ISSN: 2476-2377

Case Report

International Journal of Cancer Research & Therapy

Malignant Mesenchymal and Fibroepithelial Breast Tumors - Presentation of Three Cases

Oscar García-Angulo[1], Johan Durán[2], Claudia Cubillos[1], Juan Hidalgo[2], Juan Zambrano[3] and Ana Mejía[4]

[1]*Breast and soft tissue surgeon, member of the Breast Multidisciplinary Board, Colmédica Prepaid Medicine.*

[2]*Specialist in radiology and breast imaging, member of the Breast Multidisciplinary Board, Colmédica Prepaid Medicine*

[3]*Specialist in plastic and reconstructive surgery, member of the Breast Multidisciplinary Board, Colmédica Prepaid Medicine*

[4]*Breast surgeon, leader of the Breast Multidisciplinary Board, Colmédica Prepaid Medicine*

***Corresponding author**

Oscar García-Angulo, Breast and soft tissue surgeon, member of the Breast Multidisciplinary Board, Colmédica Prepaid Medicine, USA, E-mail: osaga72@gmail.com

Submitted: 06 Sep 2019; **Accepted**: 16 Oct 2019; **Published**: 23 Oct 2019

Abstract

Introduction: *Malignant mesenchymal breast tumors, as is the case also with malignant phyllodes tumors, are rare malignancies that share several clinical and pathological characteristics. They are often locally aggressive and have a high potential for distant metastasis.*

This paper reports two cases of malignant phyllodes tumors and one case of breast sarcoma managed by our breast surgery team. One of the malignant phyllodes tumors showed rapid progression with early multiple visceral involvement and death.

Discussion: *Presentation of an updated review of the literature covering clinical, pathological, radiological and therapeutic considerations related to breast sarcomas and malignant phyllodes tumors.*

Conclusion: *Breast sarcomas and malignant phyllodes tumors are rare breast malignancies that share more similarities than differences and require a multidisciplinary approach to management.*

Introduction

Phyllodes tumors, first described in 1838 by Mulle, are rare mixed epithelial and stromal neoplasms accounting for less than 1% of all breast neoplasms [1]. They may be classified as benign, borderline or malignant. Malignant phyllodes tumors account for 10% to 30% of all phyllodes tumors and have the potential for aggressive local growth and distant metastasis. They harbors in their stroma a neoplastic component with sarcomatous differentiation (myoid, adipose, angiosarcomatous, bony or chondroid) [2].

On the other hand, primary breast sarcomas are a rare type of malignant neoplasms of mensenchymal origin, accounting for at least 1% of all breast malignancies and less than 5% of all sarcomas [3]. Incidence is estimated at 4.6 new cases in one million women per year [4]. Breast sarcomas comprise a range of subtypes. The majority of primary breast sarcomas appear in women in the fourth decade of life, usually as a rapidly growing, solid, solitary, painless, unilateral mass [4].

We present one case of breast sarcoma and two cases of malignant phyllodes tumors seen at the Colmedica private insurance healthcare service network in Bogotá, Colombia.

Case 1

A 39-year-old patient with a long-standing, progressively growing right mammary mass initially studied elsewhere in 2015 using fine needle biopsy. Given that the pathology report described a benign proliferative mastopathy with no atypia, the patient was put under observation. The mass grew progressively and, in 2017, a trucut biopsy revealed a fibroepithelial biphasic lesion suggestive of cellular fibroadenoma. Surgery was proposed given the size of the mass, but it was not performed. The patient came back in 2018, with the lesion having grown rapidly, reaching 8 cm in diameter. At that point a round-block circular periareolar resection was performed, with removal of a solid mass. The pathology result showed a malignant phyllodes tumor of heterologous characteristics, 8.5 x 7.5 cm in size and marginal involvement. The proposed treatment was to complete the oncologic surgery by means of skin-preserving mastectomy with immediate reconstruction using a prosthetic expander implant. Sacrificing the nipple-areolar complex was the selected option given the high probability of necrosis due to the type of periareolar incision used in the first procedure. The patient underwent surgery

in June 2018, and evolved satisfactorily. No adjuvant treatments were administered since the oncologist and radiation oncologist considered that surgery as local treatment was sufficient. After 11 months of follow-up, the patient is relapse-free (Figures 1a and 1b).

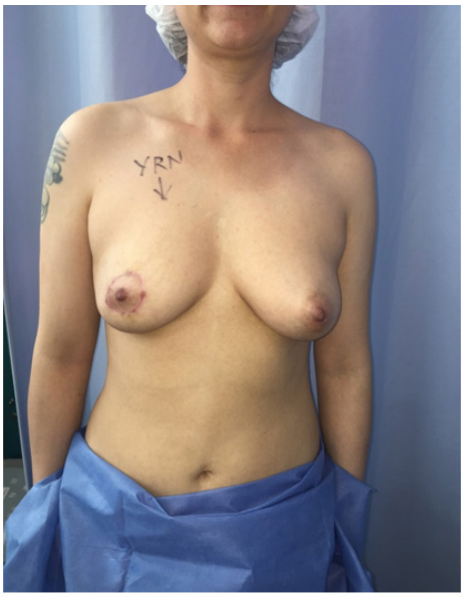

Figure 1a: Patient before simple mastectomy

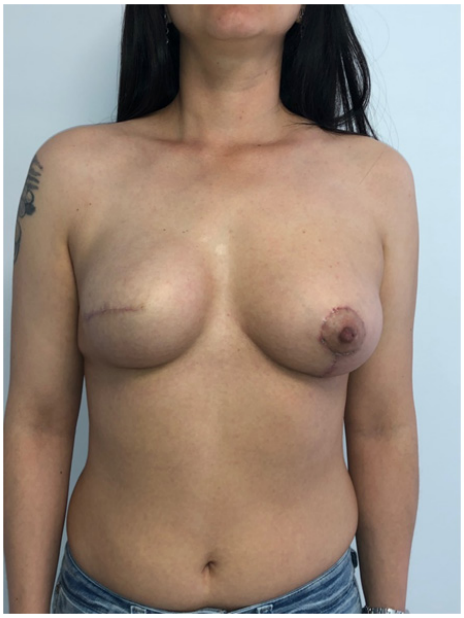

Figure 1b. Patient after right mastectomy with immediate prosthetic reconstruction and contralateral compensation mammoplasty

Case 2

A 45-year-old patient with a history of augmentation mammoplasty performed in 2011, and a painless, progressively growing mass in the right breast since 2017. The initial ultrasound in February 2018 showed a large mass with cystic degeneration occupying all quadrants and displacing an intact-looking implant, with a volume of 159 cc. An ultrasound-guided trucut biopsy was performed in March 2018 and the pathology result was reported as a biphasic tumor with moderate increase in cellularity, areas of necrosis and occasional mitoses (0-1 per 10 high-power fields), initially suggesting a phyllodes tumor. Computed tomography (CT) of the chest showed a large right mammary mass 156x111x145 mm in size (Figure 2). The patient was taken to surgery in March 2018 for simple mastectomy with wide skin removal and immediate reconstruction with latissimus dorsi flap and prosthesis. The definitive pathology report confirmed the diagnosis of a malignant phyllodes tumor 18.5 cm in size. All margins were tumor-free. Adjuvant radiotherapy was proposed, but during the CT simulation in April 2018, multiple bilateral lung nodules were identified, associated with right pleural effusion and solid lesions of the right thoracic wall. Moreover, the abdominal CT showed focal hypodense lesions 7 mm in size in segment III of the liver and 16 mm in size in segment VII. A bone scan performed in May 2018 showed abnormal focal uptake in the caudal edge of the right scapula.

A trucut biopsy taken of a nodule recently appearing after right anterior thoracic surgery showed scarce fragments of a high-grade spindle cell sarcomatous neoplasm. Immunohistochemistry reported a high-grade spindle cell and pleomorphic sarcomatous component arising in a malignant phyllodes tumor. Systemic chemotherapy was initiated on May 21 with ifosfamide and doxorubicin. After six cycles, there was a reduction in the number and size of the pulmonary lesions and disappearance of the liver lesions. However, there was progression of bone metastases and new brain metastatic lesions were identified in September 2018, which progressed until the patient died in October 2018.

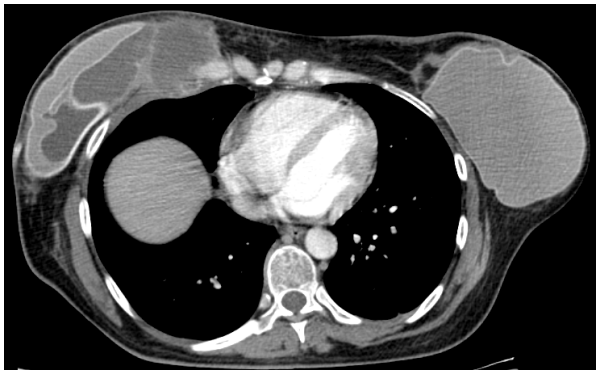

Figure 2: Axial section of contrast chest CT. An infiltrating hypodense solid mass with peripheral enhancement located in the costosternal junction can be seen on the right thoracic wall

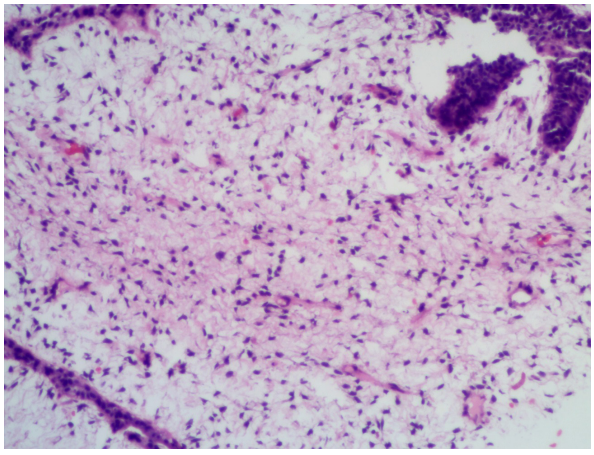

Figure 3: Pathology of high-grade spindle cell sarcomatous lesion

Case 3

A 47-year-old patient with a rapidly progressing, painful mass in the right breast present since the past six months. Ultrasound performed in May 2018 showed a lesion of mixed echogenicity, partial cystic content, irregular contours, 50 x 40 mm in size towards the 12 o'clock position in the right breast (Figure 3). The complementary mammogram showed a dense mass in the superior lateral quadrant of the right breast (Figure 4). A trucut biopsy of the mass showed an area of fibrosis and a cluster of oval-shaped spindle cells with giant multinucleated cells, suggesting an inflammatory, more so than neoplastic process. Given the size of the mass, surgical removal was performed in June 2018, with the finding of a heterogenous 9 x 8 cm mass with solid and cystic components. Pathology confirmed a tumor lesion with necrotic center and pleomorphic cells, consistent with a high-grade, poorly differentiated sarcoma with osteoclast-type cells. Margins were less than 1 mm, prompting oncologic surgery with a new local resection considering good breast-tumor ratio due to the large volume of the patient's breast. The patient received adjuvant radiotherapy but no systemic chemotherapy, and she is relapse-free after eight months of follow-up.

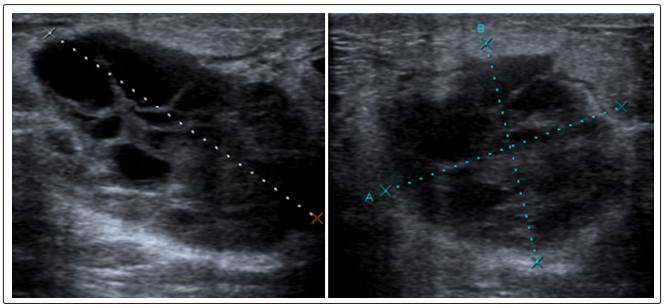

Figure 3: Ultrasound scan of the same patient shown in Figure 3. The image shows a circumscribed heterogenous, predominantly solid mass with cystic areas and antiparallel orientation, 50x40x36 mm in size

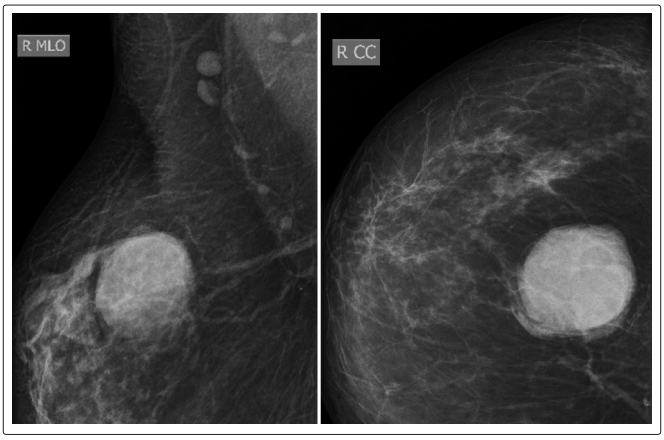

Figure 4: Mid lateral oblique and craniocaudal image of the right breast. An oval-shaped hyperdense circumscribed mass is observed on the superior inter-quadrant line, with the largest diameters of 50x40 mm

Discussion

Breast sarcomas are a heterogenous group of mesenchymal tumors designated in accordance to cell differentiation (angiosarcoma, fibrosarcoma, leiomyosarcoma, osteosarcoma, liposarcoma, chondrosarcoma, malignant fibrous histiocytoma and Kaposi sarcoma) [5]. Some arise from the periductal stroma of the mammary gland, hence their name of stromal sarcomas [4]. Among primary breast sarcomas, angiosarcoma is the most common subtype, generally associated with prior radiotherapy administration [4]. On the other hand, apart from its sarcomatous mesenchymal component, a malignant phyllodes tumor has an epithelial component in its structure, leading to its classification under the category of fibroepithelial breast tumors.

The most frequent clinical presentation of these tumor lesions is the palpable mass. Mean size at the time of diagnosis es 3 to 5 cm, although rapidly growing tumors may be as large as 15 cm in size. The size of the primary tumor is a significant prognostic factor. These tumors are usually not associated with other signs such as nipple secretion, nipple or skin retraction or skin edema, except for angiosarcomas [5].

The appearance of breast sarcoma on the mammogram is non-specific. The most common finding is a non-circumscribed mass or an area of focal asymmetry [6]. Although it is not the most frequent presentation, hyperdense circumscribed masses have been described on the mammogram (Figure 4). Malignant phyllodes tumors are more frequently seen on mammography as circumscribed masses without intralesional calcifications [7]. Many of the women are young and have a dense mammary parenchyma. This may hinder visualization of a lesion due to the effect of the overlying fibroglandular tissue that may obscure its edges.

In the study by Yang et al., 19% of the patients had no mammographic evidence of a tumor, while it was visible on ultrasound. Consequently, ultrasound is useful to confirm the presence of a mass when a palpable abnormality is found [6]. On ultrasound, these tumors appear as a solid oval-shaped mass with circumscribed or microlobulated contours. Small lesions might not be distinguishable from a fibroadenoma [8]. Larger tumors are heterogenous and may show cystic components (Figure 3) and some of them may appear hypervascular on color Doppler assessment [9].

Despite the possibility of achieving an adequate initial diagnosis by means of fine needle aspiration, this type of biopsy has a limitation when it comes to definitive immunohistochemical sub-classification and the determination of the degree of differentiation. Consequently, trucut needle biopsy is the recommended strategy for diagnosis [3].

These two types of tumors share a potential of hematogenous spread, mainly to the lungs, bones and liver and, therefore, plain chest films of the lung and liver and hepatobiliary ultrasound are mandatory. Recently, thoracoabdominal contrast CT has been used to rule out metastatic lesions to those organs [4].

The most important differential diagnoses include breast metaplastic carcinomas, breast metastatic sarcomas of extramammary primary tumors, and juvenile fibroadenomas, which may reach a significant size [3].

The main goal of treatment in primary sarcomas and malignant phyllodes tumors is surgical resection with broad margins, including the biopsy site. Complete resection with adequate negative margins is the most important determining factor of long-term survival. Obtaining an oncologic margin of at least 1 cm is recommended, and if these margins can be achieved without compromising the cosmetic appearance of the breast, a breast-conserving surgery can

be offered [10,11]. However, given the large mean size of primary tumors, mastectomy has been the strategy most frequently reported in the literatura [2].

The rate of regional lymph node involvement in sarcomas in general is less than 3%, so lymph node dissection is not required in these tumors, except in the cases of lymph node involvement documented by pathology testing [12]. Sentinel lymph node biopsy is not indicated either [3,4].

Clinical studies based mainly on case series have shown better local control when resection with breast-conserving surgery is complemented with adjuvant radiotherapy, in particular when the resection is marginal or inadequate. This approach may also be recommended for patients with sarcoma or malignant phyllodes tumor of high grade or more than 5 cm in size, due to the high rate of local recurrence. However, this approach is still very controversial given the lack of sound scientific evidence due to the small number of cases included in the studies [4]. Kim et al. published a univariate and multivariate analysis using the SEER database (Survelliance, Epidemiologic and End Results) with the aim of assessing the impact of radiotherapy on cancer-specific survival. They included 1974 patients with malignant phyllodes tumors and although patients with poor prognostic factors such as larger tumor size and high histologic grade were treated more frequently with postoperative radiotherapy, its use did not translate into a difference in disease-specific survival, regardless of the type of surgery performed [13].

In the event the use of adjuvant therapy is considered, case series studies suggest that it should be administered within a period of time of less than 30 days after surgery at a dose not lower than 48 Gy [4]. This approach has resulted in five-year disease-specific survival rates as high as 91%, both in sarcoma as well as phyllodes tumor patients [14].

The role of chemotherapy in the adjuvant setting is even more controversial because no benefit on overall survival has been observed, despite an advantage on disease-free survival. An ifosfamide/doxorubicin-based regimen is recommended [4]. When distant metastatic disease appears, systemic cytotoxic chemotherapy plays a very important role, using anthracycline-based regimens, although other agents like trabectedin and pazopanib have been introduced [11]. The two patients were discussed together with the clinical oncologist, and given that adjuvant chemotherapy was found to be of minimum benefit, it was not provided.

The overall 5-year survival reported in the clinical studies ranges between 14% and 91% and that variability depends on factors such as histological type, tumor size, the degree of differentiation and the presence of metastasis at the time of diagnosis [5]. Consequently, early diagnosis is the best way to improve survival. Lim et al. reported similar five-year overall and disease-free survival rates for patients with breast sarcomas and patients with malignant phyllodes tumors (86.5% versus 78.5% p=0.792, respectively, and 59.1% versus 57.4% p=0.816, respectively) [2]. The disease-free survival rate varies between 33% and 52% [15]. A meta-analysis of 54 studies including a total of 9234 reported a local recurrence rate of 18% for malignant phyllodes tumors. Local resection with breast-conserving surgery was shown to be associated with a higher risk of relapse (OR 2.32; 95% CI 1.01–5.30; p = 0.05) and, in general, a positive margin compared with negative margins is associated with a five-fold increase in the risk of local recurrence (OR 6.85; 95% CI 1.58–29.64) [16].

Despite the differences in diagnostic pathologic criteria, the two tumor groups considered in this study share more similarities than differences in terms of clinical behavior, therapeutic strategies and prognosis, and this is the reason why many series include both types of tumors. Recurrences of malignant phyllodes tumors are usually in the form of typical high-grade sarcomatous lesions, as was the case in one of the patients reported. In order to improve future prognosis, the recommendation is to identify these conditions early and provide timely management.

References

1. Nathan Roberts, Dianne M Runk (2015) Aggressive Malignant Phyllodes Tumor, International Journal of Surgery Case Reports 8: 161-165.
2. Lim SZ, Selvarajan S, Thike AA, Nasir ND, Tan BK, et al. (2016) Breast sarcomas and malignant phyllodes tumours: comparison of clinicopathological features, Treatment strategies, prognostic factors and outcomes. Breast Cancer Res Treat 159: 229-244.
3. Klopcic U, Lamovec J, Luzar B (2009) Fine neddle aspiration biopsy of primary breast myxofibrosarcoma. Acta Cytol 53: 109-112.
4. Duncan MA, Lautner MA (2018) Sarcoma of the breast. Surg Clin N Am 98: 869-876.
5. Matsumoto RAEK, Hsieh SJK, Chala LF, de Mello GGN, de Barros N (2018) Sarcomas of the breast: findings on mammography, ultrasound, and magnetic resonance Imaging. Radiol Bras 51: 401-406.
6. Yang WT, Hennessy BT, Dryden MJ, Valero V, Hunt KK, et al. (2007) mammary angiosarcomas: imaging findings in 24 patients. Radiology 242: 725-734.
7. Liberman L, Bonaccio E, Hamele-bena D, Abramson AF, Cohen MA, et-al. (1996) Benign and malignant phyllodes tumors: mammographic and sonographic findings. Radiology 198: 121-124.
8. Wurdinger S, Herzog A, Fischer D, Marx C, Raabe G, et al. (2005) Differentiation of Phyllodes Breast Tumors from Fibroadenomas on MRI. AJR 185: 1317-1321.
9. Glazebrook KN, Magut MJ, Reynolds C (2008) Angiosarcoma of the breast. AJR Am J Roentgenol 190: 533-538.
10. Yogi V, Singh OP, Malviya A, Ghori HU (2018) Effect of postoperative time for Adjuvant radiotherapy in malignant phyllodes tumor: an institutional experience. J Can Res Ther 14: 1054-1058.
11. Yamazaki H, Shimizu S, Yoshida T, Suganuma N, Yamanaka T, et al. (2018) A case of undifferenciated pleomorphic sarcoma of the breast with lung and bone metastases. Int J Surg Case Rep 51: 143-146.
12. Hocevar M, Marinsek ZP, Zidar A (2004) Myxofibrosarcoma of the breast as an unusual variant of malignant fibrous histiocytoma: report of a case. Surg Today 34: 752-754.
13. Yi-JunKim, KyuboKim (2017) Radiation therapy for malignant phyllodes tumor of the breast: an analysis of SEER data. The Breast 32: 26-32.
14. McGowan TS, Cummings BJ, O´Sullivan B, Catton CN, Miller N, et al. (2000) An analysis of 78 breast sarcoma patients without distant metastases at presentation. Int J Radiat Oncol Biol Phys 46: 383-390.

15. Lino de Faria A, Moreno-García C, de Andrade-Rodriguez G, Dumbra Toloni LH, Uyeda GBK, et al. (2018) Advanced stage breast sarcoma Treatment in a third world country public hospital. Case Rep Ob Gyn 2018.

16. L Yu, Chen Y, Zhu L, Cartwright P, Song E, et al. (2019) Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. Ann Surg Oncol 26: 1263-1275.