Breast angiosarcoma: A case report

Ayadi Mouna, Berrazaga Yosra, Adouni Olfa, Meddeb Khadija, Gamoudi Amor, Mezlini Amel

ABSTRACT

Introduction: Breast angiosarcomas are rare but aggressive malignant endothelial cell tumors. There are two entities: primary angiosarcoma and secondary angiosarcoma to breast irradiation. This neoplasia is characterized by absence of typical features at radiological examination.

Case Report: We report a case of a 40-year-old female with a history of invasive ductal breast carcinoma presented with a bilateral breast angiosarcoma. The main treatment is a large surgery with free tumor margins. The role of adjuvant chemotherapy and radiotherapy is still a subject of debate. For inoperable and metastatic disease, chemotherapy is the pillar of treatment.

Conclusion: The prognosis of breast angiosarcoma is still poor. Many prospective trials are needed to establish more clear therapeutic strategies.
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Introduction: Breast angiosarcomas are rare but aggressive malignant endothelial cell tumors. There are two entities: primary angiosarcoma and secondary angiosarcoma to breast irradiation. This neoplasia is characterized by absence of typical features at radiological examination. Case Report: We report a case of a 40-year-old female with a history of invasive ductal breast carcinoma presented with a bilateral breast angiosarcoma. The main treatment is a large surgery with free tumor margins. The role of adjuvant chemotherapy and radiotherapy is still a subject of debate. For inoperable and metastatic disease, chemotherapy is the pillar of treatment. Conclusion: The prognosis of breast angiosarcoma is still poor. Many prospective trials are needed to establish more clear therapeutic strategies.

Keywords: Breast angiosarcoma, Chemotherapy, Post-irradiation, Radiotherapy, Surgery

INTRODUCTION

Angiosarcomas are rare and aggressive blood vessel tumors with high recurrence rates and poor overall survival. Due to the increasing use of radiation therapy in breast cancer, secondary neoplasia is induced. The most common secondary neoplasia of the breast is angiosarcoma. It occurs 4–7 years after radiation therapy. A primary neoplasia can also be observed but less commonly. No evidence-based guidelines exist concerning the ideal treatment of angiosarcoma. Radical surgical resection of the tumor with a sufficient margin of safety is the treatment of choice for angiosarcoma.

CASE REPORT

On September 2007, a 40-year-old woman underwent breast-conservative surgery and axillary dissection for invasive ductal carcinoma of the right breast. Immunohistochemical analysis revealed estrogen and progesterone receptor positivity. The tumor was classified as pT2 pN0 M0 SBR 3 according to the UICC–TNM classification. She received four cycles of adjuvant chemotherapy (adriamycin 60 mg/m² and cyclophosphamide 600 mg/m² every 21 days). She had radiotherapy as follows: 50 Gy for the right...
breast and chest wall in 25 fractions of 2 Gy/daily with boost of 14 Gy in 7 fractions of 2 Gy/daily. She received adjuvant hormone therapy (tamoxifen 20 mg daily for five years). The patient did not suffer from chronic lymphedema.

On January 2016, we observed a painful, bluish and nodular mass occupying the interne quadrants of the right breast. On examination the size of lesion was 4 cm. An excisional biopsy was performed. Histopathological examination revealed a vascular tumor proliferation. Tumor cells were positive for CD34, CD31, factor VIII and negative for EMA, CK, CD68, ER and PR, indicating an endothelial origin. More than 50% of the cells in the solid component were positive for Ki67. The diagnosis of cutaneous grade-II angiosarcoma of the breast was made. It was probably a radiation-induced angiosarcoma.

No metastases were found at total body computed tomography scan. A right mastectomy was performed. Histopathological examination revealed a grade-II angiosarcoma measuring 4 cm of long axis that ulcerated the skin and dissociated the breast parenchyma. In addition to that, a low grade angiosarcoma measuring 7 mm was identified as a skin lesion. Margins of resection were tumor-free. Adjuvant chemotherapy and radiotherapy were not prescribed.

On October 2016, cutaneous angiosarcoma recurred on the inner end of the right mastectomy’s scar as a 1 cm nodular mass. An excisional biopsy was performed confirming the recurrence.

A body computed tomography scan showed three left axillary lymphadenopathies. Mammography and ultrasound mammary of the left breast did not show any lesion except axillary lymphadenopathies. Left breast magnetic resonance imaging scan showed in addition to lymphadenopathies, a 10 mm nodular lesion isointense on T1 images and hypo-intense on T2 with intense and early contrast enhancement. This lesion was located in the left upper outer breast’s quadrant. The tumor was classified as T1 N1 M0. An excisional biopsy of the left axillary lymphadenopathy was performed. Histopathological examination revealed an axillary localization of an angiosarcoma.

A left mastectomy and axillary node lymph dissection were performed. Histopathological examination revealed a grade-II angiosarcoma measuring 5 cm. The tumor proliferation invaded the dermis and hypodermis and reached the muscular layer. Margins of resection were tumor-free. Five nodes were metastatic from nine. Four nodes had a capsular rupture. Macroscopic and microscopic aspects of tumor are shown in Figure 1 and Figure 2.

The patient received three cycles of adriamycin and ifosfamide with appearance of liver metastases and deterioration of general condition. The patient passed away on March 2017.
Angiosarcomas are highly aggressive and malignant tumors which arise from endothelial cells lining vascular channels. They usually develop on the head and neck [1]. Breast angiosarcomas are exceedingly rare accounting for less than 1% of malignant breast tumors [2]. Breast angiosarcoma can be either observed as primary tumors or, more commonly, secondary to irradiation for breast carcinoma [2].

In 1929, radiation induced angiosarcoma was first reported in literature [3]. It represents 0.04% of all breast tumors.

The diagnostic criteria for radio-induced angiosarcoma include a previous history of radiotherapy, peak incidence between 5 and 10 years, development of sarcoma within a previous irradiated field and histology confirmation [4]. It is characterized by an aggressive nature. The prognosis is poor and local recurrence rates reach 70% after mastectomy [4].

In a series of 55 cases of breast angiosarcoma, 42% of patients were irradiated. These patients were on average 30-year-old and less likely to present with distant metastatic disease than patients presenting with primary breast angiosarcoma. Radiation-naïve angiosarcoma mainly occurs in 3–4th decade [5].

Twenty-one percent of Bilateral cases are reported. It may be either really primitive bilateral forms or early contralateral metastases [6]. In this report, the patient presented a bilateral breast angiosarcoma. The right breast angiosarcoma is probably secondary to radiation of right breast. The left breast angiosarcoma can be either a metastasis of the right one or secondary to radiation of the chest wall with no protection of left breast.

Clinically, the lesion presents as a rapidly growing, painless breast mass within a previous irradiated field. The overlying skin may be blue or purple [7, 8].

LYMPH NODE INVOLVEMENT

Lymph node involvement is rare. However, the risk increases in locally advanced tumor [9].

The mammography does not suggest a tumor and this is typical of angiosarcoma [8] due to its superficial localization. Ultrasound mammography’s findings include ovoid shape, hyperechoic or heterogeneously echoic solid masses associated with architectural distortion. The vascular nature of angiosarcoma can account for the hyperechogenicity feature. Hyperechogenicity is remarkable since most of the breast carcinomas are very rarely hyperechoic [10].

Advanced imaging modalities like MRI scan can bring a profit [11]. Pathologists should keep this diagnosis in mind when dealing with a breast skin lesion in a patient with a previous history of breast cancer and radiation therapy. Microscopically, angiosarcoma composed of vascular channels lined by proliferated endothelial cells with atypical and hyperchromatic nucleus.

Immunohistochemical stains for epithelial markers (pancytokeratin), endothelial markers (CD34 and CD31) and other sarcoma markers should help in making the correct diagnosis [12].

The SEER database revealed that the histologic grade is a significant predictor of survival for patients with localized primary breast angiosarcoma (a study about 226 patients) [13]. However, another study interesting 49 cases of primary angiosarcoma suggested that histologic grade is not prognostic [14].

Due to the rarity of the disease, prospective studies concerning adjuvant, neoadjuvant or palliative therapy are limited and no evidence-based guidelines exist. The response to chemotherapy seems to be poor.

The main treatment of breast angiosarcoma is early and complete surgical excision of the mass with tumor-free margins. Although R0 resection is performed, the five-year survival rates are 20–30%.

Unless there are palpable nodes, lymph node dissection is useless [15].

Adjuvant chemotherapy that includes doxorubicin for patients with poorly differentiated breast angiosarcoma results in a higher proportion of patients who are relapse-free compared to patients not receiving adjuvant chemotherapy [16].

For locally advanced inoperable or metastatic disease, chemotherapy is the pillar of treatment [17].

The response rate to doxorubicin, the standard frontline chemotherapy for advanced sarcoma as a single agent or in combination, is reported to the range between 40% and 65% [18]. Taxanes can be active, both as single agents and in combination with gemcitabine or with anthracyclines, with response rates between 20% and 65% [19].

Tolerability of gemcitabine plus docetaxel is acceptable, with less cardiac toxicity compared with anthracyclines but still carrying a significant incidence of neutropenia and thrombocytopenia [20].

The MD Anderson Cancer Center study of 69 patients with breast angiosarcoma found that the response rate to anthracycline-ifosfamide or gemcitabine-taxane combination in the metastatic setting (29 patients) was 48% [21]. Anthracyclines alone or with ifosfamide has led to disease control after several months (between 7 and 24 months) [22]. A control of the disease for five months was observed with weekly paclitaxel as a single agent in the initial treatment of unresectable, radio induced angiosarcoma [23].

Radiotherapy is reserved after lumpectomy, and following total mastectomy if the tumor is larger than 5 cm, the margins are positive, or if the skin or regional nodes are affected [24]. Of all breast cancers, angiosarcoma has the poorest prognosis. The median overall survival is 24 months [25].

CONCLUSION

Breast angiosarcoma is a rare entity characterized by poor prognosis despite optimal surgery and systemic
therapy. Many therapeutic strategies are needed to be explored to improve the outcomes.

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Author Contributions
Ayadi Mouna – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Adouni Olfa – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published
Meddeb Khadja – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published
Gamoudi Amor – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Mezlini Amel – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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