Cardiac metastasis in cervical cancer

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ABSTRACT
Metastasis of cervical carcinoma to the heart is uncommon. Most cases are found during autopsy. These type of metastasis occur mostly in epicardium and myocardium. We present a case report of a patient with carcinoma cervix stage IIIB who presented to the hospital with pitting edema of right lower limb, post 1 year of completion of treatment. PET-CT scan showed FDG avid inguinal, iliac and retroperitoneal lymph nodes, which were bulky on right side causing pedal edema. There was FDG avid uptake seen in right atrial wall and in the atrioventricular groove indicative of metastasis to the heart. Patient refused biopsy or further treatment and hence received best supportive care only. She had a disease free survival of 12 months, and survived for 11 months after being diagnosed with recurrence. Overall survival was 23 months.

SUMMARY
Cardiac metastasis from cervical cancer is uncommon, with an incidence of 1.23% based on autopsy findings. Owing to the rarity of the condition, the diagnosis is made almost exclusively post-mortem; there are few cases of pre-mortem diagnosis and it has been shown that when cardiac metastasis has been found in vivo, the prognosis has been extremely poor. A literature search has shown that the longest survival after the diagnosis of cardiac metastasis from cervical cancer has been 13 months. Aggressive therapy may lengthen patients' survival and quality of life; but owing to the rarity of the condition, it is very difficult to standardize care for these patients.

The metastatic sites in the heart include the epicardium (60%), myocardium (30%) and endocardium (6%), as well as formation of an intraventricular tumour (3%). Approximately 80% of intracavitary, endocardial or valvular type metastasis occurs in the right chambers of the heart; rarely does metastasis occur in the left chambers. This is attributed to the filtering role of pulmonary circulation and the slower flow in the right chambers.

Here we report a case of carcinoma of the cervix after primary radical treatment with chemoradiotherapy presenting with symptoms suggestive of recurrence that was confirmed on whole-body positron emission tomography (PET)-CT scan that showed recurrence in the pelvic and the para-aortic nodal region, and also in the heart.

CLINICAL PRESENTATION
The patient, a 47-year-old obese female, P3L3, postmenopausal for 3 years had initially presented in April 2012 with post-coital bleeding and bilateral lower limb pain. On examination, there was a bulky proliferative growth involving both lips, all fornices and upper one-third of anterior vaginal wall. The left parametrium was medially involved and the right parametrium was involved up to the lateral pelvic wall. Biopsy from the lesion was reported as squamous cell carcinoma of the cervix. Further imaging with MRI of the pelvis, ultrasound scan of the abdomen plus pelvis and X-ray postero-anterior view of the chest was performed. It showed a 4.3 × 5.1 × 5.4-cm mass involving the cervix, with no evidence of hydrenephrosis or infiltration into the surrounding organs such as the bladder or the rectum, or grossly enlarged pelvic or para-aortic nodes, and no distant metastasis into the lungs or the liver. No evaluation of any tumour marker was performed. She was diagnosed with International Federation of Gynecology and Obstetrics Stage IIIB cervical cancer (squamous cell carcinoma). She received external beam radiotherapy (EBRT) using 15 MV photons with four-field box technique to a dose of 45 Gy in 25 fractions over 40 days, with a treatment gap of 4 days owing to machine breakdown. She also received five cycles of concurrent chemotherapy of weekly cisplatin at 40 mg m$^{-2}$. After 10 days of EBRT, the patient received high dose-rate intracavitary brachytherapy using the Vienna applicator to a dose of 7 Gy to Point A (2 cm lateral to on either side of tandem, and 2 cm above the ring of the applicator) for four fractions in 1 week. The overall treatment time was 8 weeks.
MRI performed after 3 months showed complete response and the patient was advised for regular follow-up. At the 12-month post-treatment follow-up, she presented with bilateral lower limb pedal oedema of 15 days duration that was associated with pain. There was a history of fever for 3 days, 2 weeks prior to presenting to the hospital. No history of cough, chest or abdominal pain; difficulty in breathing; increased sweating; reduced appetite or weight loss was present. On general examination, a palpable centimetre-sized left supraclavicular lymph node was found. Per vaginal and rectal examination revealed no evidence of disease.

Ultrasonography with colour Doppler of bilateral lower limbs ruled out deep vein thrombosis but showed bilateral lower limb oedema (right > left).

Other than a low haemoglobin level of 9.8 g dl\(^{-1}\), other haematological and biochemical investigations did not reveal any significant abnormality. Her electrocardiogram was normal. Owing to normal blood counts and absence of fever, cellulitis was also ruled out.

The PET-CT scan showed increased \(^{18}\text{F}\)-fluodeoxyglucose (\(^{18}\text{F}\)-FDG) uptake in the retroperitoneal, bilateral pelvic and right inguinal nodes and also the presence of disease in the walls of the heart and the aortopulmonary (AP) window lymph node.

Since PET-CT findings showed disseminated disease in a known case of carcinoma of the cervix, the diagnosis of recurrence of carcinoma of the cervix was made. No histological correlation was obtained from the lymph nodes or the cardiac deposits. The deposits in the heart were determined to be metastatic deposits from carcinoma of the cervix based on the PET-CT findings.

**DIFFERENTIAL DIAGNOSIS FOR THE CARDIAC DEPOSITS**

- Metastasis from carcinoma of the cervix;
- atrial myxoma;
- thrombus;
- brown fat;
- mediastinal node;
- variable uptake in a normal heart.

Correlational imaging such as 2D echocardiography or cardiac MRI is required to differentiate between metastasis,
| Author           | Age (years) | Stage | Type | Primary treatment | Interval to cardiac metastasis (months) | Recurrence diagnosis modality | Pathology confirmation | Recurrence treatment | Cause of death | Time to death from cardiac metastasis (months) | Overall survival (years) |
|------------------|-------------|-------|------|-------------------|---------------------------------------|------------------------------|------------------------|---------------------|---------------|---------------------------------------------|--------------------------|
| Ando et al⁹      | 41          | IIB   | SCC  | Sx                | 8                                     | MRI                          | Autopsy                | CTx                 | RHF           | 5                                           | 13                       |
| Lemus et al⁷     | 53          | IIB   | SCC  | Sx                | 14                                    | MRI                          | Autopsy                | CCRT                | RHF           | 1                                           | 15                       |
| Lemus et al⁷     | 49          | IIVB  | SCC  | ERT               | 3                                     | MRI and CT scan              | None                   | CCRT                | RHF           | 7                                           | 13                       |
| Inamura et al¹⁹  | 58          | IB1   | SCC  | CTx               | 44                                    | Echocardiogram and CT scan    | Open excision          | None                | RHF           | 4                                           | 48                       |
| Nakao et al²⁰    | 57          | IIB   | SCC  | CCRT              | 10                                    | Echocardiogram and CT scan    | Open excision          | None                | RHF           | 2                                           | 12                       |
| Borsaru et al¹⁷  | 42          | IIVB  | SCC  | CCRT              | 6                                     | Echocardiogram and CT scan    | Open excision          | -                   | -             | -                                           | -                        |
| Kim et al²²      | 64          | IB1   | SCC  | CCRT              | 5                                     | Echocardiogram, TEE and CT scan| Pericardiocentesis      | CTx                 | RHF           | 7                                           | 12                       |
| Miller et al²³   | 48          | IIB   | Adeno| CCRT              | 48                                    | MRI                          | TEE-guided biopsy        | CTx/RT               | RHF           | 8                                           | 56                       |
| Byun et al¹³      | 32          | IIA   | SCC  | Sx                | 15                                    | Echocardiogram and CT scan    | Open excision          | CTx                 | Cachexia      | 13                                          | 32                       |
| Togo et al⁹⁵     | 39          | IIA   | SCC  | Sx                | 23                                    | MRI and CT scan              | Biopsy via right UV    | RT                  | Cardiac tamponde | 7                                           | 30                       |
| Ferraz et al¹⁵   | 63          | NK    | SCC  | Sx f/b CCRT       | -                                     | CT scan                     | Open excision          | None                | -             | 4                                           | -                        |
| Current study    | 47          | IIB   | SCC  | CCRT              | 12                                    | PET-CT scan                 | -                      | None                | -             | 11                                          | 23                       |

- no available data; Adeno, adenocarcinoma; CCRT, concurrent chemoradiotherapy; ERT, external radiotherapy; f/b, followed by; IUV, internal jugular vein; PET, positron emission tomography; RHF, right heart failure; RT, external radiotherapy; SCC, Squamous cell carcinoma; Sx, surgery; TEE, transoesophageal echocardiogram.
atrial myxoma, thrombus and variable normal uptake in the heart. The diagnosis of metastasis could only be absolutely confirmed with a biopsy or open excision of the lesion. Response to salvage therapy is another way to determine that the lesion is a metastasis from the cervix. Other differential diagnoses such as a mediastinal node and brown fat can be excluded by studying the CT images. For clinical purposes, normal myocardial $^{18}$F-FDG activity can be defined as absent, or diffusely (with or without some heterogeneity), locally (e.g., papillary muscles) or regionally increased. Knowledge of these normal physiological patterns and the appearance of benign lesions that can mimic malignant disease is important to help differentiate benign from malignant diseases involving the heart.

**INVESTIGATIONS/IMAGING FINDINGS**

PET-CT scan: discrete $^{18}$F-FDG-avid mass lesions involving the wall of the right and left atrium [maximum standardized uptake value (SUV$_{max}$) 11.8, largest 3.7 $\times$ 3.2 cm] (Figure 1). Discrete hypodense $^{18}$F-FDG-avid lesion in the right atrioventricular groove, measures 30 $\times$ 27 mm, SUV$_{max}$ 12.7 (Figure 2). Also seen are discrete $^{18}$F-FDG-avid enhancing nodes in AP window (largest 12 mm, SUV$_{max}$ 4.8) region. Liver and lungs are unremarkable. Metastatic $^{18}$F-FDG-avid nodes are noted in following regions: right inguinal (16 mm, SUV$_{max}$ 12.6); bilateral external iliac (largest 27 mm, SUV$_{max}$ 6.4); bilateral common iliac (subcentimetre, SUV$_{max}$ 5.5); multiple retroperitoneal (renal hilar to aortic bifurcation, largest 14 mm, SUV$_{max}$ 7.6). Adnexal structures are otherwise unremarkable (Figures 3 and 4). A 2D echocardiography correlation was suggested for the cardiac deposit.

**TREATMENT**

The patient was given analgesics for her pain and advised to see the pain and the lymphoedema clinic. Medical oncology reference was taken for an opinion on palliative chemotherapy but the patient was not willing to undergo any further investigations or treatment. Hence she was advised best supportive care and follow-up after 6 months.

**OUTCOME AND FOLLOW-UP**

The last follow-up date was March 2014. When contacted over the phone, her relative informed that she had passed away. In this case, the survival after diagnosis of cardiac metastasis was 11 months.

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