



Case Report

Successful Surgical Treatment of a Patient with a Solitary Asymptomatic Cardiac Metastasis from Breast Cancer, Identified by Elevated Tumor Markers and Circulating Tumor Cells

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Abstract

Introduction: Cardiac metastases are a not infrequent autopsy finding in patients dying of metastatic cancer, but are less commonly diagnosed during life (1). Although the autopsy incidence of cardiac metastases ranges may be as high as 25%, solitary cardiac metastases in the absence of metastatic involvement of other organs are rare (2).

Case Presentation: We report here the case of a 66-year old woman with a history of bilateral breast cancer, where a solitary metastasis in the right atrium was successfully resected.

Conclusion: In the absence of any symptoms or clinical findings on physical examination, the presence of metastatic disease was first suggested by the detection of elevated tumor markers and circulating tumor cells during routine follow up after treatment for early stage breast cancer.

Keywords: cardiac metastases; circulating tumor cells; tumor markers

Academic Editor: Xiaoning Peng, Hunan Normal University School of Medicine, China

Received: May 23, 2016; **Accepted:** July 21, 2016; **Published:** August 6, 2016

Competing Interests: The authors have declared that no competing interests exist.

Consent: Consent was taken from the patient for publication of this case report.

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Introduction

Cardiac metastases are a not infrequent autopsy finding in patients dying of metastatic cancer, but are less commonly diagnosed during life [1]. Although the autopsy incidence of cardiac metastases ranges may be as high as 25%, solitary cardiac metastases in the absence of metastatic involvement of other organs are rare [2].

We report here the case of a 66-year old woman with a history of bilateral breast cancer, where a solitary metastasis in the right atrium was successfully resected. In the absence of any symptoms or clinical findings on physical examination, the presence of metastatic disease was first suggested by the detection of elevated tumor markers and circulating tumor cells during routine follow up after treatment for early stage breast cancer.

Case Report

The patient first came to Cancer Treatment Centers of America at Midwestern Regional Medical Center (CTCA) in February 2007. At that time she was a 64 year old African American woman with the following history:

In August 1997, at the age of 51, she had a screening mammogram, which revealed a 1.2 cm mass in the upper outer quadrant of the right breast. Biopsy confirmed a high-grade estrogen receptor and progesterone receptor (ER/PR) positive invasive ductal carcinoma, and patient had a right partial mastectomy and axillary node dissection. Final pathologic stage was T1cN1M0 with 3/17 axillary nodes positive.

Post-operatively she received 4 cycles of adjuvant chemotherapy with doxorubicin and cyclophosphamide followed by radiation to the breast and 5 years of tamoxifen. Of note she did not receive radiation to the axilla or supra-clavicular area.

In April 2006 she first felt a right axillary mass. This slowly enlarged, and a fine needle aspirate of the mass in January of 2007 confirmed metastatic breast cancer. At that time, ER was positive but PR and human epidermal growth factor receptor (HER2) were negative. She then elected to come to our institution.

When first seen at CTCA in February 2007, a right axillary mass was readily palpable. Computed tomography (CT) scan confirmed a 5.5 cm lobulated right axillary mass with no other definite evidence of metastatic disease. Of note, CEA was 4.3, while CA 27.29 and CA 15.3 were normal.

Clinical impression at that time was of a right axillary recurrence of ER positive breast cancer after an approximate nine-year disease free interval.

She was treated at that time with surgical excision of the right axillary mass, followed by 6 cycles of post-operative docetaxel and radiation to the axilla and supra-clavicular area. Pathology of the resected tumor revealed high grade triple negative invasive ductal carcinoma.

The patient had a past history of long-standing hypothyroidism and was on replacement thyroxine. Her family history was notable for breast cancer in a sister diagnosed in her 30s; another sister had ovarian cancer in her 40s. Additionally, a cousin also had breast cancer. The patient tested negative for BRCA mutation.

From May 2007 until December 2010, the patient remained without further evidence of breast cancer. Annual mammograms and serum tumor markers were persistently normal (Figure 1). In December 2010, CA19-9 was added to our regular panel of breast cancer markers, and was noted to be slightly elevated. At the same time circulating tumor cells (CTC) were measured for the first time, with negative result.

She remained apparently cancer free until a screening mammogram in March 2011 showed a new

mass at 6 o'clock in the left breast, and biopsy revealed a grade 2 ER/PR positive, HER2 negative invasive ductal carcinoma. A pre-operative PET scan on April 12 2011 showed non-specific increased metabolic activity in the thyroid gland, but no other abnormality. Of particular note, no abnormal activity was seen in the left breast or the heart.

On April 19 2011, she had a left partial mastectomy and sentinel node biopsy. Final pathologic stage was T1cN0M0. Tumor was strongly ER/PR positive HER2 negative with Oncotype Dx score of 8. Following surgical removal of the tumor, the elevated CA 19-9 returned to normal, when measured in August 2011 (Figure 1).

Patient received post-lumpectomy radiation to the left breast, and was started on adjuvant Anastrozole, which she tolerated well except for arthralgias. She was followed uneventfully from the completion of radiation in September 2011 until March 2012, although the CA 19-9 was again noted to be slightly elevated in December 2011.

She complained of left breast pain in March 2012, and was found on physical examination to have post radiation edema of the left breast but no suspicious mass. Of note, serum CEA and CA 19-9 were markedly elevated. The CTC, which had been persistently zero, were 34. (Figure 1).

Date	CA				
	CEA	CA 15-3	CA 19-9	27.29	CTC
	[0.0-3 .0 ng/mL]	[1.0-35.0 U/mL]	[2-37 U/mL]	<=38.6 U/mL	>=5 U/mL
12/21/2010	1.3	10	39.5	16.6	0
4/12/2011	1.7	11	46.8	17.2	0
5/16/2011	1.4	11	40.6	19.5	0
8/4/2011	1.4	13	35	20	0
12/5/2011	2.6	12	77.6	15.7	0
3/19/2012	18.2	23	826.3	29.6	34
4/3/2012	17.3	23	746.2	43.1	6
5/1/2012					
Surgery					
6/5/2012	1.1	15	32.2	16.6	0
7/17/2012	0.9	14	31.5	18.2	0
9/4/2012	0.9	12	28.5	18.7	0
12/5/2012	1.1	13	30	16.4	0
2/27/2013	1.4	13	38.5	20	0
10/2/2013	1.2	13	30.5	14.1	0
3/17/2014	1.6	14	36.4	19.3	0
7/14/2014	1.7	11	27.1	12.5	0
1/15/2015	1.3	12	20.2	15	0
7/15/2015	2	16	26.5	17.7	0
1/18/2016	2.3	15	29.2	18.2	0

Fig 1 Serial tumor markers and circulating tumor cells (CTC)

Based on these results a PET scan was done on 04/01/12, and this revealed a new finding of increased

metabolic activity in the right atrium. (Figure 2) The remainder of the PET scan was entirely normal, except for increased activity in the thyroid gland, which was unchanged from April 2011.

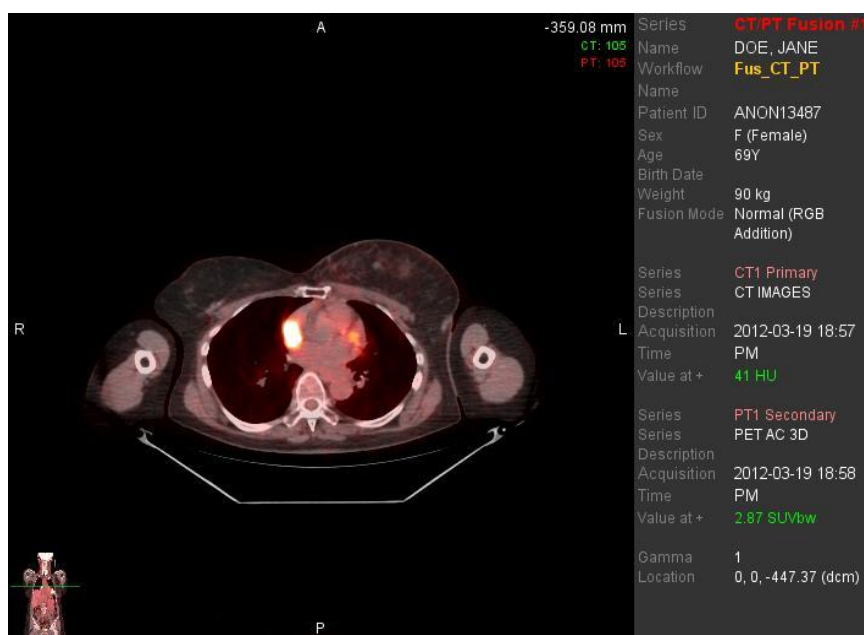


Fig 2 PET scan shows a hyper-metabolic focus in right atrium

Following the PET scan, A CT scan of the chest, abdomen and pelvis on 04/03/12 confirmed the presence of a 3 x 2.4 cm mass within the right atrium (Figure 3).

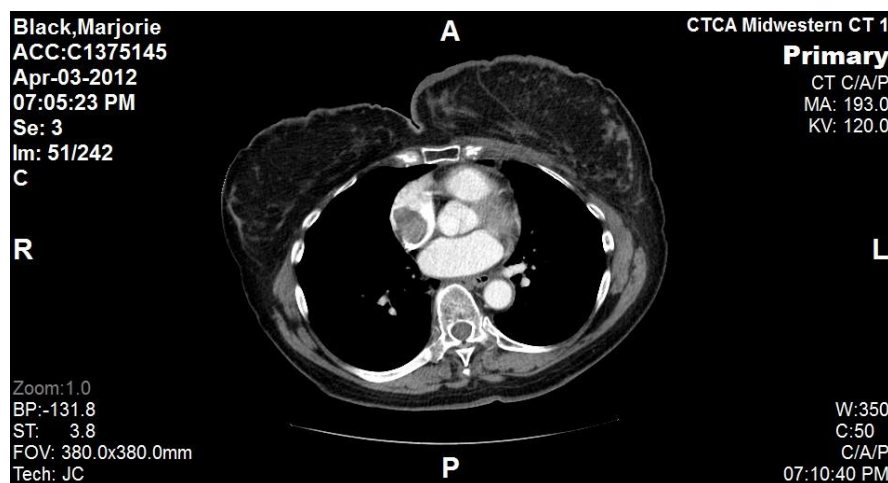


Fig 3 CT scan shows pedunculated tumor mass in right atrium

She was referred to Mid America Heart Institute in Kansas City Mo (Dr Michael Borkon), where she had surgical excision of the right atrial mass under cardio-pulmonary bypass, with a pericardial patch and reconstruction of the right atrium on 05/01/2012.

Pathology of the resected specimen revealed a 2.5 cm pedunculated tumor extending into the myocardium. (Figure 4). Sections of the mass showed sheets of malignant cells with oval nuclei and prominent nucleoli and moderate amounts of eosinophilic cytoplasm (Figure 5). Immunoperoxidase

staining was positive for Pancytokeratin, Cytokeratin 7 and Estrogen receptor, consistent with metastatic breast cancer

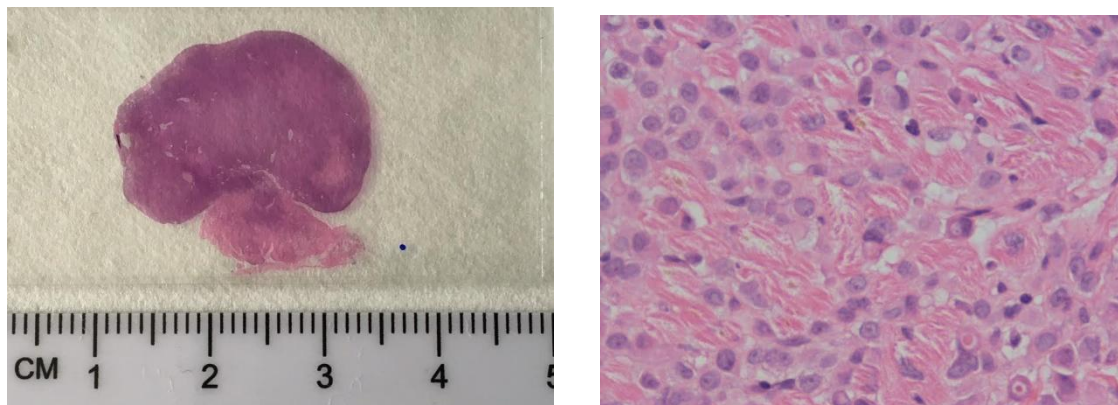


Fig 4(left) Whole mount section of 2.5 cm pedunculated mass from right atrial wall (H&E).

Fig 5(right) Metastatic breast cancer cells infiltrating cardiac muscle (H&E magnification X 400).

Her post-operative course was complicated by a period of hypotension requiring IV pressors, pulmonary edema, and bilateral pleural effusions with atelectasis. She recovered from these issues and was well enough to be discharged home on 05/09/12. Post-operatively she resumed her Anastrozole.

Following surgical resection of the right atrial tumor, her tumor markers and CTC quickly normalized, and have remained in the normal range throughout follow-up, which now extends to almost four years (Fig.1).

When seen last in January 2016, she continues to take daily Anastrozole, with no complaints to suggest recurrent breast cancer and no evidence of recurrent disease on physical examination. All tumor markers are within normal range and circulating tumor cells are persistently zero. Throughout this period, repeated PET scans continue to show no evidence of tumor recurrence.

Discussion

Cardiac metastases are generally identified in patients with extensive metastatic disease, and are frequently associated with cardiac symptoms, which may include dyspnea, persistent tachycardia arrhythmias, or thrombo-embolic phenomena [3].

What is most striking about the present case was the demonstration of a single intra-cavitary metastasis in an asymptomatic patient with no other evidence of metastatic disease. As such, she was an excellent candidate for surgical resection.

Numerous case reports have previously described surgical resection of isolated metastatic disease (“oligo-metastases”) resulting in long disease-free survival [4, 5]. Most reported cases describe patients with lung, liver, brain or bone metastasis. Although rare, there have also been previous reports of successful resection of cardiac metastases [6,7].

The other notable issue in this patient is how the diagnosis of metastatic disease was made. In our patient elevation of serum tumor markers and the presence of CTC were the only indicator of recurrent disease and led to the imaging studies, which identified a single metastasis in a wholly asymptomatic patient.

Current guidelines do not recommend the use of serum bio-markers to monitor patients for tumor recurrence following primary treatment of early stage breast cancer [8]. In the same way, surveillance CT and PET scanning to detect “early” metastatic disease in asymptomatic patients are not currently recommended [9].

These recommendations may require re-examination in the light of advances in the available treatment for patients with recurrent breast cancer. In that context the results of the current on-going randomized study of intensive versus standard post-operative surveillance in high-risk breast cancer patients by the Japan Clinical Oncology Group will be of interest [10].

We can certainly speculate in the current case, that if the diagnosis of isolated cardiac metastasis had not been made in 2012, and the diagnosis delayed until more extensive disease rendered the patient symptomatic, the favorable outcome we have observed would likely not have been achieved.

As surgical resection of oligo-metastases frequently results in long-term disease-free survival, and on occasion may even be curative [4], it may be appropriate to re-evaluate surveillance guidelines in selected patients.

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