CASE REPORT

Biventricular metastatic invasion from cervical squamous cell carcinoma

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SUMMARY

Metastasis to the heart has been previously described with primary lung and breast carcinoma, lymphoma, leukaemia, mesothelioma and melanoma. However, left-ventricular cardiac metastasis from primary cervical squamous cell carcinoma is poorly described. This report describes the clinical presentation of a patient with cardiac metastatic invasion from cervical cancer.

BACKGROUND

Primary cardiac tumours are exceedingly rare with an incidence of <0.1%. In contrast, metastatic invasion to the heart is nearly 20 times more common.^{1–5} The majority of cardiac metastases arise from primary lung cancer (36–39%), breast cancer (10–12%) and haematological malignancies (10–21%).^{6–7} Within the genitourinary tract, only ovarian and renal cancers are known to manifest cardiac metastatic potential.^{1–6} Cardiac metastasis from cervical carcinoma is much less common, with an estimated incidence of 0.3%.⁷ Indeed, regardless of the primary source, risk of cardiac metastasis increases with disease burden.⁶

Compared to pericardial lesions, intracavitary, myocardial and endocardial lesions occur far less frequently (<6% of cases), and are hypothesised to result from haematogenous spread.⁸ Of particular interest is the observation that 80% of such metastases occur in the right-sided chambers.⁹ Concerning metastatic cervical cancer in particular, only two prior reports have demonstrated concomitant involvement of the left ventricle.^{10–11}

The clinical manifestations of cardiac metastases vary widely depending on tumour burden and location. The majority of patients are asymptomatic and are diagnosed postmortem. When present, the most common symptoms and signs include dyspnoea, palpitations, lower extremity oedema, chest pain and atrial fibrillation or flutter.^{12–13}

CASE PRESENTATION

A 35-year-old woman, an immigrant from Thailand, with a history of stage IIB cervical cancer treated with primary chemoradiation, presented with a 1-month history of intermittent, exertional chest pressure localised to the mid-chest. She had last received cisplatin and concomitant radiation therapy 8 months prior to her current presentation and was noted to have a complete response. Her episodes of chest pressure lasted a few minutes and subsided without intervention. Over the 24 hours

preceding admission, her symptoms had worsened, prompting her to seek treatment.

Vital signs were all within normal limits. Physical examination was unremarkable. ECG revealed sinus rhythm and T-wave inversions in the inferolateral leads. Cardiac troponin I was elevated to 0.24 ng/mL. Transthoracic echocardiography revealed normal left ventricular size and function as well as a large, poorly delineated, cavernous mass at the basal posterior/inferolateral free wall, which appeared attached to the posterior mitral leaflet (figure 1, video 1). Trace mitral regurgitation was also present. In addition, a round echodensity in the distal right ventricle measuring 1.3×1.1 cm was noted (figure 2, video 2).

Cardiac MRI demonstrated a 4.2×2.5 cm necrotic intramyocardial mass in the lateral wall of the

Figure 1 Transthoracic echocardiography demonstrating a large, poorly delineated, cavernous mass at the basal posterior/inferolateral free wall, suggestive of metastatic cervical carcinoma.

Video 1 Apical four-chamber view of the left ventricular mass, which appears attached to the mitral valve. Trace mitral regurgitation is also noted.

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Figure 2 Transthoracic echocardiography demonstrating a round echodensity in the distal RV, measuring 1.3×1.1 cm. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Video 2 Apical four-chamber view of the right ventricular mass.

left ventricle, with a central necrotic component, and a 1.3×1.2 cm lesion in the lateral wall near the right ventricular apex (figure 3A). Perfusion imaging demonstrated enhancement of the peripheral portion of the left ventricular mass with lack of central enhancement. Postcontrast delayed imaging demonstrated avid enhancement of the left ventricular mass relative to the myocardium, with a central circular area lacking enhancement believed to be necrosis. Milder enhancement was seen in the lesion in the right ventricle (figure 3B).

Positron emission tomography (PET)/CT demonstrated a large metabolically active intramyocardial mass with central necrosis involving the lateral wall of the left ventricle (standardised

uptake values (SUV)=13.4; figure 4) and an additional metabolically active lesion in the right ventricular apex (SUV=8.9; figure 5). A soft tissue lesion in the left lower quadrant of the abdominal wall, an enhancing nodular focus in the right gluteal muscle and scattered metabolically active lytic lesions in bilateral iliac bones, sacrum and right acetabular margin were also observed. Mild enhancement of the cervix was additionally noted.

Endomyocardial biopsy of the right ventricle under transthoracic echocardiographic guidance was performed. Biopsy results revealed unremarkable myocardium, although sampling error was strongly suspected. Given the difficult technical considerations surrounding biopsy of the left ventricular mass, ultrasound-guided core biopsy of the aforementioned left anterior pelvic lesion was performed, which revealed metastatic squamous cell carcinoma.

A diagnosis of recurrent squamous cell carcinoma of the uterine cervix was made, and the patient was dispositioned to palliative chemotherapy.

INVESTIGATIONS

After the initial transthoracic echocardiogram demonstrated biventricular masses, cardiac MRI was obtained in order to further characterise these lesions. PET/CT was used to help determine the metabolic activity of these masses, as well as to aid in identifying a possible primary lesion. For a definitive histological diagnosis, tissue was obtained from the right ventricle and the left anterior pelvic lesion.

DIFFERENTIAL DIAGNOSIS

This case involved a young woman presenting with a clinical history suggestive of ischaemic chest pain with corresponding T-wave inversions and positive cardiac biomarkers, making acute coronary syndrome the most likely initial diagnosis. As part of her initial evaluation, however, a transthoracic echocardiogram demonstrated biventricular masses.

The differential diagnosis of cardiac masses includes benign tumours (such as myxomas, lipomas and papillary fibroelastomas), primary malignant tumours (sarcomas, typically angiosarcomas or rhabdomyosarcomas), secondary metastatic tumours and thrombi.

Cardiac MRI allowed for differentiation between a solid tissue mass and thrombus. PET/CT allowed for determination of the metabolic activity of these lesions as well as the extent of metastatic burden. PET/CT also aided in the detection of the anterior pelvic lesion that was ultimately biopsied subsequent to the negative endomyocardial biopsy.

Figure 3 Steady-state free precession (A) and four-chamber delayed enhancement (B) imaging demonstrating enhancement of the left and right ventricular lesions relative to the myocardium, consistent with metastatic carcinoma. In 3A, note the spared circular area in the LV, most likely due to central necrosis. LV, left ventricle; RV, right ventricle.

Figure 4 Positron emission tomography/CT demonstrating a large metabolically active intramyocardial mass with central necrosis involving the base of the LV (standardised uptake values=13.4). LV, left ventricle; RV, right ventricle.

Despite the PET/CT findings suggestive of metastasis, endomyocardial biopsy of the right ventricle was deemed necessary for several reasons. First, the patient had received chemoradiation therapy only 8 months prior to her presentation, and was noted to have achieved complete remission, therefore making recurrence of cervical carcinoma a less likely diagnosis than one of the aforementioned aetiologies of a cardiac mass. Indeed, the progression-free survival of locally advanced cervical carcinoma treated with primary chemoradiation is 63% at 30 months and 58% at 60 months.¹⁴ Second, the patient's marked absence of abdominal and genitourinary symptoms (and prominence of cardiac symptoms) guided the investigation of the cardiac lesion prior to the pelvic lesion. Third, anticipation of potential downstream therapies (eg, possible cardiac radiotherapy) mandated that a histological diagnosis at least be attempted.

TREATMENT

The management of endocardial tumours secondary to cervical carcinoma varies on a case-to-case basis. Surgical resection was not considered in this case, given the patient's metastatic disease and the inherently high surgical risk associated with biventricular resection. Moreover, the risk of transmural rupture was thought to outweigh any potential benefit of targeted cardiac radiotherapy. In light of all these considerations, the decision was made to pursue palliative chemotherapy.

Figure 5 Positron emission tomography/CT demonstrating an additional metabolically active lesion in the right ventricular apex (standardised uptake values=8.9). LV, left ventricle; RV, right ventricle.

OUTCOME AND FOLLOW-UP

Three months following her initial presentation, the patient continued to experience mild, intermittent chest-wall discomfort, for which analgaesics were prescribed. Her original symptoms of exertional chest pressure had mostly resolved. The inferolateral T-wave inversions seen on her initial ECG normalised, and her cardiac troponin I levels persisted. It remained unclear why the character of her symptoms changed, but we hypothesised that she may have been experiencing some component of anxiety on her initial presentation. Despite antineoplastic therapy, repeat PET/CT demonstrated no change in the overall dimensions or metabolic activity of either ventricular lesion.

DISCUSSION

Carcinoma of the uterine cervix carries a relatively good prognosis, with a 5-year survival rate of more than 80% when the tumour is confined to the uterus.¹⁵ When present, extrapelvic metastases typically occur in the lungs, liver, bones and lymph nodes.¹⁶ Few reports exist describing cardiac metastasis in cervical cancer (table 1).^{10 11 16–22} Median age at the time of diagnosis is 49 years and the majority of patients had stage II disease or higher. Median interval from initial diagnosis of cervical cancer to cardiac metastasis was 10 months (8 months in our patient), and all patients presented insidiously, with dyspnoea being the predominant symptom. Unfortunately, prognosis was poor in all reported cases, with a median time to death from diagnosis of cardiac metastasis of 6 months.

Only two such cases demonstrated evidence of concomitant left-ventricular involvement, as seen in this particular patient.^{10 11} The more recent case reported by Schawkat *et al*¹¹ was that of a 33-year-old woman (also with history of stage IIb cervical cancer) who presented with fever and was noted to have biventricular metastatic invasion. Important differences between our two cases include the fact that in their case, 1 year prior to presentation with cardiac involvement, the patient had two presentations with isolated pulmonary metastases

Table 1 Literature review of cardiac metastasis from cervical cancer cases

Author	Age (years)	Stage	Histology	Chief symptom of cardiac metastasis	Overall survival (months)
Ando <i>et al</i> ¹⁷	41	IIB	SCC	Dyspnoea	13
Lemus <i>et al</i> ¹⁸	53	IB2	SCC	Dyspnoea	15
Lemus <i>et al</i> ¹⁸	49	IVB	SCC	Dyspnoea and tachycardia	13
Inamura <i>et al</i> ⁷	58	IB1	SCC	Dyspnoea and purpura of extremity	48
Nakao <i>et al</i> ¹⁹	57	IIIB	SCC	Mild chest pain and shortness of breath	12
Borsaru <i>et al</i> ²⁰	42	IVB	SCC	Not reported	Not reported
Kim <i>et al</i> ¹⁵	64	IB1	SCC	Dry cough and dyspnoea	12
Miller <i>et al</i> ²¹	48	IB2	Adeno	Chest pain	56
Byun <i>et al</i> ¹⁶	32	IIA	SCC	Dyspnoea and purpura of extremity	32
Sergi <i>et al</i> * ¹⁰	50	IIA	SCC	Dyspnoea	6 days
Schawkat <i>et al</i> * ²¹	33	IIB	SCC	Dyspnoea and fever	Not reported

*Indicates report of biventricular involvement.
Adeno, adenocarcinoma; SCC, squamous cell carcinoma.

necessitating wedge resections of bilateral lower lobes. Moreover, a third recurrence of pulmonary metastasis was present at the time her cardiac lesions were discovered, as was a moderate pericardial effusion (suggestive of direct extension from adjacent viscera). Ostensibly, cardiac involvement in their case may have been a result of the preceding pulmonary lesions. Pulmonic involvement and pericardial effusion were notably absent in our case.

Overall, the generalised predilection for right-sided metastases is hypothesised to result from the filtering role of the pulmonary circulation and the slower rate of blood flow in the right-sided chambers. Furthermore, the genetic basis for cardiac involvement of cervical cancer has not been clearly established.¹⁷ Treatment options are generally considered palliative, and surgical excision has only been offered in cases of isolated right ventricular involvement, and otherwise limited metastatic burden and excellent functional status.⁷

Classically, there are four pathways of cardiac metastatic involvement: (1) retrograde lymphatic spread, (2) direct extension from adjacent viscera, (3) haematogenous spread and (4) transvenous extension through the vena cava into the right-sided chambers.¹⁷ It is thought that myocardial involvement (as opposed to endocardial, pericardial or valvular metastatic disease) is attributable to haematogenous spread,¹⁷ consistent with the findings of widespread disseminated disease seen in the abdominal wall and bones in this patient.

Interestingly, our patient's endomyocardial biopsy revealed normal myocardium, despite a total of eight samples obtained. The definitive false-negative rate of endomyocardial biopsy has not been established, although the potential for sampling error is well recognised. A retrospective analysis of 1200 patients with an initially unexplained cardiomyopathy revealed that, although a clinical diagnosis was established in 50% of patients, a specific histological diagnosis was established in only 15%.²³ Technical considerations and more readily accessible biopsy sites precluded pursuit of the left ventricular mass, which was much larger and therefore presumably more easily biopsied.

We are confident that the left ventricular lesion was an intracavitary metastasis, given its appearance on PET/CT. It would be highly unlikely for this patient to have had two distinct primary cardiac tumours in the clinical context of otherwise widely metastasised cervical cancer. Furthermore, in the majority of other reported cases, pathological confirmation was established via open excision as opposed to endomyocardial biopsy.¹⁷

The clinical presentation of cardiac metastases, regardless of primary source, is highly variable.¹⁷ However, cardiac metastases should be considered in the differential diagnosis of cardiopulmonary symptoms among oncology patients, particularly when

symptoms are new or otherwise unexplained. Echocardiography is valuable and convenient for initial imaging in these patients, but MRI remains the modality of choice in the non-invasive evaluation of intrinsic myocardial abnormalities.^{11 24}

Contributors KK and MCE were involved in the admission of the patient to the hospital, and also involved with the completion and interpretation of the patient's echocardiogram. MS and RS were involved in the patient's cardiac catheterisation and endomyocardial biopsy. RS and DMR were further involved in the biopsy of the patient's thigh, as well as the initiation and maintenance of the patient's antineoplastic therapy. DMR and CSW were involved in the completion and interpretation of the patient's imaging studies.

Competing interests None declared.

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Learning points

- Cardiac metastasis from cervical cancer, particularly with involvement of the left ventricle, is very uncommon and the clinical presentation highly variable.
- There are no definitive screening guidelines for cardiac metastases in patients with cervical cancer, but the diagnosis should be considered in patients presenting with cardiopulmonary symptoms in the absence of an alternative aetiology.
- Echocardiography is a useful initial imaging modality, but MRI is the gold standard for diagnosis of cardiac tumours.

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