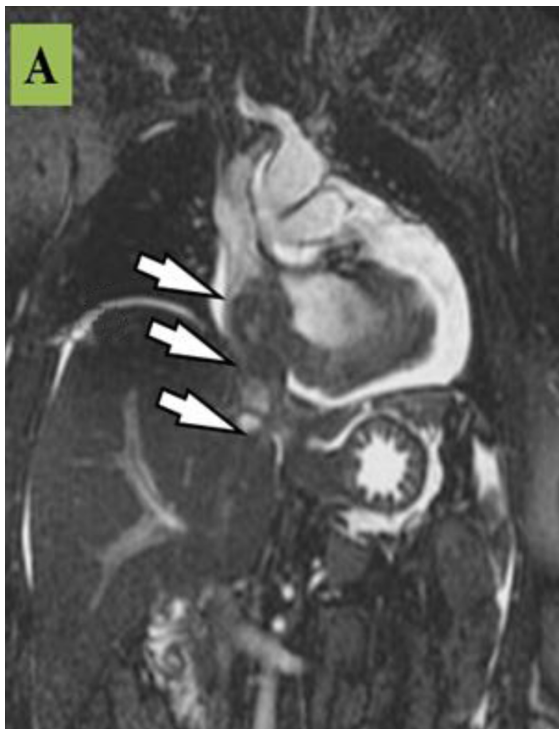
with stage IIa uterine cervical carcinoma and had undergone extended hysterectomy and pelvic lymphadenectomy after one cycle of intraarterial injection of cisplatin 100 mg/body into the bilateral internal iliac arteries. This treatment had resulted in successful reduction of the tumor. In consideration of her age, the ovaries were conserved. Pathologic diagnosis indicated squamous cell carcinoma of the keratinizing type (Fig. 1), pT2aN1M0, with metastasis into the left obturator lymph nodes. After surgery, a total dose of 46 Gy of radiation was administered over the whole pelvis.

At 1.9 years after the initial treatment, she experienced an episode of arrhythmia. The results of electrocardiography and echocardiography performed at a nearby clinic showed no significant pathological condition. Four months later, she had nausea and vomiting, and underwent CT and MRI scan tests. The results revealed a beaded intramyocardial tumor in the region from the inferior vena cava to the right atrium and a structure retaining pericardial fluid in the right atrium (Fig. 2). She underwent pericardiocentesis for cytodiagnosis in the Department of Cardiovascular Internal Medicine, and no prominent malignant cancer cells were detected.

Despite the lack of malignancy, it was determined that the right atrium tumor had probably infiltrated into the ventricular septum, and that radical resection of the tumor would be difficult by thoracotomy. After the patient gave informed consent, a biopsy of the tumor mass was performed by approaching the focus via the right internal jugular vein under angiography.



**Fig. 1** Primary specimen showing squamous cell carcinoma with inflammation in the uterine cervix (H&E stain, x 40).

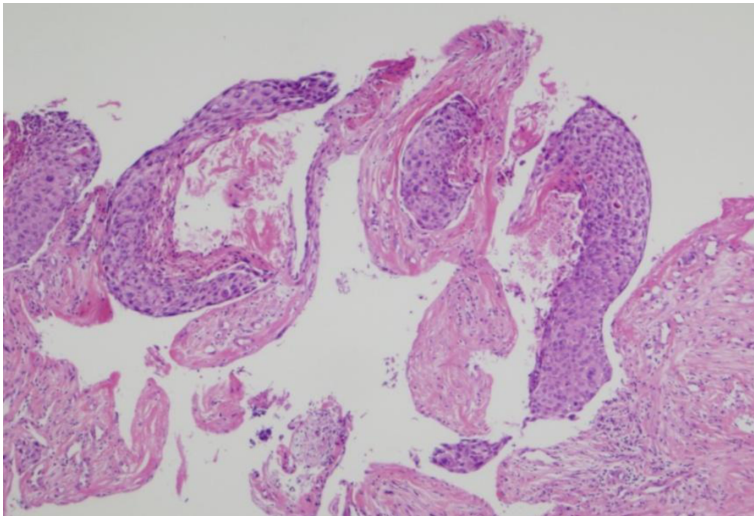


**Fig. 2** A; Thoracic MRI (coronary image)  
Intramyocardial tumor emboli through the inferior vena cava to the right atrium (arrows).  
B; CT scan (axial image)  
Arrow a: metastatic tumor in the right atrium.  
Arrow b: pericardial effusion.

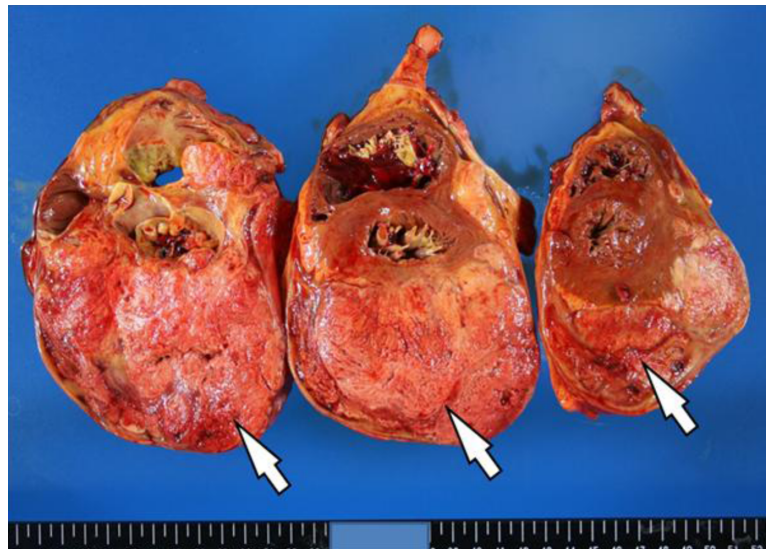
Coronary angiography showed that vasa vasorum (branches) had grown out from the trunk of the left circumflex artery for alimentation to the tumor. Pathologic diagnosis of the biopsy specimen indicated squamous cell carcinoma (Fig. 3) and based on this result the patient was diagnosed with a right atrium metastatic tumor originating from the uterine cervical carcinoma. After the biopsy, 60 Gy of radiation was administered to the right atrium tumor mass using a linac. This reduced the tumor size and alleviated pericardial fluid retention, leading to lower levels of tumor

markers. Her symptoms improved and five days after radiotherapy she was discharged from the hospital under the condition that she would receive follow-up as an outpatient.

However, seven month later she developed chest pain and respiratory disturbance, and returned to the hospital. A significantly enlarged shadow was observed in the heart on a chest X-p image and pericardial fluid retention was detected by cardiography. Based on these findings, the pathology was determined to be cardiac tamponade. Pericardiotomy-guided sur-



**Fig. 3** Biopsy of the tumor in the right atrium. Pathologic analysis indicated a metastatic squamous cell carcinoma (H&E stain, x 40).



**Fig. 4** The heart at autopsy showing that the intramyocardial tumor occupied the right atrium (arrows).

gery and continuous drainage were applied, with a resultant improvement of symptoms. But respiratory disturbance worsened, the patient died on day 23 of hospitalization. A pathological autopsy performed on the next day revealed that the weight of the heart was 1350 g and a metastatic cancer focus had developed in the bilateral atrium and the region from the inside of the ventricular muscle coat to the epicardium (Fig. 4). The findings also included tumor infiltration into the right bronchus, multiple tumor metastases into the lung and the liver, bilateral tumor metastasis into the adrenal glands, and tumor metastasis into the subcutaneous tissue.

### DISCUSSION

Cancer metastasis to the heart is generally thought to be unlikely due to the dynamic diastolic and systolic movements of the myocardium, the myocardium-specific metabolic mechanism, rapid blood flow through the heart, and limited communication of the heart with multiple organs and lymphatic vessels [5, 8–12]. A tumor may spread into the heart by metastasis via pathways such as direct infiltration via the lung or the mediastinum, dissemination from the paraaortic lymph nodes via the mediastinal lymph nodes, and

blood flow (hematogenous metastasis) through the coronary artery into the cardiac plexus aorticus. As mentioned above, involvement of the epicardium and myocardium is found in 90% of cases of metastasis to the heart. The endocardium is rarely affected, but in such cases the metastasis is more likely to develop on the right side of the heart [5, 6, 13, 14].

The metastasis of a uterine cervical tumor to the right atrium in our patient is particularly rare, with only one similar case in the literature (Table). In this case, Nakao *et al.* [15] described a 57-year-old female patient with stage IIIb uterine cervical squamous cell carcinoma, which had treated with radiation and chemotherapy. At the early stage after these therapies, the tumor spread into the paraaortic lymph nodes by metastasis. Eight months later, the patient suffered chest pain and a cardiac ultrasonogram showed a tumor mass of 2 cm in diameter in the right atrium. This mass was surgically removed from the heart, but it grew upward via the inferior vena cava (IVC) to the inside of the heart. A pathologic diagnosis indicated that the specimen was squamous cell carcinoma identical to that of the primary uterine cervical cancer [15]. As in our case, imaging diagnosis suggested that the tumor spread via the IVC to the right atrium. During



**Table** Characteristics of published cases and our case.

| Informant                | Year | Age | Stage | Treatment | Symptom          | Rec. period | Metastasis | Prognosis     |
|--------------------------|------|-----|-------|-----------|------------------|-------------|------------|---------------|
| Nakao <i>et al.</i> [14] | 2006 | 57  | III b | C + R     | chest pain       | 8           | IVC-RA     | 2 months DOR  |
| Our case                 | 2009 | 39  | II a  | C + Op    | nausea, vomiting | 21          | IVC-RA     | 12 months DOR |

Rec. period: recurrent period (month from the initial treatment), Treatment; C: chemotherapy, R: radiation therapy, Op: operation, IVC-RA: Metastatic tumor extending through the inferior vena cava (IVC) into the right atrium (RA), DOR: dead of recurrence

the initial surgical treatment the bilateral ovaries were conserved, and radical hysterectomy and pelvic lymphadenectomy were performed due to left obturator lymph node metastasis. It was assumed that the recurrent tumor had spread into the endocardium of the right atrium via the remaining ovarian veins.

The clinical symptoms of a cardiac tumor include chest pain, cardiac failure, cardiac tamponade, various types of arrhythmia, and channel block. Compared with benign cardiac tumors, metastatic cardiac tumors induce rapid changes in systemic symptoms that lead to poor outcomes. The patient in our case developed pericardial fluid retention due to tumor metastasis into the right atrium, with concomitant cardiac tamponade that led to cardiac failure. Pericardiocentesis was performed initially, but did not alleviate the pericardial fluid retention. Subsequent pericardiectomy and drainage did alleviate the systemic symptoms and resulted in life extension. Malignant cancer cells are seldom definitely observed in these cases [16, 17], and cytological diagnosis of the pericardial fluid in our case did not indicate malignancy. Therefore, particular attention should be paid to chest symptoms in cancer patients, including chest pain, dyspnoea, and arrhythmia, to avoid sudden death due to cardiac failure.

### CONCLUSION

A diagnosis of metastatic uterine cervical tumor in the right atrium was made by cardiovascular angiography. The tumor grew upward via the IVC into the right atrium, with concomitant induction of cardiac tamponade. Although gynecological malignant tumors rarely metastasize to the heart, it is important to consider this possibility in patients with chest symptoms, and to make an early definite diagnosis and give appropriate treatment.

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### CONFLICT OF INTEREST

We declare that there is no conflict of interest.

### REFERENCES

- 1) MacGee W: Metastasis and invasive tumors involving the heart in a geriatric population: A necropsy study. *Virchows Arch A Pathol Anat Histopathol* 1991; 419: 183–189.
- 2) Abraham KP, Reddy V, Gattuso P: Neoplasms metastatic to the heart: Review of 3314 consecutive autopsies. *Am J Cardiovasc Pathol* 1990; 3: 195–198.
- 3) Lam KY, Dickens P, Chan AC: Tumor of the heart: A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med* 1993; 117: 1027–1031.
- 4) Butany J, Leong SW, Carmichael K, Komeda M.A 30-year analysis of cardiac neoplasms at autopsy. *Can J Cardiol*. 2005; 21: 675–680.
- 5) Klatt EC, Heitz DR. Cardiac metastases. *Cancer*. 1989; 65: 1456–1459.
- 6) Thurber DL, Edwards JE, Achor RW. Secondary malignant tumors of the pericardium. *Circulation*. 1962; 26: 228–241.
- 7) Brenner DE. Carcinoma of the cervix—a review. *Am J Med Sci*. 1982; 284: 31–48.
- 8) Prichard RW. Tumors of the heart; review of the subject and report of 150 cases. *AMA Arch Pathol* 1951; 51: 98–128.
- 9) Senzaki H, Uemura Y, Yamamoto D, Kiyozuka Y, Ueda S, Izumi H, Tsubura A. Right intraventricular metastasis of squamous cell carcinoma of the uterine cervix: an autopsy case and literature review. *Pathol Int*. 1999; 49: 447–452.
- 10) Lemus JF, Abdulhay G, Sobolewski C, Risch VR. Cardiac metastasis from carcinoma of the cervix: report of two cases. *Gynecol Oncol*. 1998; 69: 264–268.
- 11) Greenwald EF, Breen JL, Gregori CA: Cardiac metastasis associated with gynecologic malignancies. *Gynecol Oncol*. 1980; 10: 75–83.
- 12) Mukai K, Shinkai T, Tominaga K, Shimamoto Y. The incidence of secondary tumors of the heart and pericardium: a 10-year study. *Jpn J Clin Oncol*. 1988; 18: 195–201.
- 13) Hanfling SM. Metastatic cancer to the heart. Review of the literature and report of 127 cases. *Circulation*. 1960; 22: 474–483.
- 14) Charles EH, Condori J, Sall S. Metastasis to the pericardium from squamous cell carcinoma of the cervix. *Am J Obstet Gynecol*. 1977; 129: 349–351.
- 15) Nakao Y, Yokoyama M, Yasunaga M, Hara K, Nakahashi H, Iwasaka T. Metastatic tumor extending through the inferior vena cava into the right atrium: a case report of carcinoma of the uterine cervix with para-aortic lymph node metastases. *Int J Gynecol Cancer*. 2006; 16: 914–916.
- 16) Dibadj A. Intracavitary cardiac tumor secondary to squamous cell carcinoma of cervix. Report of a case and review of literature. *Am J Clin Pathol*. 1967; 48: 58–61.
- 17) Ritcher N, Yon JL Jr. Squamous cell carcinoma of the cervix metastatic to the heart. *Gynecol Oncol*. 1979; 7: 394–400.