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Case Report

Iatrogenic Disease of Success Radiation-Induced Angiosarcoma of the Breast: A Case Report

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Abstract

Radiation induced angiosarcoma of the breast is considered the iatrogenic disease of success for breast conservative surgery. Its diagnosis and management remains a challenge and there is no standardized treatment for this type of malignancy. Herein, we report a case of radiation induced angiosarcoma of the breast in a middle aged female patient.

Keywords: Angiosarcoma; Breast; Iatrogenic disease; Malignancies

Introduction

In the last decade major advancements have been achieved in the treatment of various malignancies, which has led to a major increase in the numbers of patients who are considered long term survivors. These survivors are at risk of developing a set of therapy related complications, of which secondary cancer is a subset known as "iatrogenic disease of success" [1]. Having said this, breast conserving therapy also known as breast conserving surgery has evolved as an alternative to traditional mastectomy for patients with breast cancer, whereby it offers similar oncologic outcome regarding survival and recurrence rate and a cosmetically acceptable treated breast. However, breast conserving therapy should be followed by moderate-dose radiation therapy to eradicate any microscopic residual disease. From here, the "iatrogenic disease of success" of breast conserving therapy or surgery followed by radiotherapy is radiation induced angiosarcoma of the breast. Radiation induced angiosarcoma of the breast is diagnosed based on the presence of three criteria [2]: evidence of an initial malignant tumor of a different histology than the putative radiation-induced sarcoma, development of the sarcoma in an irradiated field, a prolonged latency period (typically >4 years) between the two malignancies. The exact incidence of radiation induced breast angiosarcoma is extremely rare with an incidence of 0.9 per 1,000 breast cancer cases in the past 15 years [3]. Herein, we report a case of a woman with histologically verified radiation induced angiosarcoma of the breast.

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Case Presentation

A 50 year old female patient Gravida 3 Para 3 known to have hypertension controlled by medication , with no family history of breast or ovarian cancer with a previous diagnosis of left breast invasive ductal carcinoma (T2N1M0,ER positive, PR positive, HER-2/neu negative) for which she underwent left breast conserving surgery followed by adjuvant treatment with chemotherapy and radiotherapy to left breast and left axillary, supraclavicular and infraclavicular region with 50 Gray, a total of 25 sessions, 6 years prior to presenting to our breast care center for management of radiation induced angiosarcoma of the left breast. At 6 year follow-up, she reported noticing skin retraction and purple discoloration over the left breast, for which she was investigated by mammography showing thickening of the skin, with no obvious breast parenchymal lesion. Incisional biopsy of the left breast skin thickening showed poorly differentiated angiosarcoma. Following these results, PET scan was done and it was negative for metastatic disease. Consequently, patient was referred to our center for surgical management of radiation induced angiosarcoma of the left breast. Radical mastectomy was done, with the widest possible margins permitting primary closure. Final pathology turned out to be radiation induced angiosarcoma of the breast.

Microscopically sections of skin and subcutaneous tissue show a poorly demarcated neoplastic proliferation made up of papillary and tubulo-papillary structures as well as sheets of anaplastic cells (Figures 1 and 2). The neoplastic cells are large round to polygonal, with a large round to oval vesicular nucleus having one or two prominent nucleoli and a moderately abundant acidophilic cytoplasm with indistinct cell borders. Frequent mitotic figures and apoptotic bodies are identified. Immunohistochemistry showed strong diffuse positivity for vimentin, CD34, C31 consistent with angiosarcoma (Figures 3-5). Furthermore, epithelial, mealnocytic and neural markers were negative (S100, HMB45, cytokeratin cocktail).

Patient opted against adjuvant therapy. At 6 month of follow-up patient is disease free on clinical and radiological examination.

Discussion

Breast sarcomas are rare; histologically they are heterogeneous non-epithelial malignancies that arise from the connective tissue

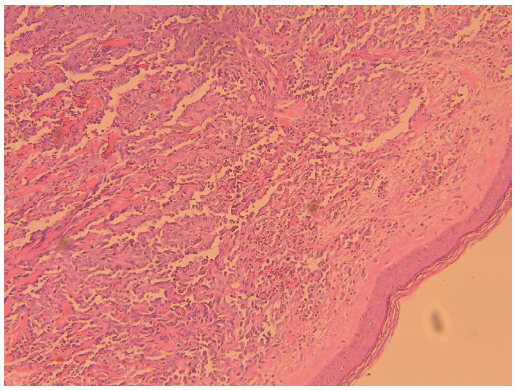

Figure 1: Low power view of poorly demarcated neoplastic proliferation, with intact overlying epidermis.

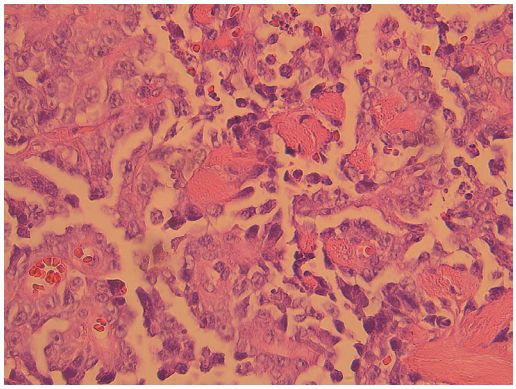

Figure 2: At higher magnification; sheets of neoplastic cells forming papillary and tubulo-papillary slit like spaces.

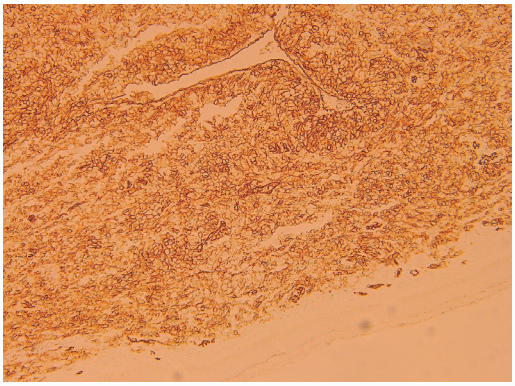

Figure 3: CD34; strong diffuse positivity.

within the breast [4]. Even rarer is angiosarcoma of the breast, first described by Schmidt in 1887 [5], it is a malignant tumor with a vascular endothelial origin, divided into primary angiosarcoma of the breast if it arises without a known precursor and secondary angiosarcoma of the breast, if it occurs at the site of previously irradiated skin, in this case it is known as a radiation induced angiosarcoma of the breast. Radiation induced angiosarcoma of the breast is diagnosed based on the presence of three criteria [6]: evidence of an initial malignant tumor of a different histology than the putative radiation-induced sarcoma, development of the sarcoma in an irradiated field, and a prolonged latency period (typically >4 years) between the two malignancies.

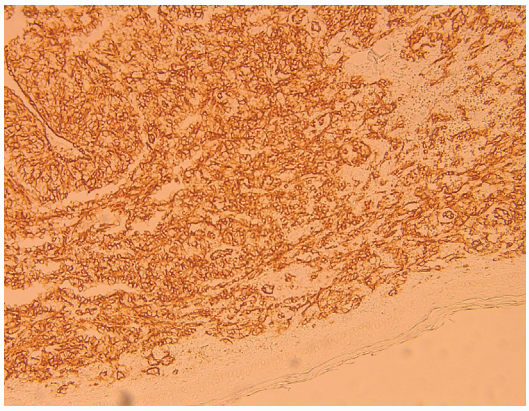

Figure 4: CD31; strong diffuse positivity.

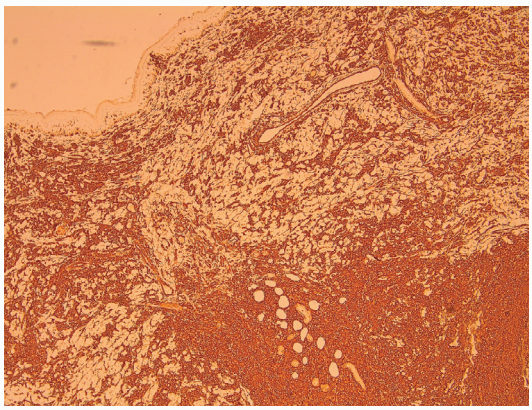

Figure 5: Vimentin; diffuse positivity.

The improvement in screening and detection of breast cancer in parallel with advancement in the adjuvant therapy has led to an increase in the numbers of breast cancer survivors. Add to this, the emergence of breast conserving therapy with radiotherapy as an alternative to the traditional mastectomy with its similar outcome regarding the oncologic result and better cosmetic result for the treated breast also increased the numbers of breast cancer survivor who will live long enough to develop late effects of treatment, which include secondary malignancies such as radiation induced angiosarcoma.

Radiation induced angiosarcoma of the breast is a rare entity accounting for approximately about 3% of all soft-tissue sarcomas [7] and <1% of breast tumors [8]. It develops in approximately 1% of patients who have been treated with breast conserving therapy for primary breast cancer [9]. It has a high recurrence rate and poor outcomes. The diagnosis of radiation induced angiosarcoma of the breast is usually delayed. This delay in diagnosis is attributed to its benign looking appearance and difficulty in differentiating it from the nonspecific skin changes induced by prior radiotherapy. In fact, radiation induced angiosarcoma of the breast often present as multiple, distinct lesions. Thus, a thorough clinical examination is important in order not to overlook satellite lesions. It can have different colors, but are mostly described as purple, blue, or black. Furthermore, the radiologic findings are also nonspecific which further delay the diagnosis. Imaging findings include the development of progressive skin or trabecular thickening in an area of the breast that is separate from the patient's original breast cancer, and enhancing cutaneous nodules. Mammography may show increased skin thickening,

typically without an overt mass. Radiation induced angiosarcoma typically develops 10 years after radiation; however the latency period can range from 6 months to 20 years. From here, some believe that its true incidence is being under reported.

Treatment of radiation induced angiosarcoma remains a challenge, with no universal guidelines regarding the optimal approach. Surgical resection with negative margins remains the cornerstone for a successful outcome. Although an excision margin of at least 10 mm is considered acceptable, there is no evidence to support this and the optimal resection is performed by appropriately trained surgeons with the aim to achieve the widest possible margins [10].

Furthermore, the role of adjuvant chemotherapy and radiotherapy remain unclear. In fact, there are no trials specifically addressing the benefit of adjuvant chemotherapy for breast sarcomas, including radiation induced angiosarcoma. Furthermore, results from retrospective series are contradictory, hence it is difficult to obtain a solid base stating that adjuvant chemotherapy is definitely beneficial.

In addition, radiation induced angiosarcoma of the breast have a particularly high rate of local recurrence and distant metastasis, including sites such as the lung, liver, bone marrow, and brain. In fact, Torres et al in their report of 95 cases of radiation induced angiosarcoma of the breast, after a median follow-up of 10.8 years, local recurrences developed in 48 percent of patients, while distant metastases occurred in 27 percent [8]. Having said this, the median overall survival is less than 6 years [11].

In summary, due its rarity management of radiation induced angiosarcoma of the breast is a challenge to the unaware. To date, early detection and radical surgical treatment is the only potentially curative option. Hence the importance of increased awareness and knowledge regarding the presenting symptoms and maintaining a low threshold to further investigate patients complaints post radiotherapy to the breast.

Conclusion

The iatrogenic disease of success of breast conserving surgery along with radiotherapy is radiation induced angiosarcoma of the breast. Radical surgery remain the cornerstone for a successful outcome, however, with an incidence of 0.9 per 1000 patients with breast carcinoma over 15 years, most breast surgeons may encounter only one case in their career. And hence, the surgical approach for radiation induced angiosarcoma remains a challenge.

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