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Breast Leiomyosarcoma: A Systematic Review and Recommendations for Management

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Background: Leiomyosarcomas of breast are very rare tumors, with only 54 cases reported in the literature to date.

Methods: We report a case of leiomyosarcoma in a 52-year-old woman who presented with a painless left breast mass in the upper outer quadrant of her left breast. It measured about 6 cm in diameter and was located within the breast parenchyma with no skin involvement. Mammogram was suggestive of BI-RADS IV lesion, and core biopsy of the lesion was inconclusive.

Results: Histopathology and immunohistochemistry of the excision biopsy of the mass confirmed the diagnosis of leiomyosarcoma approaching the specimen margins. The patient underwent simple mastectomy, which did not reveal any residual tumor or additional lesions. Follow-up for a year after her mastectomy did not show any local or systemic recurrence.

Conclusions: We reviewed the literature and summarize our findings as recommendations for management of leiomyosarcoma of breast.

Key words: Leiomyosarcoma – Breast cancer – Sarcoma breast, Immunohistochemistry – Mammogram – Radiation therapy

Sarcomas of the breast are a heterogeneous group of malignant tumors arising from the breast stromal cells. They account for less than 1% of all malignant lesions arising from breast. The most common subtypes of breast sarcoma include angiosarcoma, liposarcoma, malignant fibrous

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histiocytoma, fibrosarcoma, and leiomyosarcoma. Leiomyosarcomas of the breast are extremely rare tumors, with only 54 cases reported in the entire literature to date.

Case Presentation

We report on a 52-year-old woman with a diagnosis of leiomyosarcoma in her left breast. She presented with a solitary, painless breast lump of 6 months' duration without any other local or systemic symptoms. Her past medical, social, and family histories were noncontributory. Clinical examination revealed a 6-cm firm mass in the upper outer quadrant of the left breast. The mass was located within the breast tissue, free from skin and chest wall, and did not involve the nipple-areolar complex. Ultrasonography of the mass showed a well-circumscribed, heterogeneous, and hypoechoic mass measuring 5 cm in diameter. Mammography classified the lesion as a Breast Imaging Reporting and Data System (BI-RADS) score of IV. Core biopsy was performed but was inconclusive. In light of high clinical suspicion, the mass was surgically excised with wide margins. Histopathology diagnosis of high-grade leiomyosarcoma with vascular invasion was rendered, and sarcoma was less than 1 mm from the surgical margins. Hence, simple mastectomy was performed. The final pathology did not show any residual tumor or additional lesions. The patient was followed up for 12 months and was found to have no recurrence and is clinically well.

Discussion

Primary sarcomas of the breast are nonepithelial malignancies of the breast with an estimated SEER (Surveillance, Epidemiology and End Results Program of the National Cancer Institute) database incidence of 4.5 cases per 1 million women.[1] Leiomyosarcoma subtype represents 2.5% to 6% of all primary breast sarcomas. Primary breast sarcoma was first described in 1887, and the first case of leiomyosarcoma was published by Crocker and Murad[2] in 1968. It was initially reported as fibrosarcoma and was then characterized appropriately as leiomyosarcoma based on optical and electron microscopy findings.

Primary sarcomas of breast arise *de novo*, whereas secondary sarcomas result from previous radiotherapy or after chronic lymphedema. The origin of leiomyosarcoma of breast is unknown and is postulated to originate from the smooth muscle cells of the lactiferous ducts or blood vessels, or the erector pili muscle at the periphery of the areola. Clinical information about leiomyosarcomas of the breast is limited by the rarity of their occurrence. As a result, case reports are the only available literature on primary breast leiomyosarcoma. Literature search for leiomyosarcoma of the breast from the PubMed, Embase, and Google Scholar databases showed only 54 cases to date (Table 1). Our review also included non–English-language literature in view of the rarity of this tumor.

Leiomyosarcomas of breast present clinically as a large, painless, firm mass within the breast. They are typically found in postmenopausal women, although several case reports describe younger patients (age 18–37 years; Table 1).[11,17,19,30,37,42,47,55] The mean age of the patients was 56.1 years (range, 18–80 years) in our review. The size of the mass at presentation varied from 0.9 to 23 cm, with a mean size of 5.6 cm. Imaging modalities were not very specific and were more often suggestive of a hypoechoic, heterogeneous mass or phyllodes tumor on both ultrasound and mammogram. Similarly, magnetic resonance imaging evaluation was also nonspecific and was more often suggestive of phyllodes tumor, demonstrating a phyllode-shaped hypointense mass on T1 imaging and intermediate/heterogenous intensity on T2 imaging.

Fine-needle aspiration cytology (FNAC), core biopsy, incisional biopsy, or excisional biopsy was performed in 34 patients (63%) to obtain preoperative tissue diagnosis. FNAC of the mass was reported preoperatively in 18 reported cases and showed sarcomatous cells in 11 of them (61%). Other FNAC features of leiomyosarcoma breast include the following: histiocytic-like plump spindle cells, abundant vacuolated cytoplasm, and large hyperchromatic nuclei with irregular nuclear contours and nucleoli.[28] But features that overlap with malignant fibrous histiocytoma, metaplastic carcinoma, and high-grade phyllodes tumor make subtype-specific diagnosis with FNAC difficult. Core biopsy was also found to be more nonspecific and showed spindle cell neoplasms (Fig. 1). Excision biopsy was shown to be more specific, with 7 of the 8 patients who underwent excision biopsy receiving their final diagnosis with it (87.5%). Ultrasound-guided suction biopsy has also been shown to provide a specific preoperative diagnosis of leiomyosarcoma.[49] Histopathology of the final resected specimen showed the tumor to be composed of pleomorphic and hyperchromatic spindle-shaped

Table 1 Literature search results

Source	Year	Age, y	Size, cm	Mitosis (per 10 hpf)	IHC	Treatment	Ct/Rt	Recurrence	Final follow-up
Crocker Murad	1969	51	5	Common	n/a	RM			—
Haagensen [35]	1971	77	8	Very frequent		SM	—		Alive, 14 y
Pardo Mindan et al. [25]	1974	49	7	16		SM	—		Alive, 6 mo
Barnes and Pietruszka	1977	55	3	10		SM	—		Died 4 y 4 mo later with CVA
Hernandez	1978	53/M	4	15		MRM	—		Alive, 1 y 2 mo
Chen	1981	59	5.6	3		SM	—	Liver mets after 15 y	Alive, 16 y
Callery	1984	56	2			SM	—	—	Alive, 39 mo
Callery	1984	54	3			SM	—	—	Alive, 53 mo
Yatsuka	1984	56	1.5	21		RM	—	—	Alive, 4 y 7 mo
Gobardhan	1984	50	9	5		MRM	—	—	Alive, 2 y
Nielsen	1984	24	1.5 (1962), 1 (1965), 2 (1966)	2 (1962), 8 (1965), 14 (1966)	SMA	WLE (1962, 1965, 1966), SM (1966)	—	Local, lung, scalp	Died 20 y later
Yamashina	1987	62	2.5	11	Actin, desmin, vimentin, myosin	SM	—	—	Alive, 2 y 2 mo
Arista-Nasr	1989	50	4.5 (1980), 2.3 (1986)	4		WLE	—	—	Alive, 6 y 4 mo
Parham	1992	52	3	29		SM	—	—	Alive, 6 mo
Lonsdale and Widdison	1992	60	2, 4 (18 mo later)	10	SMA, desmin, vimentin	SM	—	—	Alive, 3 mo
Waterworth	1992	58	4	10	SMA, desmin, vimentin	WLE + AC	—	—	Alive, 1 y
Wei	1993	36	4			MRM	—	—	Died 14 mo later
Boscaino	1994	56	2.5/4	2		WLE (1981)/RM (1984)	—	—	Alive, 9 y
Boscaino	1994	45	1.9 (1985)/ 2.2 (1989)	2		E (1985)/WLE (1989)	—	—	Alive, 40 mo
Levy	1995	35	4	2	SMA, actin	SM	—	—	Alive, 6 mo
Falconieri	1997	83	6	20	Muscle-specific actin, vimentin, desmin	RM	—	—	Alive, 10 mo
Falconieri	1997	86	8	11	Muscle-specific actin, vimentin, desmin	SM	—	—	Alive, 8 mo
Uğraş	1997	47	2	3	SMA	SM	—	—	Alive, 1 y 6 mo
González-Palacios [10]	1998	62	3	10		SM	—	—	Alive, 17 y
Gupta	2000	80	6.5	5–8		SM + AC	—	—	Alive, 2 y
Hussien	2001	49	2	12	SMA, desmin	WLE / SM + axillary node dissection	—	—	Alive at 18 mo
Székely	2001	73	4.8	20–22	SMA, vimentin, desmin	SM + axillary lymphadenectomy	—	—	Aliver, 12 mo
Kusama	2002	55	1 cm (1996 – leiomyoma)	Few	SMA, vimentin but negative for desmin	WLE (1996, 1997)/SM (1998)	Ct	Lung, lumbar spine	Alive, 4 y 8 mo

Table 1 Continued

Source	Year	Age, y	Size, cm	Mitosis (per 10 hpf)	IHC	Treatment	Ct/Rt	Recurrence	Final follow-up
Shinto	2002	59	12	19		SM, Ax lymphadenectomy	Ct	Local, lung	Died at 8 mo
Wei	2003	52	4	22	SMA, vimentin, desmin	WLE	—	—	Alive, 3 mo
Markaki	2003	42	14	50	SMA, vimentin, desmin, fibronectin	MRM	Ct		Alive, 3 y
Markaki	2003	65	5,2	10	SMA, vimentin, desmin, fibronectin	E	—	—	Alive, 18 mo
Liang	2003	25	4	5	Actin	EB	—	—	Alive, 32 mo
Adem	2004	67	2			EB	—	—	Died 7 mo later
Adem	2004	55	4			SM	—	—	Died 77 mo later
Jayaram	2004	55	12			MRM	—	—	Local recurrence
Lee	2004	44	3	6–12	SMA, desmin, vimentin	SM	—	—	Alive, 13 mo
Lee	2004	52	4.5	6–12	SMA, desmin, vimentin	SM	—	—	Alive, 17 mo
Stafyla	2004	53	23			MRM	Rt	—	Alive, 2 y
Munitiz	2004	58	4	14	SMA, desmin, vimentin	MRM	Ct	—	Alive, 1 y
Gür	2006	40	8	10	SMA, vimentin	SM		—	Alive, 4 y
Gupta	2006	37	8	15	MSA, desmin, vimentin	WLE	—	—	Alive, 36 mo
Vu	2006	61	23			SM	—	—	Alive, 10 mo
De la Pena and Wapnir	2008	50	3.2		SMA, desmin, calponin	SM	—	—	Alive, 11 mo
Wong	2008	52	1.5	7	SMA, vimentin	SM	—	—	Alive, 4 days
Cobanoglu et al. [5]	2009	64	3.5	12		MRM	—	—	Alive, 22 mo
Fujita	2010	18	7	10	SMA, vimentin, desmin	SM + SNL	—	—	Alive, 5 y
Kamio	2010	46	0.9	8 – Jan	SMA, vimentin, desmin	WLE		—	Alive, 8 y 4 mo
Karabulut	2012	48	10	Frequent	SMA	TM + Ax lymphadenectomy	—	—	Alive at 1 mo
Rane	2012	19	7	20–25	SMA, vimentin	WLE	—	—	Alive, 3 y
Amaadour	2013	44	9.2	6	Desmin, H-caldesmon	—	Ct	Lung	Died at 1 mo
Oktay	2011	44	3.5	Few	n/a	WLE	Rt	—	Alive, 12 mo
Sandhya	2010	54	7	10	SMA, desmin	TM+ Ax lymphadenectomy	—	—	Alive, 12 mo
Bassett	2014	20	2.2	Frequent	SMA	EB, TM + Ax lymphadenectomy	—	—	—
Ilyas	2015	52	6	Frequent	SMA, actin, vimentin	EB, SM	—	—	Alive, 12 mo

Ct, chemotherapy; hpf, high-power fields; n/a, not applicable; Rt, radiotherapy; SMA, smooth muscle actin.

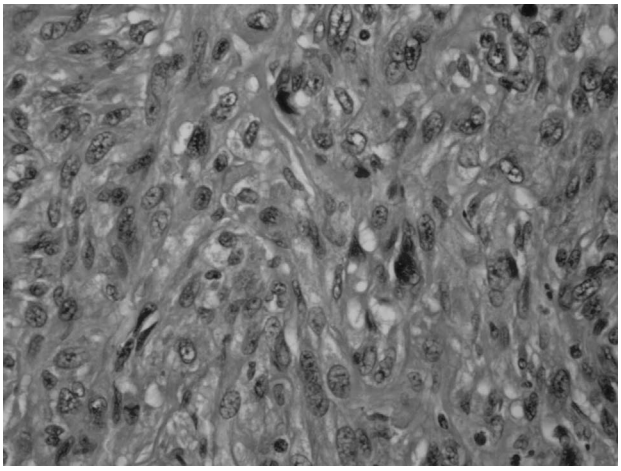

Fig. 1 Microscopic examination reveals tumor composed of hypercellular spindle cells resembling smooth muscle with moderate to severe nuclear pleomorphism (hematoxylin-eosin, original magnification ×10).

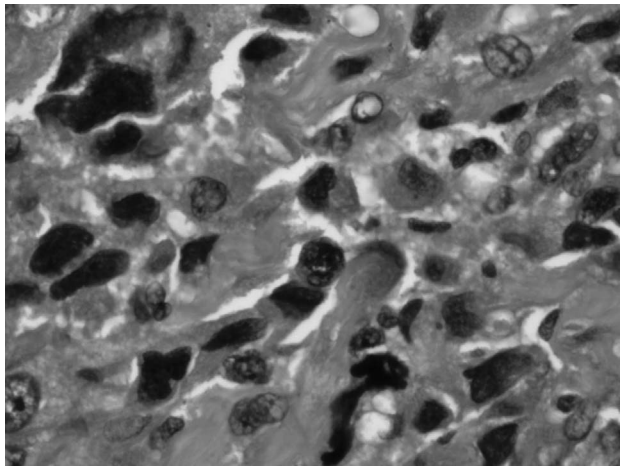

Fig. 2 Higher-power magnification showed osteoclast-like giant malignant cells with bizarre nucleus and high mitotic activity (hematoxylin-eosin, original magnification ×40).

cells arranged in an interdigitating fascicle, with mitoses within tumor cells ranging from 2 to 50 per 10 high-power fields (Fig. 2).

Since 1984 immunohistochemistry has been shown to be essential in confirming a diagnosis. The most consistent proteins identified with immunohistochemistry include muscle-specific or smooth muscle actin and vimentin. Desmin was the third most common protein reported to be positive but has also been reported to be negative with immunohistochemistry in a few cases.[25,26] Metaplastic carcinoma also exhibits a prominent sarcomatous component, and some leiomyosarcomas have epithelioid features. And leiomyosarcomas of the breast need to be differentiated from metaplastic carcinoma with mesenchymal metaplasia, which has an adenocarcinomatous component.[50] Stromal component of metaplastic carcinoma is positive for cytokeratin, vimentin, and S100. Another cytopathologic differential diagnosis is myoepithelial carcinoma. Leiomyosarcoma and myoepithelial carcinoma are positive for actin; S100 and focal cytokeratin expression suggests a diagnosis of myoepithelial carcinoma. Other cytopathologics differentials include pleomorphic lobular carcinoma, melanoma, and metastatic lesions within the breast. Morphologically and immunohistochemically, primary and secondary breast leiomyosarcomas are identical, and hence a thorough workup to exclude other organ involvement is mandatory.[51,52]

Surgery has been the only accepted curative treatment option. As with other sarcomas, adequate surgical margins are essential. Simple mastectomy with or without axillary lymph node biopsy or lymphadenectomy was performed in 51.9% of patients (28 patients), wide local excision in 27.8% (15 patients), and radical or modified radical mastectomy in 20.3% (11 patients). Axillary lymph node evaluation was performed in 20 patients (36.3%) as part of mastectomy or with wide local excision, and it was not positive for malignancy in any of them. Local recurrence was recorded in 7 patients (12.7%), with 6 of the recurrences reported after wide local excision with resection margins varying from 5 mm to 2 cm, and occurred between 18 months and 4 years after excision. Local recurrence after mastectomy has only been reported in a case of locally advanced leiomyosarcoma of breast involving the pectoral muscles.[27] Systemic recurrence has been reported in 7 patients (12.7%) and has been shown to occur in liver, lung, brain, bones—including lumbar spine—and in contralateral breast.

The size of the primary tumor or the type of excision (local excision or mastectomy) does not appear to affect prognosis, although this is difficult to ascertain based on case reports only. Also, because of the rarity of its incidence, consensus recommendations on surgical resection margins are not available. Fujita *et al*[42] from their review of the data recommend a 3-cm margin as an adequate margin, although such margins may not be possible in all cases.[42] No role for lymph node evaluation has been noted unless the preoperative diagnosis of leiomyosarcoma is not certain. Mitotic activity of the

tumor also does not appear to be of any prognostic value.[26]

Data on adjuvant chemotherapy are limited, with 9 of the reported patients having had either chemotherapy or radiotherapy. No treatment recommendations could be deciphered from these reports on adjuvant chemotherapy or radiotherapy, and they need to tailored to individual cases in liaison with medical oncologists.

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