ISSN 2689-8268 | Volume 8

American Journal of Surgery and Clinical Case Reports

Review Article Open Access

Radiation-Induced Breast Angiosarcoma Following Breast- Conserving Therapy. Report of Two Cases

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Received: 08 Jan 2025
Accepted: 06 Feb 2025
Published: 12 Feb 2025
J Short Name: AJSCCR

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Citation:

G Bassir. Radiation-Induced Breast Angiosarcoma Following Breast- Conserving Therapy. Report of Two Cases. Ame J Surg Clin Case Rep. 2025; 8(4): 1-4

1. Resume

Adjuvant radiotherapy plays an essential role in the prevention of locoregional recurrences of breast cancer and its efficacy has been demonstrated in several randomized trials. Radiation-induced angiosarcoma, an exceptional complication of radiotherapy, characterized by its malignancy and its polymorphic clinical and radiological presentation, has a very poor prognosis. We report two cases of radiation-induced mammary angiosarcoma in two patients with a history of breast cancer treated by conservative surgery and radiotherapy.After having presented our two observations, we will discuss through this observation, the epidemiological, diagnostic and therapeutic aspects of this type of rare aggressive tumors.

2. Abstract

Adjuvant radiotherapy plays an essential role in the prevention of locoregional recurrences of breast cancer and its effectiveness has been demonstrated in several randomized trials. Radiation-induced angiosarcomais an exceptional complication of radiotherapy, characterized by its malignancy and by its polymorphic clinical and radiological presentation, it has a very poor prognosis. We report two cases of radiation-induced breast angiosarcoma in two patients with a history of cancer breast treated with conservative surgery and radiotherapy. After having exposed our two observations, we will discuss through this observation, the epidemiological, diagnostic and therapeutic aspects of this type of rare aggressive tumors.

3. Introduction

Mammary angiosarcoma (MA) is a rare malignant mesenchymal tumor that develops at the expense of mammary vascular tissue. It represents 0.004 to 1% of all malignant breast tumors [1], and 8 to 10% of mammary sarcomas [2]. They generally affect the skin, rarely the chest wall or the mammary parenchyma [3]. Its definitive diagnosis is purely histological. Authors have reported cases of radiation-induced mammary angiosarcoma (MA)in patients who have had conservative treatment for breast cancer. Although only about a hundred cases have been reported to date, the incidence of these tumors is likely to increase, given the growing number of patients who are candidates for conservative radio- surgical treatment of breast cancer. We report twonew cases.

3.1.Observation

This is a 68-year-old patient. Her history was marked by an infiltrating ductal carcinoma for which she underwent conservative surgery in 2015 (lumpectomy and axillary lymph node dissection) associated with radiotherapy (50 Gy on the mammary gland with an overprint of 10 Gy at the tumor bed). Anti-estrogen hormone therapy was prescribed for aperiod of five years due to the positivity of the hormone receptors. The patient was followed up regularly. Six years after the radio-surgical treatment, a mastectomy was performed with angiosarcoma grade II. The patient consulted 1 year after the appearance of a macular lesion along the mastectomy scar.Clinical examination revealed purplish macules throughout the mastectomy scar.

3.2. Observation

This is a 54-year-old patient, type 2 diabetic under ADO. At 43, she presented with an infiltrating ductal carcinoma of the left breast (T1N1M0) for which she had conservative surgical treatment (lumpectomy and axillary lymph node dissection) associated with radiotherapy (50 Gy on the mammary gland with an overprint of 10 Gy at the tumor bed). The patient was followed up regularly. 11 years after the initial treatment, the patient consulted for the appearance of a permeation nodule on the lumpectomy scar (QII

of the left breast).On initial clinical examination: 2cm permeation nodule opposite the left QII tumorectomy scar without palpable nodule on an enlarged breast, free axillary areas.On ultrasound-mammography, it is a post-therapeutic QII alteration of the left breast and a 7x3mm right intramammary lymph node classified as Briards 3 bilaterally.A biopsy of the permeation nodule was performed and histological analysis revealed the presence of a high-grade sarcoma, initially suggesting a high-grade leiomyosarcoma. grade, a rereading came back in favor of a post-radiation angiosarcoma The extension assessment, including in particular a thoraco-abdominopelvic CT scan, found micronodules in the 2 lung fields of secondary origin. The patient received 5 courses of chemotherapy; the follow-up clinical examination found an indurated breast with ulcerated lesion (Figure 2), with a large retro-nipple mass on the echo-mammogram, heterogeneous hypoechoic, with a hyperechoic center of 6 x 4.6 x 4.4 cm (Figure 3). A left mastectomy was performed and the histopathological analysis: post-radiation angiosarcoma grade II.

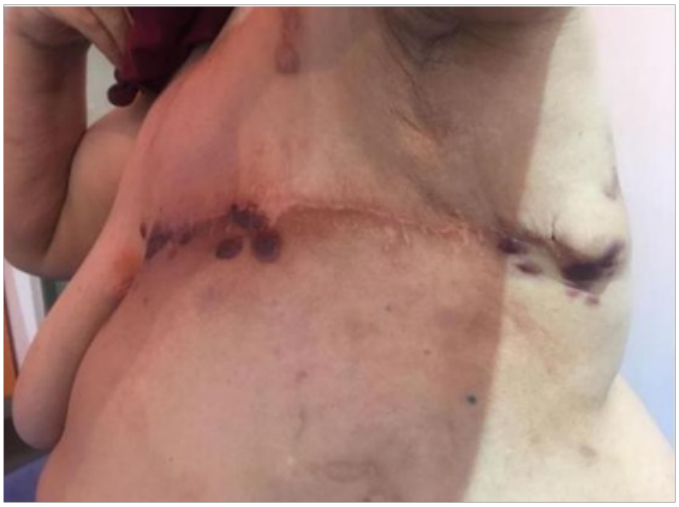

Figure 1: The patient was re-examined with excision of the entire mastectomy scar, which was diagnosed at the anapathology as grade II breast angiosarcoma.

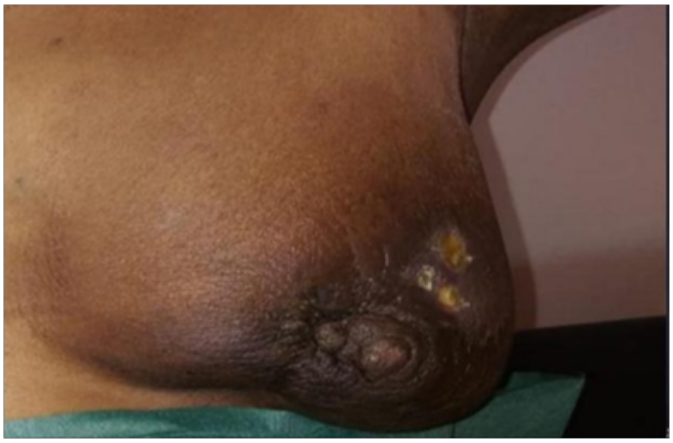

Figure 2: The patient received 5 courses of chemotherapy; the follow-up clinical examination found an indurated breast with ulcerated lesion.

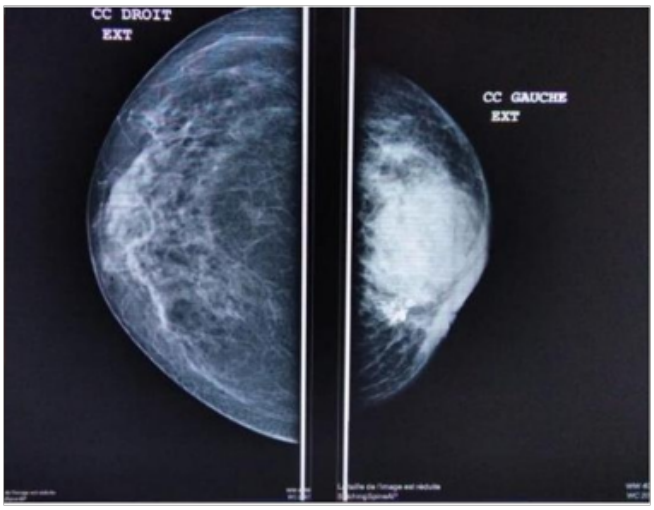

Figure 3: A left mastectomy was performed and the histopathological analysis: post-radiation angiosarcoma grade II.

4. Discussion

Breast angiosarcoma is a rare pathology, classified into 2 types: secondary angiosarcomas (80%) affecting patients who have already received radiotherapy, and primary angiosarcomas (PSA) (20%) (4) mainly affecting young women between 20 and 40 years old with no history. However, all age groups are affected, from 13 to 85 years old [1].The first case of secondary ASM after conservative radiosurgical treatment of breast cancer was reported in 1987 by Body et al.[5]. Much data comes from cohorts of patients treated with irradiation for breast cancer. Taghian et al. studied a series of 7,620 patients treated at the Gustave Roussy Institute between 1954 and 1983, 70% of whom had undergone radiotherapy. They reported a cumulative incidence rate of 0.2% at 10 years, 0.43% at 20 years, and 0.78% at 30 years. These data were taken up by Rubino et al. who established by means of a case-control study on 14 radio-induced sarcomas that the risk of sarcoma was 30 times greater for doses of more than 44 Gy than for doses of less than 15 Gy [8,9]. Proposed fourcriteria for the diagnosis of radiation-induced sarcomas [6]: a history of radiotherapy; a clinical latency of several years (more than five years); the occurrence of the sarcoma in the irradiated field; histological confirmation of the sarcomatous nature of the post- radiation lesion. Our two observations met these diagnostic criteria.ASM is discovered in the majority of cases, following a nodule with a vascular, pulsatile character, black/purplish in color, voluminous with a size often between 2 and 11 cm [7], which increases rapidly in size, this is the case for both observations (Figure 1 and 2).Two clinical signs are pathognomonic of breast angiosarcoma: the purplish appearanceof the skin next to the tumor and the pulsatile nature of the mass [8]. Axillary adenopathies are exceptional, they only concern very advanced forms [9]. The diagnosis of ASM is essentially based on the histological analysis of biopsies taken at the level of a suspicious lesion [10].The mammographic appearance is not very specific and can even be misleading, simulating a benign lesion. On ultrasound,

the mass is of heterogeneous echostructure associating both hyper and hypoechoic areas, with low attenuation of the ultrasound beam. The contribution of color Doppler is more interesting in showing the vascular nature of the tumor, the contribution of CT is important, it shows a mass that enhances very significantly after injection of the contrast product and a partial homogenization for the late times. On magnetic resonance imaging (MRI), angiosarcoma presents as a mass with a hyposignal in T1 and a hypersignal in T2 with tabular areas in the periphery presenting a more intense hypersignal in T2, suggesting the presence of blood vessels [11,12]. The definitive diagnosis is histological. However, it is faced with diagnostic difficulties, especially on biopsies. It must be carried out on the entire tumor.Macroscopically, the tumor has a size that varies between 1 and 20 cm (average 5 cm). It is poorly defined, spongy in appearance when cut and hemorrhagic. Histologically, the tumor proliferation infiltrates the lobular stroma and surrounding tissues. It is composed of irregular anastomotic vascular cavities, lined by one or more layers of endothelial cells. Mammary angiosarcomas are graded. The system proposed by Donnell et al. has proven its prognostic impact [9]. Three grades (I, II, III) are distinguished according to nuclearatypia, mitotic activity and the proportion of solid aggregates of spindle cells, ranging from the well-differentiated form to the poorly differentiated form [1,14]. The classical treatment of radiation-induced sarcomas is surgery. Robinson et al. [15] wrote that "radical surgery is the only chance of cure" [15]. Given the extreme rarity of axillary invasion, axillary dissection is useless unless there are palpable lymph nodes [1-16]. A simple lumpectomy can be proposed for small tumors less than 3 cm, with a wide safety collar greater than 1 cm. This lumpectomy must be supplemented by aexternal radiotherapy in the manner of conservative treatment for carcinomas. Postoperative radiotherapy recommended by some authors does not seem to prevent local recurrences for others [14,17]. Adjuvant chemotherapy in angiosarcomas has been disappointing. Chemotherapy seems to provide a gain in survival and a reduction in local recurrences and metastases. On the other hand, for hormone therapy, no study has justified its use in treatment.A new therapy may be offered by trials of biological treatments using anti-growth factor antibodies, notably anti-vascular endothelial growth factor (VEGF) and anti-fibroblast growth factor (FGF) [9,18].The prognosis of these tumors remains unfavorable because for the majority of them, the diagnosis is made at a late stage [19], the overall five-year survival rate is around 30% [7,11]. Tumor size at the time of diagnosis is the major prognostic factor, hence the importance of early diagnosis of this tumor [7,20]

5. Conclusion

Radiation-induced sarcomas represent a rare but serious complication of radiotherapy in the context of breast cancer. This tumor has a poor prognosis and its diagnosis must be considered in the event of any change in skin color in a patient with a history of radiotherapy. A positive diagnosis is based on histological analysis of biopsies taken from the lesion in question. Their treatment is primarily surgical and justifies long-term monitoring of irradiated patients in orderto allow early diagnosis and complete excision.

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