

Leiomyosarcoma of the Breast in a 48-Year Old Male

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This is a case of a 48-year old male with left-sided 9.0cm x 8.0cm exophytic, foul-smelling, bleeding breast mass. Core needle biopsy revealed a malignant phylloides tumor. He underwent total mastectomy and final histopathology showed a primary breast leiomyosarcoma staining positive for smooth muscle actin. A review of cases of primary breast leiomyosarcoma was done and to date, there are only 70 documented. The treatment of breast sarcomas still follows those strategies for soft tissue sarcomas in other locations. An important prognosticating factor is complete resection on initial treatment. Lymph node metastasis is rare for sarcomas in general.

Key words: Leiomyosarcoma, breast neoplasms, simple mastectomy, staining and labeling

Breast cancers in general, can be divided into two groups: the carcinomas and the sarcomas. Carcinomas arise from the epithelial component of the breast which are cells that line the lobules and terminal ducts. Carcinomas encompass majority of all breast cancers. Sarcomas, on the other hand, are rare cancers that come from the stromal (connective tissue) components of the breast i.e. myofibroblasts and blood vessel cells. 1,2,3 Primary breast sarcomas account for 0.2% to 1.0% of all breast malignancies and less than 5.0% of all soft tissue sarcomas. In a clinicopathologic study conducted by the Mayo Clinic in 2004 of 27,881 malignant breast tumors, the prevalence of primary breast sarcomas among breast cancers was found to be 0.0006%. 4,5

This report describes a rare case of primary breast leiomyosarcoma in an adult male, noting the existing cases in the literature and reviewing the main pathology, treatment and prognosis.

The Case

A 48-year old, married, Filipino male from Bicol consulted at the emergency room of this hospital for a bleeding left breast mass. The breast mass was noted six years prior with a size of 0.5cm x 0.5cm. Two years after, with a size of around 2.0 cm, he sought consult and subsequently had it excised. Result was not known to the patient. One year thereafter, the mass recurred and grew into "fist-size" and subsequently becoming ulcerated. On review of systems, there was weight loss of ten kilograms in three months. He had a brother who died due to an unknown brain tumor. For the personal and social history, he was a non-smoker, not an alcoholic drinker, worked as a jeepney driver and there was no exposure to radiation or pesticides.

Upon presentation, there was an 8.0cm x 5.0cm fungating, foul smelling mass on the central aspect of the left breast with points of bleeding, with the nipple areolar complex not anymore distinguishable from the mass (Figures 1A & B). There were no enlarged axillary lymph nodes palpated. Core needle biopsy revealed malignant phylloides. A contrast-enhanced CT scan of the chest (Figure 2) revealed a 5.3cm x 10.1cm x 9.8cm lobulated, exophytic breast mass on the left and non-calcified pulmonary nodules, right upper lobe, which cannot totally rule out an infectious process or metastatic focus. No liver masses were noted on ultrasound.

He underwent Total Mastectomy. Intraoperatively, the breast mass has areas of necrosis and bleeding, and the nipple-areola complex was not distinguishable, measuring 9.0cm x 8.0cm. Grossly, margins were negative. (Figures 1C-F).

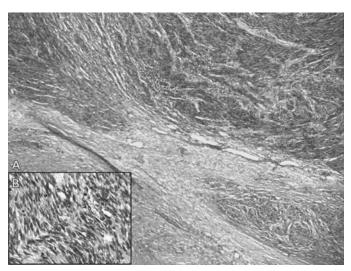
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Figures 1A-1F. The mass on the central aspect of the left breast with the nipple areolar complex no longer distinguishable from the mass (1A & 1B). The mass has areas of necrosis and bleeding (1C-1F).



Figure 2. On CT scan, a lobulated, exophytic breast mass (on the left) and non-calcified pulmonary nodules (on the right upper lobe) were seen.

Final histopathology results revealed Leiomyosarcoma, Grade II (Figures 3A & B), staining positive for smooth muscle actin (Figure 4). Final diagnosis is Leiomyosarcoma, Left Breast, Stage 1 (G2T2aN0Mx).



Figures 3A & 3B. Final histopathology results revealing Leiomyosarcoma, Grade II.

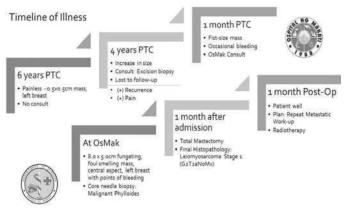


Figure 4.

Discussion

Leiomyosarcoma (sarcoma from smooth muscle) is one of the most frequent soft tissue sarcomas with an

estimate of 10% to 20% of the newly-diagnosed cases.⁶ Breast leiomyosarcomas are very rare.⁷ To date, there are only about 70 cases reported (Table 1) and six of

them are male; making the present case, the seventh case, and the first case of male breast leiomyosarcoma in the Philippines and second in Asia.

Table 1. Review of cases of primary leiomyosarcoma of the breast.

Author	Year	Sex	Age	Side	Size (cm)	Treatment
Crocker and Murad	1969	M	51	R	5.0	Radical Mastectomy
Haagensen	1971	F	77	L	8.0	Mastectomy
Cameron	1974	F	40	-	4.5	Simple Mastectomy
Pardo-Mindan	1974	F	49	L	7.0	Simple Mastectomy
Barnes	1977	F	55	L	3.0	Simple Mastectomy
Hernandez	1978	M	53	L	4.0	Modified Radical Mastectomy
Chen	1981	F	59	L	5.6	Simple Mastectomy
Callery	1984	\mathbf{F}	56	-	2.0	Simple Mastectomy
Callery	1984	F	54	-	3.0	Simple Mastectomy
Yatsuka	1984	F	56	L	1.5	Radical Mastectomy
Gobardhan	1984	F	50	L	9.0	Modified Radical Mastectomy
Nielsen	1984	F	24	R	1.5 (1962) r	Excision in 1960, 1962
					1.0 (1965) r	Excision
					2.0 (1966) r	Simple Mastectomy
Une	1986	F	62	0	2.0	Radical Mastectomy
Yamashina	1987	F	62	Ĺ	2.5	Simple Mastectomy
Arista-Nasr	1989	F	50	R	4.5 (1980)	Wide Local Excision
71115ta 14a51	1707	1	50	10	2.3 (1986) r	Wide Local Excision
Farkas	1991	M	61		2.5 (1700)1	Wide Local Excision
Parham	1992	F	52	L	3.0	Mastectomy
Lonsdale	1992	F	60	L	2.0, 4.0	Excision-Mastectomy
Lonsdate	1//2	1	00	L	(18 mos. later)	Lacision-iviastectomy
Waterworth	1992	F	58	L	4.0	Wide Local Excision with Level 2 Axillary
waterworth	1//2	1	50	L	4.0	Lymph Node Sampling
Wei	1993	F	36	R	4.0	Modified Radical Mastectomy
Boscaino	1994	F	56	R	2.5-4.0	Excision (1981)-Radical Mastectomy (1984)
Boscaino	1994	F	45	L	1.9-2.2	Biopsy (1985)-Wide Local Excision (1989)
Levy	1994	F	35	R	4.0	Simple Mastectomy
Falconieri	1997	F	83	R	6.0	Radical Mastectomy
Falconieri	1997	F	86	R	8.0	Simple Mastectomy
	1997	F	47	R	2.0	Subcutaneous Simple Mastectomy
Ugras Gonzalez-Palacios	1997	F	62	L L	3.0	Simple Mastectomy
		F	80	L	6.5	
Gupta	2000	F F				Mastectomy with Axillary Clearance
Szekely	2001		73	R	4.8	Mastectomy
Hussien	2001	F	48	- T	2.0	Radical Mastectomy
Kusama	2002	F	55	L	0.5	Excisions (1996, 1997)-Simple Mastectomy (1998)
Shinto	2002	F	59	L	12	Simple Mastectomy
Wei	2003	F	52	R	4.0	Wide Local Excision
Markaki	2003	F	42	R	14	Modified Radical Mastectomy
Markaki	2003	F	65	Ĺ	5.2	Excision
Liang	2003	F	25	Ĺ	4.0	Excision
Saeger	2003	F	61	-	22	-
Adem	2004	F	67	-	2.0	Excision
Adem	2004	F	55	-	4.0	Mastectomy
Jayaram	2004	F	55 55	R	12	Modified Radical Mastectomy
Lee	2004	F	33 44	- -	3	Simple Mastectomy
Lee	2004	r F	52	-	4.5	Simple Mastectomy Simple Mastectomy
LCC	2004	I.	32	-	7.3	omple mastectomy

Stafyla	2004	F	53	L	23	Modified Radical Mastectomy
Munitiz	2004	F	58	R	4	Modified Radical Mastectomy
Gupta	2006	F	37	R	8	Wide Local Excision
Vu and Knudson	2006	F	-	-	23	Mastectomy
Gur	2006	F	40	R	8.0	Simple Mastectomy
Yu	2007	-	-	-	-	-
Dela Pena	2008	F	50	L	3.2	Mastectomy
Wong	2008	F	52	L	1.5	Mastectomy
Cobanoglu	2009	F	64	L	3.5	Modified Radical Mastectomy
Boehm	2010	M	62	R	4.6	Modified Radical Mastectomy
Masannat	2010	M	59	R	1.5	Simple Mastectomy
Fujita	2010	F	18	R	7.2	Simple Mastectomy
Can	2011	F	66	R	12	Radical Mastectomy
M'rabet	2011	F	40	L	6.0	Radical Mastectomy
Oktay	2011	F	44	L	3.5	Excision
Karabulut	2012	F	48	R	10	Radical Mastectomy
Rane	2012	F	19	L	8.0	Wide Local Excision
Amaadour	2013	F	44	R	9.2	-
Khan	2013	M	50	R	2.5	Modified Radical Mastectomy
Bassett	2013	F	20	L	2.5	Simple Mastectomy
Sokolovskaya	2014	F	58	R	15	Simple Mastectomy
Guedes	2014	F	46	R	1.6	Wide Local Excision
Kim	2015	F	51	L	0.5	Excision
Tajima	2015	F	50	L	4.8	Wide Local Excision
Salleh	2015	F	56	L	6.5	Wide Local Excision
Hayashi	2015	F	59	L	2.0	Wide Local Excision
Lee	2016	F	49	L	8.0	Simple Mastectomy
Present	2016	M	48	L	8.0	Simple Mastectomy

Table 2. Histologic grade

[N1] considered stage IV)

no distant metastasis

distant metastasis

distant metastasis cannot be assessed

Distant Metastasis (M)

Mx

M0

M1

Tumor Grade (G)				
Gx	grade cannot be assessed			
G1	well differentiated			
G2	moderately differentiated			
G3	poorly differentiated			
G4	poorly differentiated or undifferentiated			
Primary Tumor (T)				
Tx	primary tumor cannot be assessed			
T0	no evidence of primary tumor			
T1	tumor 5.0 cm or less in greatest dimension			
T1a	superficial tumor			
T1b	deep tumor			
T2	tumor 5.0 cm or larger in greatest dimension			
T2a	superficial tumor			
T2b	deep tumor			
Regio	Regional Lymph Node (N)			
Nx	regional lymph nodes cannot be assessed			
N0	no regional lymph node metastasis			
N1	regional lymph node metastasis (presence of positive nodes			

Treatment strategies used for soft tissue sarcomas on other sites are generally applied to breast sarcomas.^{1,8} Incidence of breast sarcomas increases with age, usually at the 7th decade. Known risk factors are: 1) history of irradiation, 2) chronic lymphedema, 3) vinyl chloride exposure, and 4) Epstein-Barr Virus infection in severe immunosuppression,^{2,6} which were not present in this case. They present usually as a large, painless, mobile mass that is rarely bilateral. They are larger than epithelial breast cancers. The median size is 5cm-6cm (range = 2cm-40cm). On the genetic level, regions deleted in 10q and 13q harbor the two important tumor suppressor genes: RB1 and PTEN.⁶

Preoperative diagnosis is difficult due to its rarity. The accuracy of fine-needle aspiration is often limited in establishing the histologic diagnosis of breast sarcomas. Core needle biopsy or excisional biopsy is recommended, as both methods are reliable and can provide enough tissue for histopathologic diagnosis and grading.^{2,3} Imaging of all breast abnormalities should include diagnostic mammography, ultrasound and in some cases,

breast magnetic resonance imaging. Likewise, metastatic work-up is the same with other breast malignancies. CT scan is utilized to check for distant metastasis.

Pathology

Grossly, leiomyosarcoma is a solid, rubbery, lobulated tumor. It becomes large and soft with areas of necrosis, hemorrhage and cystic degeneration.9 Histologically, leiomyosarcoma recapitulates the morphology of the smooth muscle tissue. This tumor demonstrates a spindle cell morphology on light microscopy and is often difficult to differentiate from other tumors of the same morphology. The morphology is characterized by sheets of alternating bundles and fascicles of densely packed spindle cells with abundant fibrillar eosinophilic cytoplasm and indistinct borders. The centrally located nucleus is blunt-ended and cigar-shaped. Necrosis, nuclear pleomorphism and mitosis are additional features of the tumor. 10 The immuno-histochemical profile shows a positive reaction for smooth muscle actin, vimentin, calponin, desmin and smooth muscle myosin heavy chains and a negative reaction for S100 and CD117.9 Leiomyosarcoma of the breast may originate from two locations: the smooth muscle bundles of nipple/areola complex and smooth muscle cells of vascular walls.¹¹

Staging

The histologic grade (Table 2), tumor size, and lymph node or distant metastasis comprise the staging (Table 3) of soft tissue sarcomas, including primary breast sarcomas. Unlike epithelial breast cancers, lymph node status is less informative because metastases to regional nodes are rare^{1,3,8} for sarcomas in general. The patient has grade 2 breast leiomyosarcoma, moderately-differentiated, tumor size of 10.0cm, without lymph node metastasis, however, distant metastasis was not fully assessed. He was in Stage 1 (G2T2aN0Mx).

Management

A multidisciplinary approach is used in the treatment of breast sarcomas; usually a team made up of surgeons, radiation oncologists and medical oncologists. ¹² Surgery

remains as the cornerstone treatment of localized sarcomas. The ability to perform a complete surgical resection with negative margins at the time of treatment on initial presentation is the most important prognosticating factor for survival. A positive margin is a strong predictor of local recurrence. There is a 38% risk of local recurrence after 6 years if the margins are positive compared to 12% if the margins are negative.

In 1982, a randomized-controlled trial including 43 patients of high grade soft tissue sarcomas comparing limb-sparing surgery with radiotherapy to amputation alone found out that there is no significant difference in overall survival and disease-free survival. Furthermore, a study of 77 patients on limb-sparing surgery without radiotherapy showed a local recurrence rate of 7%. 14 The resection margin status was seen to be the most substantial predictor of local recurrence. There is a 13% local recurrence rate in resection margins of <1cm and 0% in >1cm. Radical surgery is reserved only for cases where resection or re-resection with adequate margins cannot be performed without sacrificing the functional outcome. Table 4 shows treatment options based on stage.

Stage I (tumor defined as low grade, superficial, and deep)

Table 3. Tumor staging

Stage I (tu	mor acmica as ic	w grade, supermen	ai, and accp)
G1	T1a	N0	M0
G1	T1b	N0	M0
G1	T2a	N0	M0
G1	T2b	N0	M0
G2	T1a	N0	M0
G2	T1b	N0	M0
G2	T2a	N0	M0
G2	T2b	N0	M0
Stage II (tı	umor defined as h	igh grade, superfi	cial, and deep)
G3	T1a	N0	M0
G3	T1b	N0	M0
G3	T2a	N0	M0
G4	T1a	N0	M0
G4	T1b	N0	M0
G4	T2a	N0	M0
Stage III (tumor defined as	high grade, large,	and deep)
G3	T2b	N0	M0
G4	T2b	N0	M0
Stage IV (defined as any me	tastasis to lymph	nodes or distant sites)
Any G	Any T	N1	M0
Any G	Any T	N0	M1

Table 4. Treatment options based on stage.

Stage	Treatment	
I	Surgery with at least 1cm resection margin Re-resection versus postoperative radiotherapy if margins are 1.0cm or less Tumors less than 5cm are less associated with local recurrence and may be observed	
II-III	Pre-operative chemo-radiotherapy Surgery to obtain oncologically appropriate margins Radiotherapy boost with or without adjuvant chemotherapy	
Unresectable disease	Radiotherapy Chemotherapy Chemoradiation May proceed to surgery if responsive	
īV	Metastasectomy with or without preoperative or postoperative Chemotherapy with or without radiotherapy Regional node dissection for nodal involvement with or without chemotherapy with or without radiotherapy	
	Palliation Chemotherapy, radiotherapy, surgery, observation if asymptomatic Supportive care Ablative procedures (Radiofrequency ablation, cryotherapy) Embolization procedures SBRT	

Radiotherapy. This may be recommended for patients with tumors larger than 5cm, high grade, and resected with positive margins wherein repeat surgery is not feasible. Patients receiving preoperative radiotherapy followed by surgery need postoperative radiotherapy boost in patients with positive margins. Moreover, adjuvant radiotherapy improves disease-free survival but not necessarily overall survival.

Chemotherapy. There are less conclusive data on the use of chemotherapy. Single-agent doxorubicin has response rates varying between 10% and 20%. Leiomyosarcomas, however, are less responsive than other subtypes. Ifosfamide may be used as second line regimen but has a worse toxicity profile. Chemotherapy may be recommended for high grade or those tumors larger than 5cm.

Prognosis

Leiomyosarcomas metastasize commonly to the lung, bone and liver; uncommonly to the brain, skin, subcutaneous tissue, spleen and adrenals. The 5-year overall survival rate is 50% to 66%. Most treatment failures occur during the first 15 months due to positive margins. The 5-year disease free survival rate is 33% to 52%.¹

Conclusion

In the present case, the lines of resection were noted to be adequate however, the basal margin was at 0.2cm nearest the location of the tumor. Ideally, re-resection of the basal margin should be done. However, radiotherapy was highly recommended. The patient then was eventually advised radiotherapy.

Follow-up for these patients consists of history and physical examination every 3-6 months for 2-3 years then annually. Postoperative baseline and periodic imaging of the primary site is also ideal since there is an increased risk for locoregional recurrence in the patient. A chest CT scan can be recommended every 6-12 months postoperatively.

Patient Perspective

The patient was particularly concerned about his mass since it is very uncommon for a man to develop such a breast lesion. He wanted the mass to be treated as soon as possible since he was the breadwinner and had to go back to work to provide for his family. The patient was lost to follow-up after a consult at the outpatient department one month postoperatively. He did not return to the institution due to financial constraint.

The patient gave his consent to be studied by the institution's surgical team and for his case to be presented in this report.

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