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OLGU SUNUMU / CASE REPORT

Radiation-Induced Angiosarcoma of The Breast: A Case Report with FDG PET/CT Imaging Findings

Radyasyona Bağlı Meme Anjiyosarkomu: FDG PET/BT Görüntüleme Bulgularıyla Bir Olgu Sunumu

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ÖZET

Giriş: Meme anjiyosarkomu, vasküler endotelden köken alan, tüm yumuşak doku meme tümörlerinin yaklaşık %1'ini oluşturan ve kötü prognoz taşıyan nadir görülen bir tümördür. İki farklı tipte ortaya çıkar: Primer meme anjiyosarkomu (PMAS) ve sekonder meme anjiyosarkomu (SMAS). PMAS tipik olarak meme kanseri veya radyoterapi öyküsü olmayan genç kadınları etkiler; sıklıkla meme parankiminden kaynaklanır ve ara sıra cilt tutulumuyla birlikte hızla büyüyen, genellikle ağrısız, ele gelen bir kitle olarak ortaya çıkar. Buna karşın SMAS yaşlı kadınlarda görülür, meme dermisinden kaynaklanır, bazen parankimi tutar, multifokalite gösterir. Ciltte renk değişikliği ve şişlik gibi karakteristik özellikler sunar. Mevcut literatürde, memenin radyasyonla ilişkili anjiyosarkomunu Flor-18 florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografi (FDG PET-BT) kullanılarak yapılan görüntüleme bulguları ile rapor eden vakaların eksikliği bulunmaktadır. Bu vaka raporu, sol meme kanseri nedeniyle meme koruyucu cerrahi ve ardından radyoterapi uygulanan 55 yaşındaki kadın hastayı ayrıntılarıyla anlatmaktadır.

Olgu: Spesifik olmayan mamografik ve ultrason özellikleri olan hastada radyoterapiden 48 ay sonra radyasyona bağlı anjiyosarkom gelişti. FDG PET-BT'de meme derisinde FDG tutulumunun arttığı nodüler lezyonlar görüldü. Artmış FDG tutulumu gösteren bu nodüllerin yapılan patolojik inceleme sonucunda radyasyona bağlı meme anjosarkomu olduğu doğrulandı. Hastaya tedavi amacıyla total mastektomi operasyonu yapıldı.

Sonuç: Meme koruyucu cerrahi ve radyoterapi öyküsü olan hastalarda, takip sırasında semptomların ortaya çıkması, radyasyona bağlı anjiyosarkomun gelişimini akla getirmelidir. Erken tanı çok önemlidir ve FDG PET-BT lokal görüntüleme ve uzak organ metastazı taraması açısından faydalı olabilir.

Anahtar Kelimeler: Radyasyona bağlı anjiosarkom, Meme Koruyucu Cerrahi, Radyoterapi, FDG PET-BT

ABSTRACT

Introduction: Breast angiosarcoma is a rare tumor arising from the vascular endothelium, accounting for approximately 1% of all soft tissue breast tumors and carrying poor prognosis. It manifests in two distinct types: Primary breast angiosarcoma (PBAS) and secondary breast angiosarcoma (SBAS). PBAS typically affects young women without a history of breast cancer or radiotherapy, often originating from the breast parenchyma with occasionally skin involvement presenting as a rapidly growing, usually painless, palpable mass. In contrast, SBAS occurs in older women, originates from the breast dermis, occasionally involves the parenchyma, displays multifocality, and presents characteristic features such as skin discoloration and swelling. There is a lack of cases in the current literature reporting radiation-associated angiosarcoma of the breast with imaging findings using Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET-CT). This case report details the development of radiation-associated angiosarcoma in a 55-year-old woman who underwent breast-conserving surgery and subsequent radiotherapy for left breast cancer.

Case: The patient developed radiation-associated angiosarcoma 48 months after radiotherapy, with non-specific mammographic and ultrasound features. FDG PET-CT revealed increased FDG uptake in the breast skin and nodular lesions. Pathological examination of the nodules with increased FDG uptake confirmed radiation-induced breast angiosarcoma. The patient underwent a total mastectomy for treatment.

Conclusion: In patients with a history of breast-conserving surgery and radiotherapy, presenting symptoms during follow-up should prompt consideration of radiation-associated angiosarcoma. Early diagnosis is crucial, and FDG PET-CT can be beneficial for local visualization and distant organ metastasis screening.

Keywords: Radiation-associated angiosarcoma, breast-conserving surgery, radiotherapy, FDG PET-CT

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INTRODUCTION

Breast angiosarcoma (AS) is a rare tumor arising from the vascular endothelium, comprising approximately 1% of all soft tissue breast tumors and carrying poor prognosis. It manifests in two distinct types: primary breast angiosarcoma (PBAS) and secondary breast angiosarcoma (SBAS). PBAS typically affects young women without a history of breast cancer or radiotherapy, often originating from the breast parenchyma with occasionally skin involvement presenting as a rapidly growing, usually painless, palpable mass (1,2). In contrast, SBAS occurs in older women, originates from the breast dermis, occasionally involves the parenchyma, displays multifocality, and presents characteristic features such as skin discoloration and swelling (2,3).

SBAS can occur in the ipsilateral extremity with chronic lymphedema outside the radiation field after radical mastectomy and axillary dissection (known as Stewart-Treves syndrome). It can also present as radiation-associated breast angiosarcoma (RABAS), whose frequency is increasing due to the rising prevalence of breast-conserving surgery followed by adjuvant radiotherapy. RABAS develops in the ipsilateral chest wall or breast within the "twilight zone," where radiation is not homogeneously distributed (2,3). The incidence of RABAS ranges between 0.9-1.1 per 1000 cases (4). In the literature, the latent period for AS development post-radiotherapy is reported to range from 3 to 20 years, with an average duration of 6-8 years (4,5).

In the existing literature, there is a dearth of reported cases documenting radiation-associated angiosarcoma of the breast along with imaging findings utilizing Flour-18 fluorodeoxyglucose positron emission tomography (FDG PET-CT) (6). The primary objective of this study is to present a case involving a patient who underwent breast-conserving surgery and received radiotherapy on the same breast for the treatment of breast cancer. Subsequently, during the follow-up period post-treatment, the patient developed radiation-induced secondary AS. Furthermore, our aim encompasses the presentation of the FDG PET-CT imaging findings associated with this particular patient.

CASE

A 55-year-old female patient with no family history of cancer underwent breast-conserving surgery in August 2015 due to left breast cancer. Concurrently, axillary lymph node sampling on the same side was performed. The postoperative pathology report revealed the tumor stage as pT1 pN0. The tumor exhibited positive estrogen receptor (ER) at 90%, positive progesterone receptor (PR) at 40% with a +3 intensity, negative Cerb-2, Ki-67 proliferative index at 20%, and positive E-cadherin, indicating invasive ductal carcinoma.

Following the surgery, the patient received a total radiation dose of 60 Gy over 30 days: 50 Gy to the left breast (2 Gy per day, 5 days a week) and 10 Gy to the tumor bed (2 Gy per day for 5 days in one week). Also hormonal therapy consisting of two years of tamoxifen and three years of letrozole was administered for five years following the radiation therapy. Until August 2019, the patient underwent regular follow-ups, including blood tests, tumor markers, breast ultrasounds, mammograms, and computed tomography (CT) scans, revealing no pathological findings. However, in August 2019, mammography showed non-specific features such as volume reduction in the operated area of the left breast, skin retraction in the outer quadrant, and mild thickening of the breast skin. The same day, ultrasound revealed a slightly heterogeneous area in the outer-middle quadrant of the left breast, corresponding to the operation site, with vertical irregularly bordered hypoechoic nodular lesions measuring 5x4 mm. An incisional biopsy from this area resulted in the diagnosis of AS. Magnetic resonance imaging (MRI) was not conducted; instead, FDG PET-CT imaging was performed in October 2019 for possible metastasis screening. The FDG PET-CT imaging indicated increased FDG uptake in the thickening of the breast skin in the outer-upper segment, along with millimetric nodular soft tissue lesions with elevated FDG uptake (Figure 1). The maximum standard up-take value (SUV max) of the tumor was measured as 3.2.

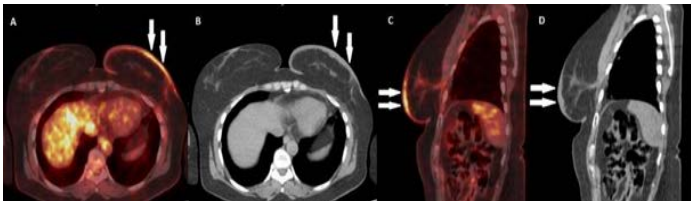

Figure 1. In the axial (A: fusion, B: CT) and sagittal sections (C: fusion, D: CT) of the left breast skin, a thickening indicating FDG uptake is observed in the area indicated by the arrows.

In February 2020, the patient underwent a left breast mastectomy and lymph node sampling on the same side. In

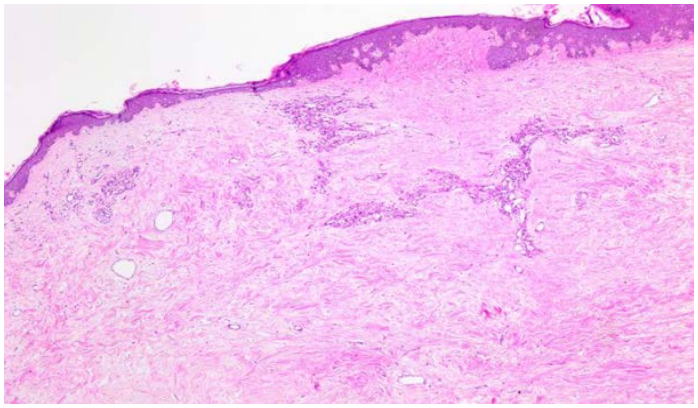

Figure 2. Microscopic appearance of angiosarcoma: A tumoral lesion consisting of irregularly shaped anastomosing vascular channels under the skin, lined with atypical endothelial cells. HE,x50

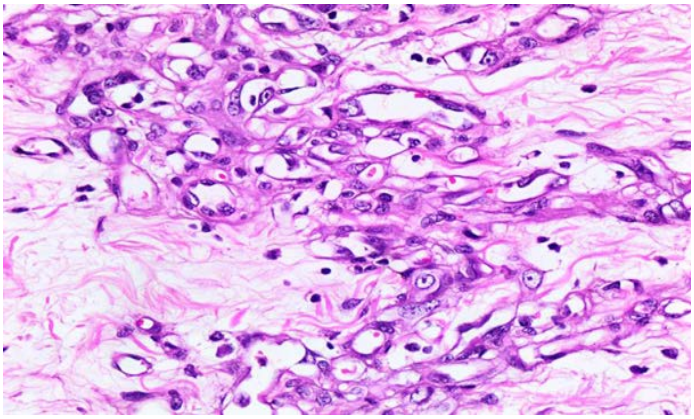

Figure 3. Microscopic appearance of angiosarcoma: Tumor cells are polygonal shaped, plump and pleomorphic cells. HE,x400

the macroscopic examination of the mastectomy material, a 3x3x1.5 cm sized lesion with a white fibrotic appearance in most areas and a dirty yellow calcified appearance in some areas was observed. In addition, the presence of nodules, the largest of which was 5 mm in diameter, in the white fibrotic area under the skin in the old incision area was noted. Microscopic examination of nodular lesions reveald a tumoral lesion consisting of irregularly shaped anastomosing vascular channels under the skin, lined with polygonal shaped, plump, atypical endothelial cells (Figures 2,3). Immunohistochemically, the tumor cells were diffusely strongly positive for CD34, CD31, and FLI-1, focally weakly positive for CD117 and negative for HHV-8, CK7 (Figure 4). Eighteen mitoses were counted in ten highpower fields using PHH3, and the Ki67 proliferation index was 40%. The surgical margins were tumor-negative. In the frozen material of the sentinel lymph node in the left axilla, one reactive lymph node was

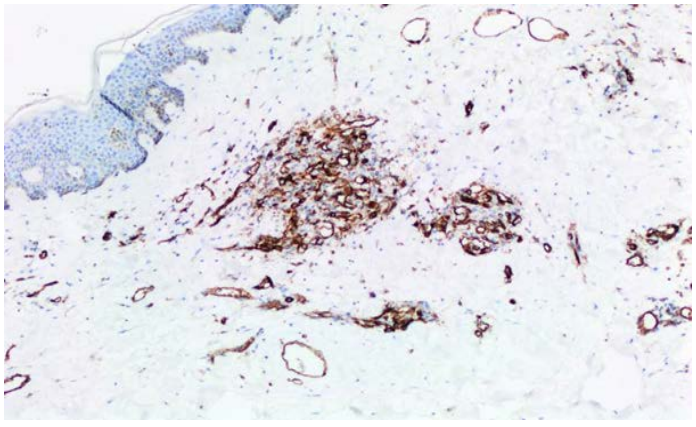

Figure 4. Immunohistochemical CD31 positivity of tumor cells in angiosarcoma. CD31x100

observed and no metastasis was detected. Based on the pathology results, the tumor in the left breast, attributed to the prior radiation therapy, was considered RABAS.

Our patient received six cycles of adjuvant chemotherapy following the surgery.

DISCUSSION

SBAS developing as a result of radiation can manifest in the early period, approximately 3-4 years after radiotherapy, or even emerge in the late period, up to 25 years later (4,5,7). In our case, the onset of the disease after radiotherapy was found to be consistent with the literature, occurring at 48 months. "Despite the 5-year overall survival rate being over 80% in breast cancer, the prognosis of RABAS is notably poor, with a 5-year overall survival rate generally ranging between 20% and 54% (1,7,8). Factors such as tumor size exceeding 5 cm, advanced age of the patient, multiple skin lesions, and high tumor grade have been reported to be associated with a poor prognosis (5,7,9). After a postoperative period of 48 months, no evidence of recurrence or metastasis has been identified in our patient. We attribute the favorable prognosis in our case to the small size of the tumor and the patient's young age. In RABAS, mammography typically shows non-specific findings such as skin retraction, skin thickening, and distortion of breast parenchyma. Despite these findings, approximately one-third of patients may not exhibit any specific symptoms (10,11). In our case, non-specific features were observed, including skin retraction and mild thickening of the breast skin in the outer quadrant. Similarly, ultrasound revealed a slightly heterogeneous area in the outer-middle quadrant of the left breast, corresponding to the operation site, with irregularly bordered hypoechoic nodular lesions measuring 5x4 mm, a pattern frequently reported in the literature (12). Although magnetic resonance imaging (MRI) was not performed in our study, MRI has been shown to be the most sensitive technique for detecting the primary tumor, recurrence, and residual lesions in RABAS (13). FDG PET-CT is commonly used for staging malignant tumors and post-treatment follow-ups. While its routine use for staging early-stage breast cancers is not recommended, FDG PET-CT is recommended in advanced-stage breast cancer and in cases where distant metastasis is suspected (14). Breast AS is not considered a commonly encountered neoplasm; therefore, there is limited research examining the use of FDG PET-CT in the imaging of this tumor (6). In our case, FDG PET-CT imaging revealed heterogeneous FDG uptake in the breast skin and increased FDG uptake in small millimetric nodular lesions on the skin. When a suspicious lesion arises in a previously irradiated area, the most suitable method for diagnosing RABAS is recommended to be the application of a core biopsy or diagnostic excision (13). Treatment decisions should be made promptly. Due to the rarity of the disease, there is no consensus on treatment, and it varies from simple wide excision to radical mastectomy. There is no clear consensus on chemotherapy (9,15).

CONCLUSION

In patients who have undergone breast-conserving surgery and received radiotherapy on the same breast for breast cancer, presenting symptoms such as thickening of the skin, bruising, discoloration, and rash on the same side during follow-up should prompt consideration of RABAS in the differential diagnosis. Early diagnosis is crucial, and for treatment planning, FDG PET-CT imaging can be beneficial for local visualization and screening for distant organ metastasis.

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