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Case report

Myofibroblastic sarcoma of the breast. Report of a case induced by radiotherapys

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ABSTRACT

Myofibroblastic sarcoma (MFS) is an uncommon tumor rarely located in the breast. Ionizing radiation is a carcinogen capable of inducing sarcomas through DNA damage. A 42-year-old woman was diagnosed with synchronous bilateral breast infiltrating ductal carcinoma with axillary lymph node metastases on the left side. After modified left radical mastectomy and simple right mastectomy, she underwent postoperative radiation with a total volume dose of 50 Gy that included the thoracic wall and the left axillary-supraclavicular region. After a latency period of 6 years and 4 months, the patient developed an MFS in the area of radiation (mammary upper outer quadrant). To our knowledge, only 11 cases of MFS have been previously published in the breast. The study of the 12 cases including the present one revealed that the ages of the patients ranged from 42 to 86 years (mean 60.3 years). There was a clear difference concerning sex (M:F, 1:5). The average duration of the lesion varied from 1 week to 8 months (mean 3.3 months). The size ranged from 2.2 to 22 cm (average 5.1 cm). The tumors showed frequent mitosis and areas of necrosis. The percentage of recurrences, metastasis, and death due to the tumor was 27.3%, 36.4%, and 27.3% respectively. MFS cases differ from those affecting extra-mammary regions. They are more common in females and show a greater degree of aggressiveness. Correct diagnosis of mammary MFS requires morphological and immunohistochemical study. We present for the first time a case of MFS of the breast induced by radiotherapy.

1. Introduction

Myofibroblastic sarcoma (MFS) is an uncommon malignant tumor composed mainly or entirely of cells having myofibroblastic features. The myofibroblastic phenotype can be immunohistochemically or ultrastructurally documented. Mentzel et al in 1988 defined this entity in a series of 18 cases (1). Later on, it was accepted and included as a distinctive neoplasm by the World Health Organization (WHO) Classification of Bone and Soft tissue tumors in 2002 [2]. Myofibrosarcoma is a synonym for this tumor.

The neoplasm occurs predominantly in adults with a preferred location in the head and neck region, including oral cavity and tongue, extremities, and trunk. It presents a slight male predominance. The lesion more commonly arises in the subcutaneous and deeper soft tissue [1,3]. The neoplasm shows a low percentage of recurrences and metastases [1,3].

The tumor rarely occurs in the breast. In fact, only 11 patients with MFS of the breast have been previously reported in the literature [4–13]. On the other hand, only one case of radiotherapy-induced MFS has been published to date. This case arose in the larynx [14].

In this report, we present for the first time a rare case of MFS of the breast induced by radiotherapy.

2. Case presentation

A 42-year-old woman presented in May 2012 with a palpable non-tender mass of about 3.5 cm in the upper outer quadrant (UOQ) of the left breast. Mammograms showed microcalcifications in the UOQ of the left breast and the upper inner quadrant (UIQ) of the right breast. An echography of the left breast revealed a hypogenic area of poorly defined limits and several enlarged axillary lymph nodes. The core biopsies showed an infiltrating ductal carcinoma not otherwise specified associated with intraductal carcinoma and axillary lymph node metastases. The tumor showed positivity for the estrogenic receptor (ER)

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and the progesterone receptor (PR). Staining for Ki67 was positive in 20% of the neoplastic cells. The HercepTest for the detection of HER2 protein overexpression was negative. The echography and core biopsies of the right breast revealed a fibroadenoma and an infiltrating ductal carcinoma not otherwise specified associated with intraductal carcinoma. This tumor was ER+, PR+, Ki67+ in 15% of cells, and HercepTest negative. Right axillary lymph nodes were tumor-free. The study of systemic tumor extension was negative and the patient received adjuvant chemotherapy (docetaxel, doxorubicin, and cyclophosphamide in 5 cycles) which ended on October 3, 2012. On November 9, 2012, a modified left radical mastectomy and simple right mastectomy were performed with sentinel lymph node removal. The tumor staging was as follows: left breast, ypT2ypN2M0; right breast, ypTisypN0M0.

A treatment in system D was planned and a dose of 50 Gy in the volume that included the thoracic wall, the left axilla, and supraclavicular region was administered in a linear accelerator with 6 MV photons, at 2 Gy/day. The treatment ended on February 14, 2013, with good tolerance presenting as acute toxicity grade 2 epidermitis. The patient had bilateral mammary implants in 2018 and treatment with tamoxifen until January 2019.

In May 2019, she noticed a hard nodule palpable in the UOQ of the left breast of approximately 3 cm. The ultrasound showed an oval, hypoechogenic nodule, with a well-defined contour of 16 x 6.5 mm (Fig. 1A). The lesion bulged the adjacent implant. The magnetic resonance imaging performed with contrast revealed a partially well-defined, heterogeneous, oval nodule of 25 x 17 mm that bulged the prosthetic capsule (Fig. 1B–D). On June 26, 2019, under general anesthesia, the breast lesion, including the adjacent prosthetic capsule, was completely removed. The surgical specimen was sent to the pathology department.

Table 1
Antibodies used in this study.

Antibody	Source	Clone	Dilution	Retrieval solution pH (Dako)
Cytokeratin 7	Dako	OV-TL12/30	FLEX RTU	High
Cytokeratin 19	Dako	RCK108	FLEX RTU	High
Pancytokeratin	Dako	AE1/AE3	FLEX RTU	High
S100 protein	Dako	Polyclonal	FLEX RTU	High
Epithelial membrane antigen	Dako	E29	FLEX RTU	High
P63	Dako	DAK-p63	FLEX RTU	High
CD99	Dako	12E7	FLEX RTU	High
CD57	Dako	TB01	FLEX RTU	High
Fibronectin	BioSite systems LTD	Polyclonal	1:200	High
Smooth-muscle actin	Dako	IA4	FLEX RTU	High
Muscle-specific actin	Dako	HHF35	FLEX RTU	High
h-Caldesmon	Dako	h-CD	FLEX RTU	High
Desmin	Dako	D33	FLEX RTU	High
Calponin	Dako	CALP	1:200	High
Myo-D1	Dako	5.8A	1:50	High
CD34	Dako	QBEND10	FLEX RTU	High
CD68	Dako	KP1	FLEX RTU	Low
Ki67	Dako	MIB-1	FLEX RTU	Low

3. Pathological findings

The surgical specimen identified as lumpectomy of the left breast included skin, hypodermis, fascia, and superficial muscular plane. The sample was marked with staples to facilitate spatial orientation. The specimen weighed 30 g. and measured 5.5 × 4 x 2 cm. Serial cuts showed a hard, solid, well-defined, grayish-white, ovoid nodule of

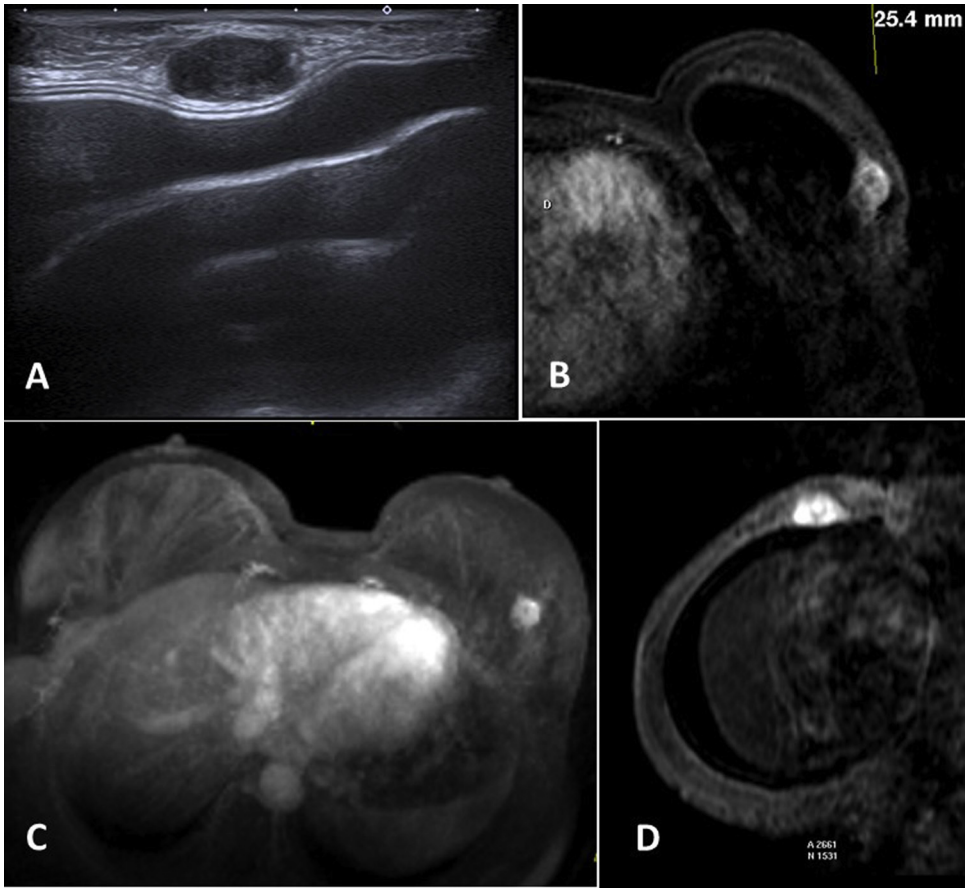

Fig. 1. Imagistic study of the left breast. (A) Echography: hypoechogenic nodule of well-defined, oval morphology, 16 x 6.5 mm in size, which contacts the prosthetic capsule to which it bulges (BIRADS 4A). Magnetic resonance imaging: (B) Axial section, dynamic sequence. Nodule with peripheral contrast enhancement. Maximum diameter of 25.4 mm. (C) Maximum intensity projection image. (D) Sagittal reconstruction of the dynamic sequence. Well-defined nodule, with intense contrast enhancement, that contacts the capsule of the prosthesis, which it bulges without infiltrating.

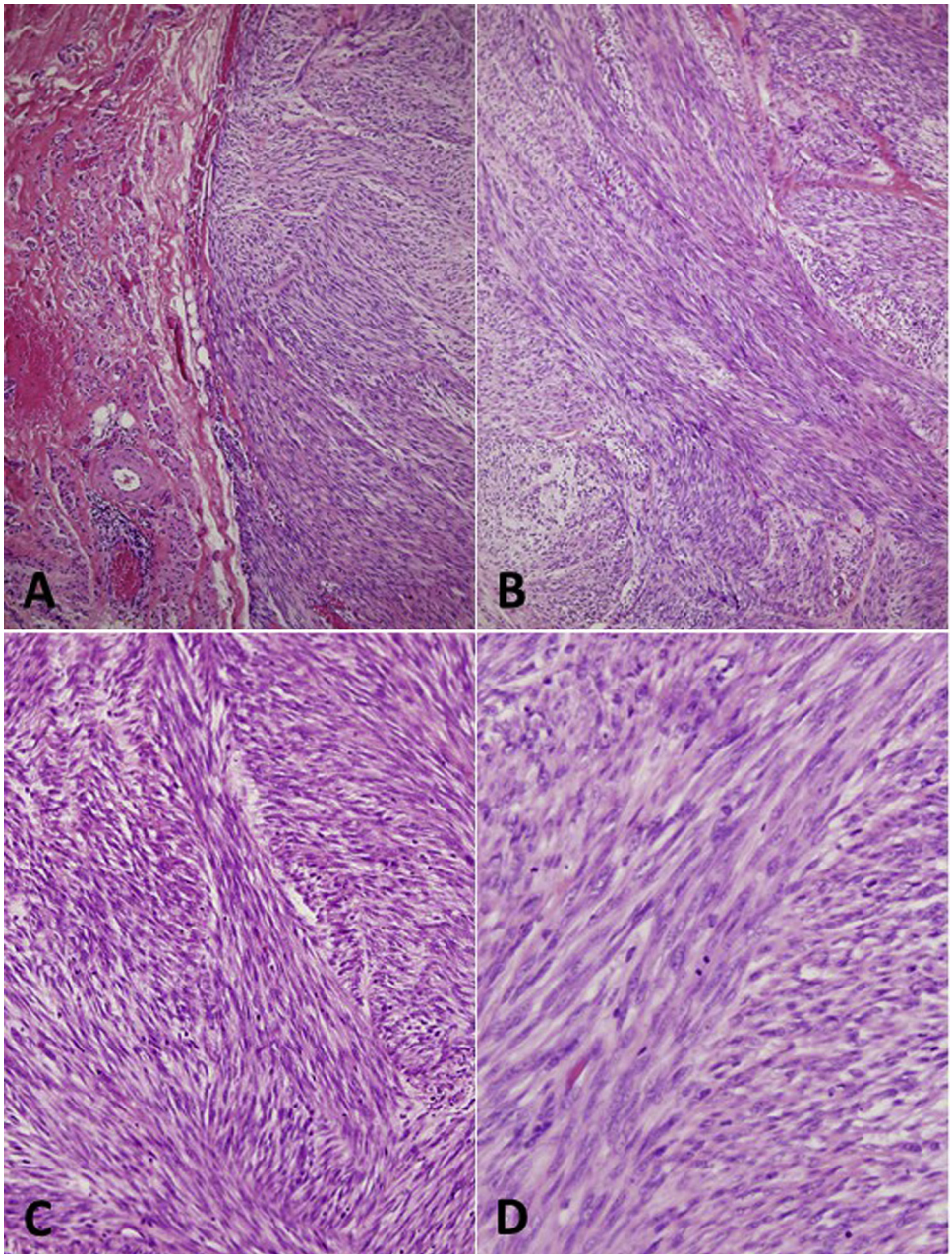

Fig. 2. Histopathology of the myofibroblastic sarcoma. (A) Well-defined neoplasm with pushing edge and peripheral lymphocyte infiltration. Groups of rhabdomyocytes are visible in the periphery (H&E, x200). (B) The tumor is made up of intersecting cellular fascicles (H&E, x100). (C) The spindle-shaped tumor cells show palely eosinophil cytoplasm and imprecise limits (H&E, x200). (D) The nuclei are elongated with a regular distribution of chromatin and one, two, or more inconspicuous nucleoli (H&E, x400).

2.8 × 1.5 x 1.2 cm. located under the hypodermis. The nodule did not affect the surgical edges. The distance from the tumor to the medial edge was 0.5 cm. On the rest of the edges, the distance was 1.5 cm.

The entire surgical specimen was fixed in 10% buffered formalin. Representative tissue samples were embedded in paraffin. For routine microscopy, 5-μm-thick sections were stained with hematoxylin and eosin and Periodic acid Schiff (PAS) procedure. Immunohistochemical (IHC) staining was performed using the EnVision FLEX + Visualization System (Dako, Agilent Technologies, SL, Las Rozas, Madrid, Spain). The IHC reaction was performed using appropriate tissue controls for the antibodies utilized. Automatic staining was performed on a Dako Omnis autostainer (Agilent Technologies, SL). Antibodies used are detailed in Table 1. Fluorescence in situ hybridization (FISH) with probes FISH SureFISH 18q11.2SS18 3´BA (Dako, Agilent Technologies, SL), and SureFISH 18q11.2 SS18 5´BA (Dako, Agilent Technologies, SL) was performed.

The histological study showed a well-delimited, partially capsulated, neoplasm of moderate-to-dense cell density with pushing edges and peripheral inflammatory infiltration in the form of lymphocyte aggregates located on the muscular plane (Fig. 2A). The neoplasm was constituted by intersecting fascicles of spindle cells (Fig. 2B) of poorly delimited palely eosinophil cytoplasm (Fig. 2C). The nuclei were elongated with chromatin distributed regularly or vesicular with indentations and small nucleoli (Fig. 2D). Nuclear atypia was sparsely represented by occasional hyperchromatic nuclei (Fig. 3A). Sometimes the growth pattern was vaguely storiform (Fig. 3B). Areas of hyalinized collagen (Fig. 3C) and focal myxoid change were observed (Fig. 3D). Vascularization showed thin-walled capillary vessels. The mitotic count

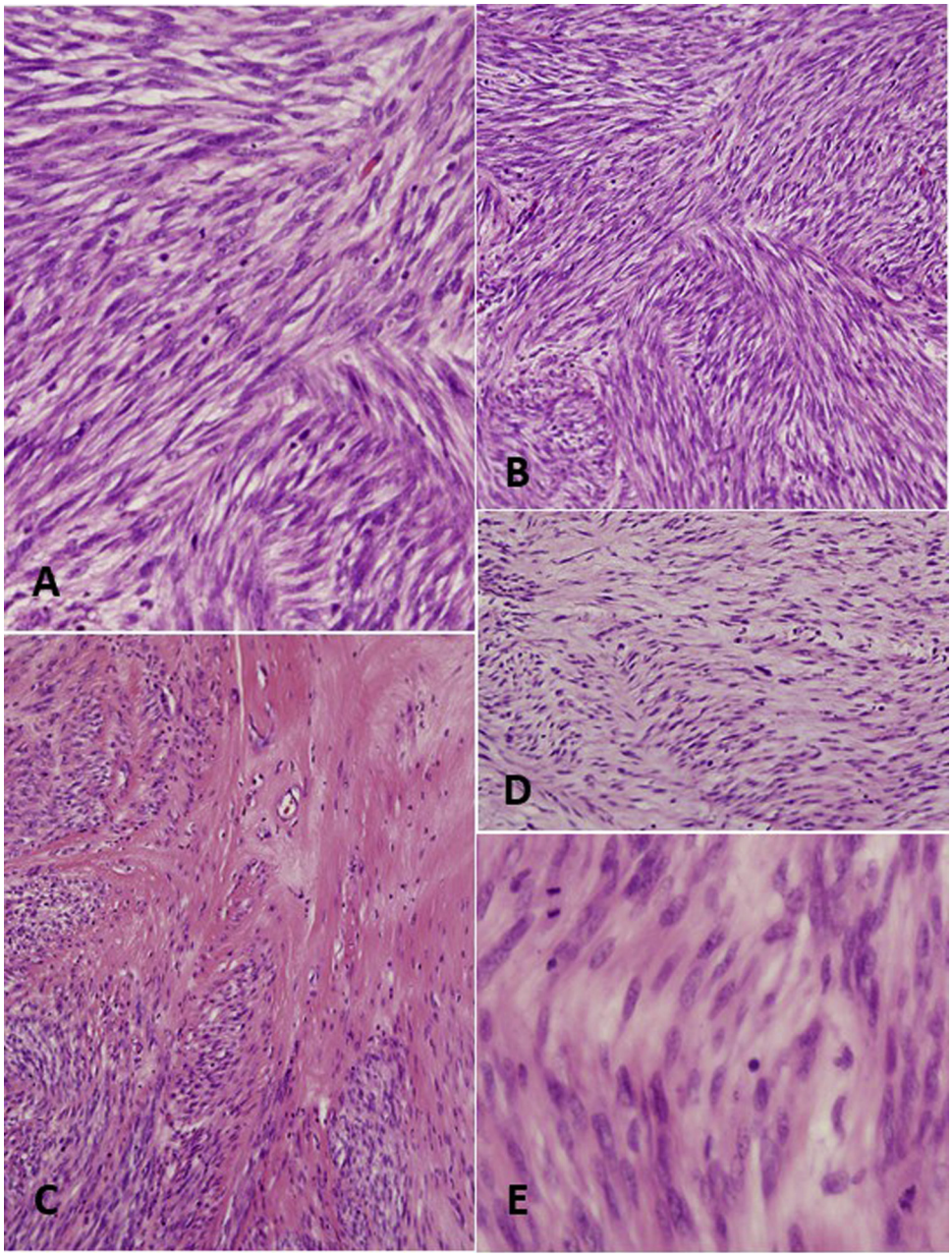

Fig. 3. Microscopic details of the myofibroblastic sarcoma. (A) Mild nuclear atypia with occasional hyperchromatic nuclei (H&E, x400). (B) Storiform growth pattern (H&E, x200). (C) Extensive area of hyalinized collagen (H&E, x200). (D) Myxoid tumor area (H&E, x200). (E) Frequent mitoses (H&E, x400).

was 16 mitoses per 10 high power field (Fig. 3E). Scattered, scarce, isolated lymphocytes were observed in the periphery of the tumor tissue. No necrosis or calcification was observed. Staining with PAS did not show basal lamina in tumor cells. The immunohistochemical study revealed diffuse cell reactivity for smooth-muscle actin (Fig. 4A), muscle-specific actin (Fig. 4B), fibronectin (Fig. 4C), calponin (Fig. 4D) and CD99 (Fig. 5A). Positivity for muscle-specific actin, calponin, and CD99 was much less intense than that of the other antibodies. Tumor cells showed negativity for desmin, h-caldesmon, myo-D1, CD34, p63, S100 protein, epithelial membrane antigen, cytokeratin (CK) 7, CK19, pancytokeratin AE1/AE3, CD57, and CD68. Ki67 labeled 35% of the neoplastic cells (Fig. 5B). FISH for the rearrangement of the SS18 gene (SYT) was negative. A diagnosis of MFS was established, and it was further classified as grade 2 (score, 2 + 2+0 = 4) according to the French grading system (FNCLCC) [15]. The histopathological study confirmed that the resection margins were tumor-free.

4. Discussion

Sarcomas of the breast, excluding phyllodes tumor, comprise < 1% of all breast tumors and < 5% of all soft tissue sarcomas [16]. Their classification should follow the same criteria used in soft tissue sarcomas including the histologic grading. MFS is recognized as a distinctive pathological entity. Until recently there has been a debate about the diagnostic criteria of this tumor. Some authors considered the tumor ultrastructure as a key to diagnosis [17]. However, given the corresponding histological appearance, the use of an antibody panel that includes smooth-muscle actin, desmin, h-caldesmon [12], fibronectin, CD34, S100 protein, and epithelial markers allows the diagnosis of MFS effectively.

Mammary MFS has been rarely reported with only 11 cases in the worldwide literature [4–13]. The clinicopathological data of these previously described cases as well as our case are summarized in

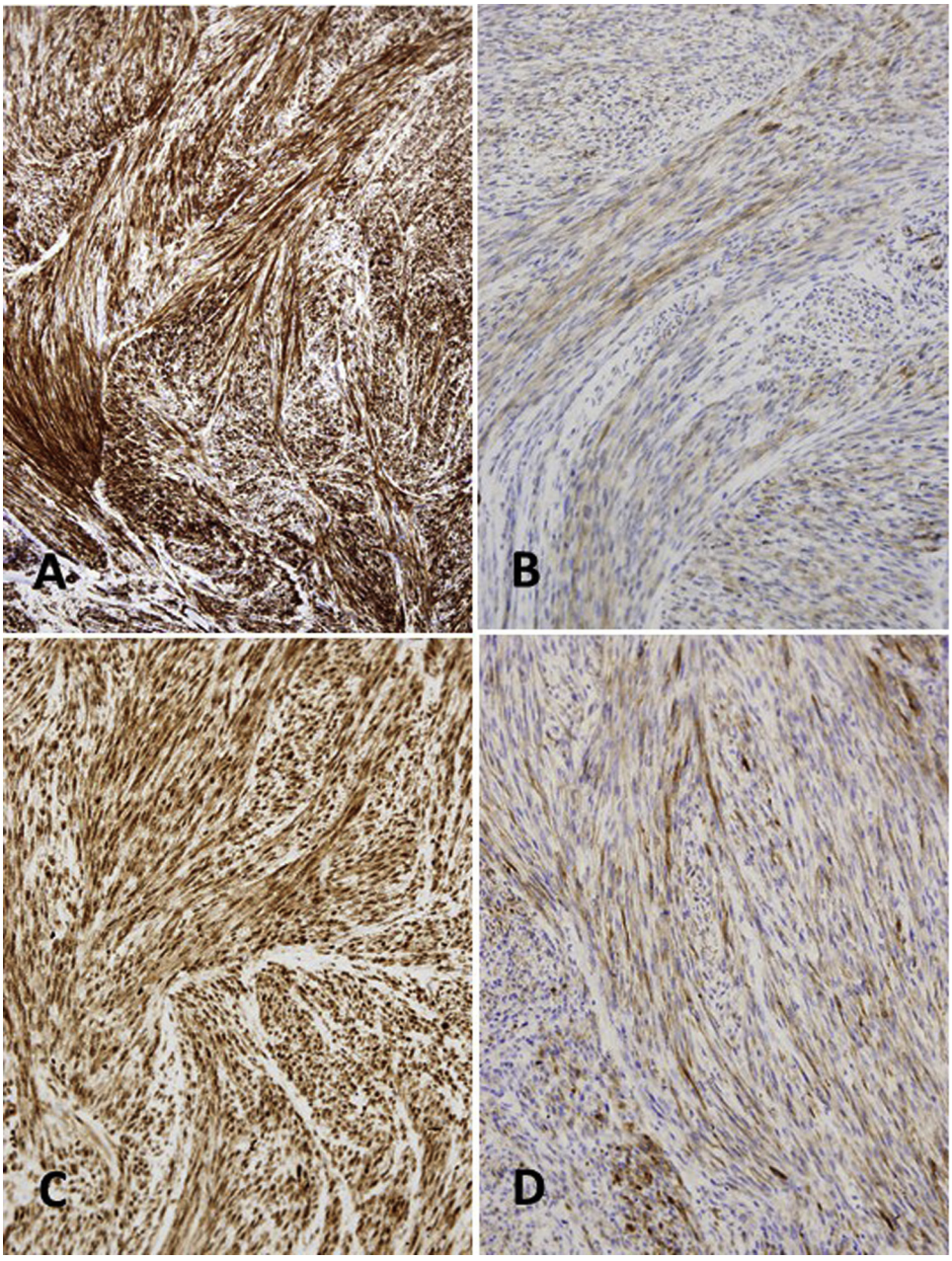

Fig. 4. Immunohistochemistry. Neoplastic cells stain positively for smooth-muscle actin (A, x100), muscle-specific actin (B, x200), fibronectin (C, x200), and calponin (D, x200).

Table 2. The study of these 12 cases revealed that the ages of the patients ranged from 46 years to 82 years, with a mean and median of 60.3 years and 58 years, respectively. There was a clear difference in the incidence concerning gender (M:F, 1:5). The duration of the lesion varied from 1 week to 8 months (mean 3.3 months, median 2 months). One case originated in fibroadenoma and another case was induced by radiotherapy treatment. The size ranged from 2.2 cm to 22 cm (mean 5.1 cm, median 3.1 cm). The tumors presented frequent mitosis with an average of at least 8.1 mitoses per 10 high power fields. Tumor necrosis was in all cases less than 50% of the tumor mass. It was present in 75% of tumors. In one case (case 5) the neoplasm showed vascular invasion [8]. In 9 evaluable cases, the histological grade using the FNCLCC criteria was grade 2 (intermediate or moderate grade). The majority of cases (75%) were studied with electron microscopy. The average and median follow-ups were 26.8 and 16 months respectively (range 2 to 120 months). The percentage of recurrences, metastasis, and death due to the tumor was 27.3%, 36.4%, and 27.3% respectively. This high aggressiveness contrasts with the low degree of malignancy of cases located outside the breast. Thus, Cai et al. [3] observed recurrence, metastasis and tumor death rates of 28.6%, 7.1%, and 7.1% respectively.

Regarding the histological grade, the current WHO classification of soft tissue tumors includes only the low-grade MFS type [18]. However, moderate-to-high grade forms of the tumor have been described including the pleomorphic MFS [19,20]. Furthermore, the comparison of histopathological data between low-grade and moderate-to-high grade cases showed significant differences in tumor size, mitotic count, and proliferative index in the two groups [3].

On the other hand, primary breast sarcomas have no pathognomonic imaging features and can mimic those of invasive breast carcinoma [21].

Radiation therapy is a component of the treatment of patients with

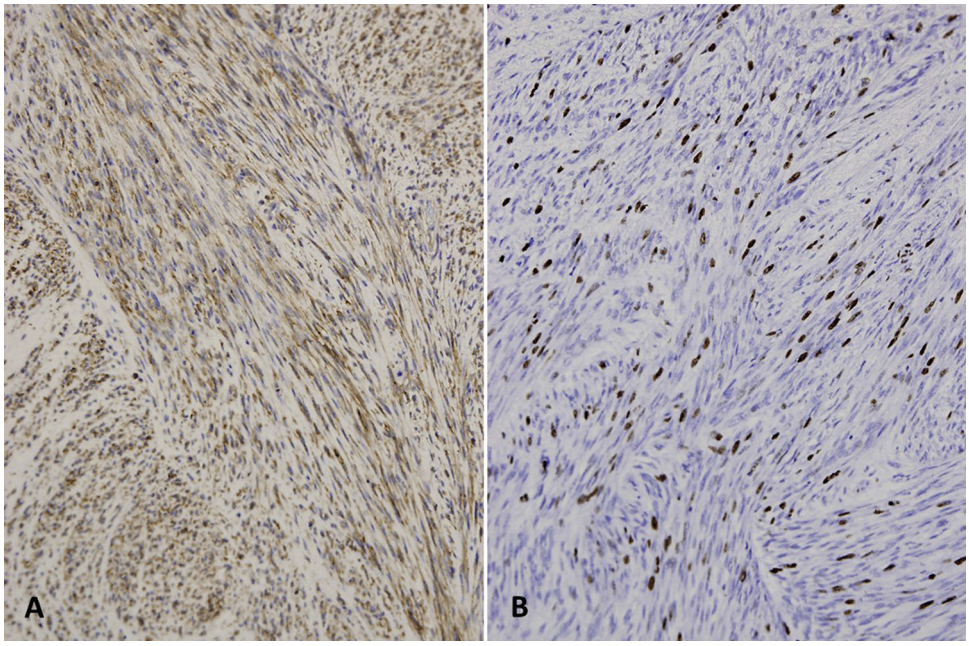

Fig. 5. Immunohistochemistry. Most neoplastic cells show reactivity for CD99 (A, x200). Approximately 35% of tumor cells are labeled with Ki67 (B, x200).

primary breast carcinoma (BC) particularly in cases of breast-conserving surgery. Radiotherapy may present with short- and long-term complications. One of the most significant late sequelae is radiation-induced sarcoma (RIS). Cahan et al. [22] stated the criteria to consider that a tumor is induced by radiation. The revised criteria include the following [23–25]: (a) the new tumor must have arisen in a previously irradiated area; (b) the new tumor must be histologically different from the original; (c) the new tumor should not be present at the beginning of radiotherapy, and; (d) there must be a prolonged period of latency (preferable > 4 years) between the two malignancies. However, the latency between radiation exposure and sarcoma development has been modified by most investigators. Some of them have suggested a minimum latency as short as 6 months [26,27]. On the other hand, patients with genetic malignancy predisposition syndrome, such as Li-Fraumeni syndrome or Rothmund-Thomson syndrome, should be excluded. The present case meets the 4 revised criteria of Cahan et al and the latency period was 6 years and 4 months.

The 15-year cumulative incidence of RIS has been reported as 0.28% among patients with BC [28]. Besides, a significant relationship between radiation dose and risk of consecutive sarcoma was found, with a relative risk of 30.6 for doses higher than 44 Gy compared to 14 Gy or lower [28]. Most patients receive a total dose of about 50 Gy [29] as happened in our patient. The most frequent RIS location is the chest wall [30]. On the contrary, sporadic sarcomas occur most commonly in the parenchyma.

Some authors suggest that cases of RIS will increase in the future. This is due to the increased use of radiation therapy and the effectiveness of cancer therapy with increased patient survival [31]. The median interval between radiation and the development of sarcoma is 11 years [29]. However, the interval can be as long as 30 years [29]. Ionizing radiation damages DNA, producing double-strand breaks, and provokes reactive oxygen species that induce direct damage to bases, single-strand breaks, and DNA cross-linking. Thus, ionizing radiation generates distinctive mutational signatures that explain its oncogenic potential [32].

Angiosarcoma was reported among RIS patients as the most common histologic subtype accounting for 52% of cases followed by undifferentiated pleomorphic sarcoma (28%), osteosarcoma (5%), fibrosarcoma (3%), extraskeletal osteosarcoma (3%), chondrosarcoma (2%), leiomyosarcoma (2%), myxofibrosarcoma (2%), extraskeletal chondrosarcoma (1%), and neurofibrosarcoma (1%) [29]. Most RISs are morphological high grade [31]. Angiosarcoma (32.1%) and undifferentiated pleomorphic sarcoma (7.9%) are also the main histologic types of primary breast sarcoma [33]. As far as we are aware MFS has not been previously reported as RIS of the breast.

The most common symptoms of RIS are skin changes, swelling or a mass, and/or pain [25]. Diagnosis includes physical examination, ultrasonography, and magnetic resonance imaging. Core needle or incisional biopsies are preferred to fine-needle aspiration cytology [34].

The main differential diagnosis of MFS includes spindle cell carcinoma (SCC), adult fibrosarcoma (AF), monophasic synovial sarcoma (MSS), low-grade malignant peripheral nerve sheath tumor (LGMPNST), and low-grade leiomyosarcoma (LGLMS). SCC usually has small foci of squamous or glandular differentiation. Epithelial markers (CK AE1/AE3, CK CAM5.2), p63, and GATA3 are positive [31]. AF show cells with less eosinophilic cytoplasm and lack immunohistochemical features of myofibroblasts. MSS is characterized by fascicles of uniform spindled cells with alternating areas of hypercellularity and hypocellularity (marbled pattern). Cells focally express CK7, CK19, and EMA. TLE-1 is diffusely positive. Genetically, tumor cells present reciprocal translocation t(X;18)(p11.23;q11)(SS18-SSX1) in about 65% of cases. LGMPNST shows high cellularity and marked mitotic activity. It is composed of cells with elongated and wavy nuclei. Cells often form perivascular whirling. Besides, the tumor stains for S100 protein (at least 50% of cases), SOX10, nestin, CD57, and HMGA2, and lacks positivity for myogenic markers. Loss of histone H3K27 trimethylation by immunohistochemistry has been observed in approximately 50% of cases. This marker seems to be highly specific for LGMPNST [34]. LGLMS displays well-developed fascicles of spindle cells with fibrillary acidophilic cytoplasm, blunt-ended nuclei, and paranuclear vacuolization. Cells show a PAS + basal cell lamina. The tumor is reactive for h-caldesmon and desmin and non-reactive for fibronectin.

Surgery with widely clear margins constitutes the basic treatment of RIS. The role of adjuvant or neoadjuvant chemotherapy remains uncertain [35].

5. Conclusion

In conclusion, mammary MFS cases differ clinically and biologically

Table 2
Reported cases of myofibroblastic sarcomas of the breast.

Case no/Reference	Age(y)/ Sex	Duration (months)	Background	Size (cm)	Mitoses(10HPF) /Focal necrosis	Grade	EM	Therapy/Follow-up (months)	Outcome
1/[4]	51/M	7.0	No	5.0	Common/Yes	2	Yes	Radical mastectomy/NR	NR
2/[5]	55/F	0.25	No	2.0	10/Yes	2	Yes	Mastectomy. Madden lymphadenectomy. CT/11	Recurrence at 1 month. Pleuropulmonary metastases. DOD after 11 months
3/[6]	59/F	NR	No	2.3	6-7-15/No	2	Yes	Mastectomy and lymphadenectomy. Radiotherapy/20	Alive and well
4/[7]	60/M	1.0	No	2.5	10/Yes	2	Yes	Mastectomy. Madden lymphadenectomy/ 120	Five local relapses. Alive
5/[8]	72/F	NR	No	3.4	2/Yes	2	Yes	Mastectomy/12	Recurrence at 5 months. Lung metastases at 12 months
6/ [9]	51/F	3.0	No	22.0	8-35/Yes	2	No	Radical mastectomy. CT. Radiotherapy/24	Alive
7/[10]	46/F	6.0	No	2.2	Numerous/NR	NR	Yes	Lumpectomy. Simple mastectomy/12	Alive
8/[11]	81/F	0.5	No	4.2	Numerous/NR	2	Yes	Lumpectomy. Simple mastectomy. Radiotherapy/16	Pleuropulmonary metastases at 14 months.Alive
9/[12]	57/F	NR	NR	NR	NR/NR	NR	Yes	NR/NR	Pulmonary and brain metastasis. DOD after 12 months
10/ [12]	82/F	NR	NR	NR	NR/NR	NR	Yes	NR/NR	DOD 15 months after presentation
11/[13]	61/F	8.0	Arising in fibroadenoma	5.0	5-10/Yes	2	No	Lumpectomy/24	Alive and well
12/Present report	49/F	1.0	Radiotherapy associated	2.8	16/No	2	No	Lumpectomy/2	Alive and well

DOD, Died of disease; NR, Not reported; CT, Chemotherapy; EM, electron microscopy.

from those affecting extramammary regions. They are more common in females and show a greater degree of aggressiveness. Precise diagnosis of mammary MFS requires morphological and immunohistochemical study. We present here for the first time a case of radiation-induced MFS of the breast. MFS should be included among radiation-induced breast sarcomas.

Compliance with ethical standards

No ethics committee approval is required at our institution for a case report involving a single patient.

Consent

Written informed consent was obtained from the patient for publication of this case report and all accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Declaration of Competing Interest

The authors declare that they have no conflict of interests.

References

[1] T. Mentzel, S. Dry, D. Katenkamp, C.D.M. Fletcher, Low-grade myofibroblastic sarcoma. Analysis of 18 cases in the spectrum of myofibroblastic tumors, Am. J. Surg. Pathol. 22 (1998) 1228-1238.
[2] C.D.M. Fletcher, K.K. Unni, F. Mertens, World health organization classification of tumors, Pathology and Genetics of Tumors of Soft Tissue and Bone, IARC Press, Lyon, 2002.
[3] Z.G. Cai, C.C. Pan, D.H. Yu, Z.Z. Feng, L. Ma, Y. Zhao, H.B. Xu, Myofibroblastic sarcomas: a clinicopathologic analysis of 15 cases and review of literature, Int. J. Clin. Exp. Pathol. 9 (2016) 1568–1577.
[4] D.J. Crocker, T.M. Murad, Ultrastructure of fibrosarcoma in a male breast, Cancer 23 (1969) 891–899.
[5] G. Taccagni, E. Rovere, M. Masullo, L. Christensen, B. Eyden, Myofibrosarcoma of the breast: review of the literature on myofibroblastic tumors and criteria for defining myofibroblastic differentiation, Am. J. Surg. Pathol. 21 (1997) 489–496.
[6] A. Gocht, H.C. Bösmüller, R. Bässler, F.A. Tavassoli, F. Moinfar, D. Katenkamp, K. Schirrmacher, P. Lüders, W. Saeger, Breast tumors with myofibroblastic differentiation: clinico-pathological observations in myofibroblastoma and myofibrosarcoma, Pathol. Res. Pract. 195 (1999) 1–10.
[7] F. González-Palacios, J.L. Enriquez, P. San Miguel, R. Vazquez, M. García-Cosío, Myofibroblastic tumors of the breast: a histological spectrum with a case of recurrent male breast myofibrosarcoma, Int. J. Surg. Pathol. 7 (1999) 11–17.
[8] E. Montgomery, J.R. Goldblum, C. Fisher, Myofibrosarcoma: a clinicopathologic study, Am. J. Surg. Pathol. 25 (2001) 219–228.
[9] K. Lucin, E. Mustać, N. Jonjić, Breast Sarcoma showing myofibroblastic differentiation, Virchows Arch. 443 (2003) 222–224.
[10] P.B. Morgan, S. Chundru, S.S. Hatch, H.K. Hawkins, P.A. Adegboyega, M.A. Eltorky, Uncommon malignancies: case 1. Low-grade myofibroblastic sarcoma of the breast, J. Clin. Oncol. 23 (2005) 6249–6251.
[11] M. Stark, A. Hoffmann, Z. Xiong, Mammary myofibrosarcoma: case report and literature review, Breast J. 17 (2011) 300–304.
[12] P. Shenjere, B. Eyden, S.S. Banerjee, B. Chakrabarty, J.H. Shanks, K.A. Sikand, L.P. Menasce, Ultrastructurally confirmed myofibrosarcoma: a series of 10 new cases, with a discussion on diagnostic criteria, Int. J. Surg. Pathol. 21 (2013) 29–36.
[13] N.H. Myong, J.W. Min, Low-grade myofibroblastic sarcoma arising in fibroadenoma of the breast: a case report, Diagn. Pathol. 11 (2016) 33.
[14] M. Almeida Branco, J.L. Vargas, F. Fernández, Sarcoma miofibroblástico post-radioterapia, Rev. Otorrinolaringol. Cir. Cabeza Cuello 76 (2016) 71–76.
[15] J.M. Coindre, Grading of soft tissue sarcomas. Review and update, Arch. Pathol. Lab. Med. 130 (2006) 1448–1453.
[16] S. Al-Benna, K. Poggemann, H.U. Steinau, L. Steinstraesser, Diagnosis and management of primary breast sarcoma, Breast Cancer Res. Treat. 122 (2010) 619–626.
[17] R. Lagacé, T.A. Seemayer, G. Gabbiani, W. Schürch, Myofibroblastic sarcoma, Am. J. Surg. Pathol. 23 (1999) 1432-1..
[18] C.D.M. Fletcher, J.A. Bridge, P.C.W. Hogendoorn, F. Mertens, WHO Classification of Tumors of Soft Tissue and Bone, IARC Press, Lyon, 2013.
[19] E. Montgomery, C. Fisher, Myofibroblastic differentiation in malignant fibrous histiocytoma (pleomorphic myofibrosarcoma): a clinicopathological study, Histopathology 38 (2001) 499–509.

[20] C. Fisher, Myofibrosarcoma, Virchows Arch. 445 (2004) 215–223.
[21] S. Wienbeck, H.J. Meyer, A. Herzog, S. Nemat, A. Teifke, W. Heindel, F. Schäfer, S. Kinner, M. Müller-Schimpfle, A. Surov, Imaging findings of primary breast sarcoma: results of a first multicenter study, Eur. J. Radiol. 88 (1–7) (2017).
[22] W.G. Cahan, H.Q. Woodard, N.L. Higinbotham, F.W. Stewart, B.L. Coley, Sarcoma arising in irradiated bone. Report of eleven cases, Cancer 1 (1948) 3–29.
[23] M. Arlen, N.L. Higinbotham, A.G. Huvos, R.C. Marcove, T. Miller, I.C. Shah, Radiation-induced sarcoma of bone, Cancer 28 (1971) 1087–1099.
[24] W.B. Laskin, T.A. Silverman, F.M. Enzinger, Postradiation soft tissue sarcomas. An analysis of 53 cases, Cancer 62 (1988) 2330–2340.
[25] E.M. Murray, D. Werner, E.A. Greeff, D.A. Taylor, Postradiation sarcomas: 20 cases and a literature review, Int. J. Radiat. Oncol. Biol. Phys. 45 (1999) 951–961.
[26] C. Cha, C.R. Antonescu, M.L. Quan, S. Maru, M.F. Brennan, Long-term results with resection of radiation-induced soft tissue sarcomas, Ann. Surg. 239 (2004) 903–909.
[27] R.A. Gladdy, L.X. Qin, N. Moraco, M.A. Edgar, C.R. Antonescu, K.M. Alektiar, M.F. Brennan, S. Singer, Do radiation-associated soft tissue sarcomas have the same prognosis as sporadic soft tissue sarcomas? J. Clin. Oncol. 28 (2010) 2064–2069.
[28] C. Rubino, A. Shamsaldin, M.G. Lê, M. Labbé, J.M. Guinebretière, J. Chavaudra, F. de Vathaire, Radiation dose and risk of soft tissue and bone sarcoma after breast cancer treatment, Breast Cancer Res. Treat. 89 (2005) 277–288.
[29] S.H. Salminen, M.M. Sampo, T.O. Böhling, L. Tuomikoski, M. Tarkkanen, C.P. Blomqvist, Radiation-associated sarcoma after breast cancer in a nationwide population: increasing risk of angiosarcoma, Cancer Med. 7 (2018) 4825–4835.
[30] N. Penel, J. Grosjean, Y.M. Robin, L. Vanseymortier, S. Clisant, A. Adenis, Frequency of certain established risk factors in soft tissue sarcomas in adults: a prospective descriptive study of 658 cases, Sarcoma 2008 (2008) 459386.
[31] J.K. Mito, D. Mitra, L.A. Doyle, Radiation-associated sarcomas. An update on clinical, histologic, and molecular features, Surg. Pathol. Clin. 12 (2019) 139–148.
[32] S. Behjati, G. Gundem, D.C. Wedge, N.D. Roberts, P.S. Tarpey, S.L. Cooke, P. Van Loo, L.B. Alexandrov, M. Ramakrishna, H. Davies, S. Nik-Zainal, C. Hardy, C. Latimer, K.M. Raine, L. Stebbings, A. Menzies, D. Jones, R. Shepherd, A.P. Butler, J.W. Teague, M. Jorgensen, B. Khatri, N. Pillay, A. Shlien, P.A. Futreal, C. Badie, I.C.G.C. Prostate Group, U. McDermott, G.S. Bova, A.L. Richardson, A.M. Flanagan, M.R. Stratton, P.J. Campbell, Mutational signatures of ionizing radiation in second malignancies, Nat. Commun. 7 (2016) 12605.
[33] M. Yin, H.B. Mackley, J.J. Drabick, H.A. Harvey, Primary female breast sarcoma: clinicopathological features, treatment, and prognosis, Sci. Rep. 6 (2016) 31497.
[34] J.R. Goldblum, Soft tissues, in: J.R. Goldblum, L.W. Lamps, J.K. McKenney, J.L. Myers (Eds.), Rosai and Ackerman´s Surgical Pathology, Eleventh Edition, Elsevier, Philadelphia, PA, 2018, pp. 1810–1914.
[35] G.R. Sheth, L.D. Cranmer, B.D. Smith, L. Grasso-Lebeau, J.E. Lang, Radiation-induced sarcoma of the breast: a systematic review, Oncologist 17 (2012) 405–418.