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A Rare Case of Post-Radiation Angiosarcoma with Pleural Metastasis

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Abstract

Soft tissue sarcomas (STS) represent 1% of all malignancies in adults. Angiosarcomas are an uncommon subtype of vascular or lymphatic origin, compromising 2% of STS. We present a rare case of secondary angiosarcoma of the breast. Following treatment for invasive ductal carcinoma and subsequent diagnosis of radiation-induced angiosarcoma two years prior, a 77-year-old female presented with dyspnea and bilateral pleural effusions. Diagnostic thoracentesis demonstrated findings consistent with metastatic angiosarcoma. Angiosarcoma of the breast is exceptionally rare among soft tissue neoplasms and is typically associated with a poor prognosis.

Keywords: Angiosarcoma, pleural metastasis, breast cancer

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1. Introduction

Soft tissue sarcomas (STS) are a heterogeneous group of malignancies, comprising approximately 1% of all malignancies in adults (1). Among STS, angiosarcomas are a rare subtype of vascular or lymphatic origin, accounting for approximately 2% of cases (2). These aggressive tumors typically arise in the subcutaneous tissue of various anatomical sites, including the head, neck, and breast (2).

Distinguishing between primary and secondary angiosarcomas is crucial, as they exhibit notable differences in median age of onset, underlying precipitating factors, and clinical presentation. Primary angiosarcoma refers to cases without a known precursor lesion, while secondary angiosarcoma arises as a consequence of prior therapeutic interventions, such as radiation therapy for breast cancer (3). These distinctions hold implications for disease management, prognostication, and therapeutic decision-making.

Breast angiosarcomas specifically arise from the endothelium of blood vessels surrounding breast lobules or within lobular capillaries, representing a subset of malignancies with unique pathophysiological characteristics. Primary breast angiosarcomas account for less than 0.04% of all malignant neoplasms. They often present as rapidly growing masses with ill-defined borders that arise in the parenchyma of the breast with occasional skin involvement, affecting women 30 to 50 years old (3). In contrast, secondary breast angiosarcomas typically arise 5 to 7 years post-radiation treatment for breast cancer with locally advanced or metastatic angiosarcoma at the time of diagnosis (4). Secondary breast angiosarcoma typically affects older women with a median age of 67 to 71 years old (3).

Despite their rarity, angiosarcomas are notable for their propensity to metastasize early and for their poor prognosis, particularly when diagnosed at advanced stages. Here, we present a rare case of secondary angiosarcoma with pleural metastases in a patient with a history of post-radiation breast cancer.

2. Case Presentation

A 77-year-old female presented to the hospital with generalized weakness, dyspnea, and hypoxia that had been ongoing for two days. The patient's past medical history was significant for heart failure with a preserved ejection fraction, end stage renal disease on hemodialysis, anemia of chronic kidney disease, and type 2 diabetes mellitus. She also has a history of invasive ductal carcinoma of the upper outer quadrant of the left breast that was treated eight years previously with a lumpectomy and radiation therapy followed by anastrozole for six years. Two years prior the patient was diagnosed with radiation-induced angiosarcoma of the left breast, which was treated with doxorubicin and paclitaxel. Her most recent PET scan five months prior to her hospital presentation revealed a new right-sided subcutaneous nodule along the inferior aspect of the of right chest wall with a maximum SUV above 3.1 measuring 12 x 7 mm, consistent with metastasis.

At the time of her presentation to the hospital, she required noninvasive ventilation for hypoxia and hypercapnia. Chest x-ray revealed near complete whiteout of the right lung with bilateral pleural effusions and airspace disease. Notably, the patient had recently been discharged from the hospital for a similar presentation. At that time, she had bilateral pleural effusions, requiring two thoracenteses to address her hypoxic hypercapnic respiratory failure. Her presumed diagnosis was decompensated acute exacerbation of chronic heart failure.

During her subsequent hospital admission, a third thoracentesis was performed. The pleural fluid revealed a pH of 7.35, LDH of 594, protein of 4.6, and fluid cell count of 96% lymphocytes. Pleural fluid cultures did not grow any organisms. Cytopathology revealed scattered abnormal cells with enlarged nuclei, high nuclear-cytoplasmic (NC) ratio, irregular chromatin, and prominent nucleoli range in clusters and single cells in a background of mixed inflammation (Image 1). Immunohistochemical stains were preformed that showed CD 31 positivity in rare atypical cells (Image 2). Based on these findings and her clinical presentation she was diagnosed with metastatic angiosarcoma of the pleura with malignant pleural effusions. Despite additional therapeutic thoracenteses, the patient continued to have recurrent pleural effusions and required supplemental oxygen. Consequently, a right-sided PleurX catheter placed for recurrent malignant pleural effusions prior to discharge.

3. Discussion

Angiosarcoma, characterized by its aggressive behavior and early metastasis, remains a rare

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malignancy with unclear etiology and pathogenic mechanisms. While several risk factors have been identified, including prior radiation therapy, chronic lymphedema, and exposure to certain chemicals, the etiology and pathogenic mechanisms remain unclear due to its rarity (5). A population based, retrospective cohort study utilizing data from the Surveillance, Epidemiology, and End Results Program (SEER) showed women treated with radiation therapy as part of their treatment for breast cancer had a 16-fold increase in the risk of angiosarcoma and a 2-fold increase in the risk of other sarcomas (6). Although women who undergo radiation therapy have an increased risk of sarcomas that persist for up to 50 years, the absolute magnitude of the risk is small (7,8).

Clinical presentation of primary breast angiosarcoma often includes rapidly growing, painless masses, occasionally accompanied by purplish-blue skin discoloration. In contrast, secondary breast angiosarcoma may manifest with rashes, ecchymosis, or skin thickening near previous surgical sites (3). While these are common presenting symptoms for secondary breast angiosarcoma, in our case, the patient did not present with such symptoms. Imaging studies, particularly breast MRI, play a crucial role in detecting angiosarcoma. Breast MRI proves a more dependable non-invasive approach for detecting breast angiosarcoma that mammography might overlook (9). Definitive diagnosis relies on pathological and immunohistochemical findings using fine needle aspiration or core need biopsy due to the lack of specificity in clinical presentation and imaging features (3).

Immunohistochemistry serves as a cornerstone in the diagnosis and differential diagnosis of angiosarcoma, with CD31 and CD34 emerging as sensitive markers for endothelial cells. Factor VIII related antigen also serves as an endothelial cell maker in vascular sarcoma cells. Novel markers such as ETS-related gene (ERG) and Friend leukemia integration 1 (FLI-1) have also showed heightened sensitivity and specificity compared to traditional markers (9).

The prognosis for angiosarcoma in general remains poor, with reported 5-year survival rates varying between 28% and 54%. It has also been reported that there is a higher mortality risk among patients diagnosed with secondary breast angiosarcoma compared to those with primary breast angiosarcoma (9). Additionally, prognosis for metastatic disease is particularly grim, with a median survival ranging from 3 to 10 months (10).

The increased use of breast conservation therapy has led to a rise in reports of radiation-induced angiosarcoma. Angiosarcoma of the breast presents diagnostic and therapeutic challenges due to its rarity, aggressive behavior, and varied clinical manifestations. Our case is unique case in that the patient was diagnosed with post radiation angiosarcoma two years prior to presenting to the hospital with pleural involvement and malignant pleural effusions. This case also highlights that further research is needed to elucidate angiosarcoma's etiology, optimize diagnostic strategies, and develop effective treatment approaches to improve patient outcomes and prognosis.

4. Conclusion

Angiosarcoma of the breast represents one of the rarest forms of soft tissue neoplasms, characterized by its aggressive behavior and poor prognosis. Specifically, post-radiation angiosarcoma with pleural involvement is very rare with estimated less than 1% of all cases of angiosarcoma. We present a unique case of a patient who presented with pleural metastasis two years after the initial diagnosis of post-radiation angiosarcoma.

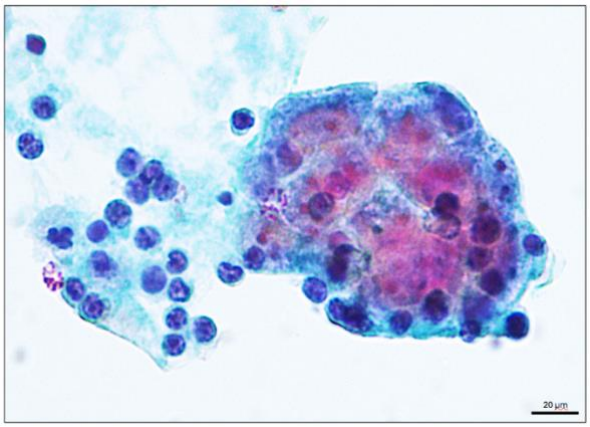

Image 1: *Clustered atypical cells with enlarged nuclei, high NC ratio, irregular chromatin, and prominent nucleoli in a background of mixed inflammation. ThinPrep, 40x.*

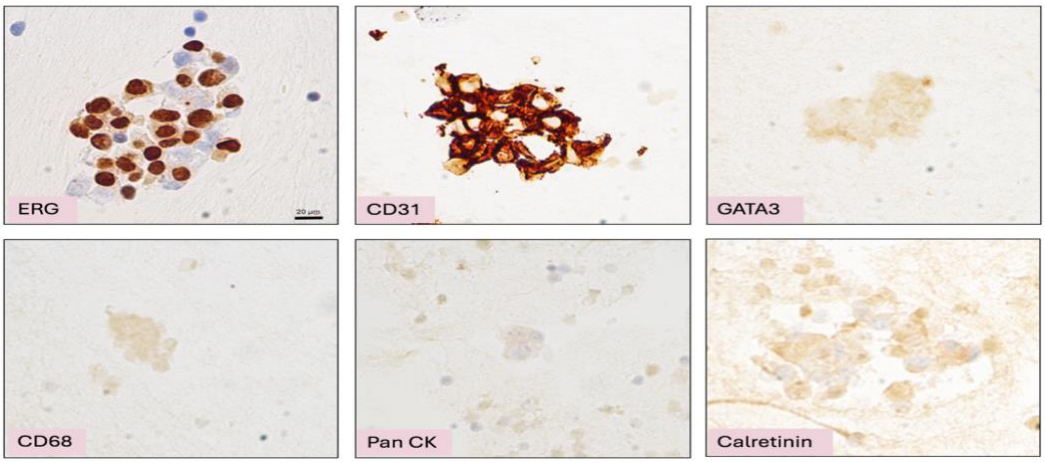

Image 2: *Immunohistochemical analysis of the cell block revealed the following pattern of expression in the atypical cells (clockwise from top left): Nuclear positivity for ERG, cytoplasmic expression of CD31, and negativity for GATA 3, CD68, pancytokeratin, and calretinin.*

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