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Case Report

Recurrent Breast Angiosarcoma

Allison M. Coy, M.D., Mark C. Meyer, M.D.
University of Kansas School of Medicine, Kansas City, KS
Department of Family Medicine and Community Health

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INTRODUCTION

Angiosarcoma of the breast is a rare and typically aggressive malignancy which is responsible for less than 1% of breast malignancies.[1] Primary breast angiosarcoma occurs spontaneously, most often within the third through fifth decade of life, while secondary breast angiosarcoma occurs in women previously treated for breast carcinoma with breast-conserving therapy and radiation or less commonly in the setting of longstanding lymphedema.[2] Primary angiosarcoma of the breast most often presents with a palpable mass which can be rapidly progressive, sometimes with blue or purple skin discoloration, while secondary angiosarcoma typically presents with rash-like skin changes or skin discoloration.[3] The latency period for the development of secondary breast angiosarcoma following radiation treatment is variable with a median of five to six years.[4] Diagnosis is difficult in that mammogram and ultrasound findings for primary breast angiosarcoma are nonspecific, though there is higher sensitivity of detection with ultrasound compared to mammogram.[5] MRI findings can be helpful in the diagnosis of breast angiosarcoma, with typical MRI findings showing high signal intensities on T1 and T2-weighted imaging.[6] Based on the limitations in diagnostic imaging in identifying breast angiosarcoma, a high degree of clinical suspicion is recommended with consideration of biopsy, especially in patients with cutaneous findings that can be missed on imaging.

Given the rarity of breast angiosarcoma, treatment recommendations are predominantly based on expert opinion. The mainstay of treatment has been mastectomy, although there is some evidence suggesting breast conservation surgery results in increased overall survival in primary breast angiosarcoma and non-inferior overall survival in secondary breast angiosarcoma when compared to mastectomy.[7] Radiation therapy has been utilized in treatment of primary and secondary breast angiosarcoma, but evidence for improved survival has not been clearly demonstrated. There is potential benefit for chemotherapy in overall survival for patients with secondary breast angiosarcoma, but this has not been demonstrated in primary breast angiosarcoma.[8]

Prognosis of breast angiosarcoma is poor, with five-year overall survival estimated to be 44.9%.[9] Disease recurrence is common with frequent sites of recurrence being local-regional (52.6%), liver (13.6%), bone (10.5%), and lung (10.5%), with reported disease recurrence occurring at 37 months.[10] In this case report, a patient was found to have recurrent breast angiosarcoma 31 years after treatment for primary breast angiosarcoma.

CASE REPORT

A 78-year-old female with past medical history significant for left primary breast angiosarcoma status post lumpectomy and radiation therapy in 1992 presented to her primary care physician with a two-to-three-week history of skin changes on the left breast. The lesion overall was not bothersome although it occasionally itched and had not displayed significant change since onset. She had no other associated symptoms. Previous mammogram obtained two years prior was stable, with follow-up recommended in one year. Physical exam (Figure 1) of the left breast was notable for approximately 2 cm diameter circular lesion with central eschar at 1 o'clock position from the nipple. No other breast masses or axillary lymphadenopathy were noted. Given her history and presentation she was referred to a breast clinic for biopsy and breast imaging was ordered.

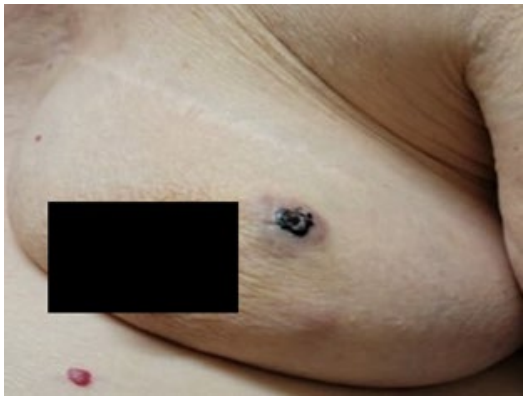

Figure 1. Breast lesion at time of presentation [Figure used with patient's consent].

Upon evaluation in the breast clinic, she underwent diagnostic ultrasound and mammogram of the left breast along with a punch biopsy of the lesion. Ultrasound (Figure 2) showed a 2.6 x 0.5 x 3.1 cm subcutaneous mass that was hypoechoic with ill-defined margins and internal vascularity. Pathology was consistent with angiosarcoma. Breast MRI was obtained which showed biopsy proven angiosarcoma with additional suspicious mass and non-mass enhancement in the left breast with concern for metastatic spread of disease given abnormal skin thickening with associated enhancement in the right breast along with irregular enhancing masses within soft tissues of the chest. CT scan of the chest, abdomen, and pelvis (Figure 3) was obtained, which showed widespread metastatic disease throughout the abdomen and pelvis including hepatic, splenic, adrenal, retroperitoneal, osseous, and subcutaneous metastases. She was referred to oncology to discuss treatment options, which unfortunately were palliative in nature given the widespread extent of her disease at presentation. Treatment options presented included conventional chemotherapy with taxane-based agent, tyrosine kinase inhibitor, or immunotherapy with shared decision making to proceed with the tyrosine kinase inhibitor sunitinib.

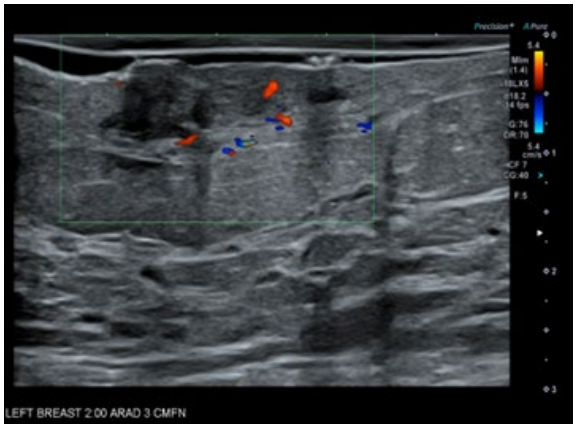

Figure 2. Ultrasound of left breast showing 2.6 x 0.5 x 3.1 cm subcutaneous mass that was hypoechoic with ill-defined margins and internal vascularity [Figure used with patient's consent].

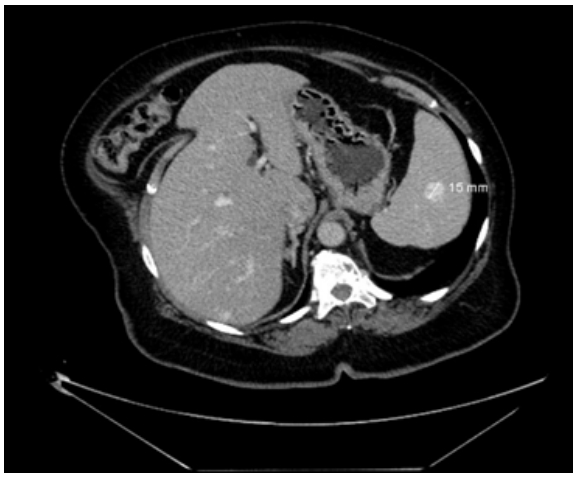

Figure 3. CT scan with contrast showing hepatic and osseous metastases [Figure used with patient's consent].

Approximately one month into treatment she presented to the University of Kansas Health Center's emergency department with nausea, vomiting, diarrhea, and progressive weakness with inability to care for herself at home. She underwent evaluation of diarrhea without identification of infectious etiology and GI symptoms were felt to be secondary to chemotherapy side effects and sunitinib was held on admission. Repeat CT scans showed stable to mild progression of disease. During her hospitalization she had acute onset of urinary retention with significant lower extremity weakness and decreased rectal tone. She underwent MRI of her lumbar spine with and without contrast (Figure 4) which revealed enhancing multifocal osseous metastatic disease with extraosseous extension of the tumor at the L2 vertebral body, along with spondylolisthesis and concomitant spondylotic change at L4-L5 with resulting marked trefoil type stenosis. Neurosurgery was consulted and recommended proceeding with L4/5 laminectomy for decompression.

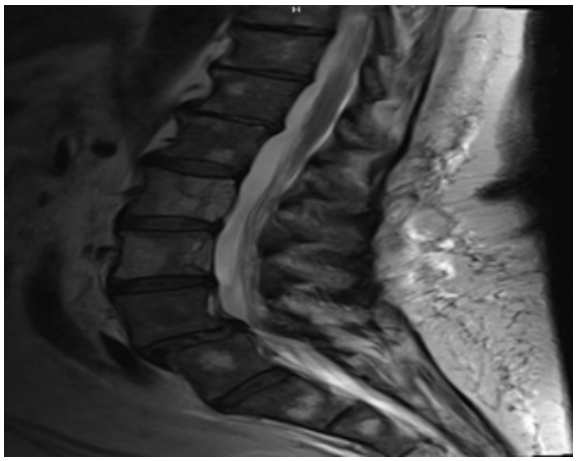

Figure 4. MRI lumbar spine with and without contrast showing enhancing multifocal osseous metastatic disease with extraosseous extension of tumor at L2 vertebral body along with spondylolisthesis and concomitant spondylotic change at L4-L5 with resulting marked trefoil type stenosis [Figure used with patient's consent].

Post-operatively she had improvement in her lower extremity strength. Urinary retention remained an ongoing issue and an indwelling Foley catheter was placed. She developed hematemesis with acute blood loss requiring transfusion post-operatively. She underwent EGD which showed grade D esophagitis with pathology negative for HSV and CMF. Given the number of medical issues facing the patient, palliative care was consulted, and patient elected for discontinuation of cancer treatment with a goal of improving strength with transition to care focused on maximizing quality of life. She completed a stay at a skilled nursing facility with improvement in her lower extremity strength and resolution of her neurogenic bladder.

DISCUSSION

This case report describes a patient with a history of primary breast angiosarcoma initially treated with lumpectomy and radiation who developed a late recurrence of breast angiosarcoma which was diagnosed at an advanced stage. Patients who have undergone radiation therapy for treatment of breast cancer are at increased risk for the development of secondary breast angiosarcoma. The pathophysiology of radiation-associated breast angiosarcoma is not well understood and it displays a variable latency period ranging from 6 months to 41 years with an average of six years.[11] Risk factors for development of secondary angiosarcoma include increasing age, White race, invasive tumor, lymph node removal, history of lumpectomy, and history of radiation therapy.[12]

Radiation-associated secondary breast angiosarcoma typically presents with cutaneous findings, which can often be missed on surveillance mammography. A retrospective review of patients with radiation-associated breast angiosarcoma showed sensitivity rates of mammography at 43%, ultrasound at 50%, MRI at 92% and CT scan at 84%.[13] Although this represents a limited data set of patients, it underscores the need for both patients and physicians to have a high degree of suspicion for patients presenting with cutaneous skin changes, especially in patients

with a history of breast radiation, and proceeding with biopsy when needed, even considering reassuring breast imaging. Treatment recommendations for both primary and secondary breast angiosarcoma are based on case series due to the overall low incidence of the disease. Overall survival rates are better for primary breast angiosarcoma versus secondary, with lack of demonstrated difference in outcomes of treatment with surgery alone versus a combination of surgery and chemotherapy or surgery and radiation therapy.[14]

Development of secondary breast angiosarcoma is extremely rare, with estimated cumulative incidence of 1 per 1,000 in patients with breast cancer who underwent radiation therapy.[15] Rates of breast conserving treatment with radiation therapy have been increasing,[16] resulting in an increased population of patients at risk. Given this patient's history, she had potential for recurrence of primary breast angiosarcoma and for development of secondary breast angiosarcoma secondary to treatment, but given the latency period and presentation, it is likely she developed secondary breast angiosarcoma as a sequela of her breast radiation.

CONCLUSIONS

Breast angiosarcoma is a rare malignancy with challenges in detection and treatment compared to other types of breast cancer. Patients with a history of radiation therapy are at increased risk for development of secondary breast angiosarcoma that can present with isolated cutaneous changes that may not be detected with mammography. Patients and physicians should maintain a high degree of suspicion in the investigation of skin changes which occur in women with a history of radiation therapy.

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