# Primary Breast Leiomyosarcoma with Metastases to the Lung in a Young Adult: Case Report and Literature Review

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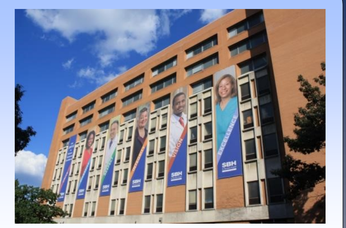

## Introduction

Primary breast sarcoma is an uncommon neoplasm with incidence of 0.5-1%. Breast leiomyosarcoma (LMS) is a rare subtype of breast sarcoma, constituting 5-10% of breast sarcomas [1], making it an extraordinarily rare malignancy. There are less than 70 documented cases in the literature, the majority of which are case reports, with the earliest appearing in 1968.

Because of this rarity, diagnosis and treatment have been historically nonuniform; however, more recent literature has described a more consistent approach.

In this case report, we describe a primary breast LMS in a premenopausal adult female who despite mastectomy, developed metastatic disease in the lung.

## Case Description

A 20 year-old female patient with a past medical history of neurofibromatosis type 1, presented with a three centimeter palpable left breast mass at the inferior aspect of the nipple-areolar complex at the 6 o'clock position.

The mass reportedly developed after sustaining blunt trauma to the left breast. Initial ultrasound revealed a likely hematoma. However, at a three-month follow up for repeat ultrasound, the mass had increased in size.

Excisional biopsy revealed a 27 millimeter leiomyosarcoma with marked nuclear pleomorphism and 30 abnormal mitotic figures for every 10 high powered field. Immunohistochemical stain was positive for smooth muscle actin, vimetin, desmin, and CD68 but negative for cytokeratin 7 and S-100. Her staging was Stage IIA.

Metastatic work-up included negative chest x-ray and positron emission tomography - computed tomography (PET-CT). PET-CT identified retroareolar soft tissue density in the left breast indicative of metabolic activity with a standardized uptake value of 8.8.

In addition, metabolic activity was seen in the left axillary lymph node. Due to the possibility of recurrence of LMS, a left breast total mastectomy was performed with two sentinel lypmh nodes sent as well. Both nodes had no evidence of LMS; however, the left breast was positive for residual LMS without lymphovascular invasion.

Two years and eight months after mastectomy, workup in the emergency department for complaints of dyspnea, coughs, and chest pain revealed a lung nodule. Chest computed tomography revealed a large right sided mass (14.3x13.9x11.1cm) involving all lobes of the right lung and extending into the mediastinum as well as a moderate-sized pericardial effusion

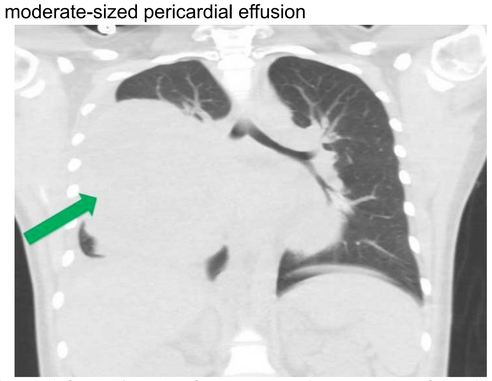

Figure 1: Coronal section from computed tomography of the chest, demonstrating large breast leiomyosarcoma metastasis to the lung in right hemothorax with mediastinal extension (GREEN ARROW).

Pericardial window drained bloody fluid of which cytology demonstrated no malignant cells. Pericardial biopsy revealed fibrinous pericarditis with neutrophils, lymphocytes, fibrin and fibroblasts without the presence of any malignant cells. Core needle biopsy confirmed metastatic LMS to the lung (FIGURE 1).

After treatment of the pericardial effusion, she was transferred to a tertiary care center with sarcoma specialists to be enrolled in a clinical trial for further treatment of her metastatic disease.

## Discussion

Although sarcomas can occur anywhere in the body, less than 1% of all breast neoplasms consist of sarcomas [1-4]. LMS is a rare subtype of breast sarcoma. The diagnosis of breast LMS is generally post-menopausal [3-4]. Due to its rarity, in all age groups, there have been 68 documented cases in the literature, mostly isolated case reports—to our knowledge, ours is the first manuscript to detail all case reports of breast LMS (TABLE 1).

Clinically, breast LMS may be difficult to distinguish from other breast neoplasms especially since physical exam and imaging findings are often identical to other types of malignancy. Typically, at diagnosis, breast LMS may be several centimeters in diameter and well-circumscribed [3,5]. Mammogram, ultrasound, and other imaging modalities are also typically non-specific [5]. The masses are often mistaken for benign etiologies, but more commonly mistaken for more common breast malignancies, as there are no characteristic imaging features of these tumors.

Definitive diagnosis relies on the results or core needle [5], or excisional biopsy. Histologically, potential origin of the malignant cells include; blood vessel smooth musculature, smooth muscle of the nipple areolar complex, or malignant transformation from benign neoplasms, such as leiomyoma or other spindle cell tumors [1,6].

Diagnostic histologic characteristics consist of interlacing spindle cell bundles [1,3] with further grading via degree of atypia, mitotic activity, cellularity, and nuclear pleomorphism [3].

Diagnosis is confirmed with immunohistochemical stains. LMS stains positive for smooth muscle actin, desmin, vimetin, and muscle specific actin [1,3, 5-6] and negative for S-100, cytokeratins, and epithelial markers [1, 5-6]. Clinical staging follows standard TMN classification for breast malignancy.

Treatment of early-stage disease is initially operative – local resection or mastectomy. LMS tends to recur locally; thus, the local resection would be inadequate unless wide negative margins are achieved [4-5, 7]. Fujita et al. have recommended a negative margin of at least three centimeter for maximum effectiveness; however two centimeter margins can be utilized for breast conservation therapy [7].

Furthermore, because hematogenous dissemination is the main route of metastasis, there have been no documented case of axillary lymph node invasion; thus, it is possible that lymph node dissection is unnecessary [2, 4, 6-7]. However, because of the rarity of this disease and limited number of studies to guide treatment decisions, sentinel lymph node biopsy is often done to confirm no lymph node involvement [7].

Chemotherapy and radiotherapy have unclear benefit. Radiotherapy has been recommended after local excision [7]. Chemotherapy, is indicated for metastatic disease however the effect on morbidity and mortality, and benefit is unclear [1,6]. Chemotherapy parallels treatment for other types of sarcoma. Anthracyclines are currently considered the first line chemotherapy with the addition of ifosfamide [5]. However, Fujita et al describe two cases that resulted in effective chemotherapy treatment with cycles of vincristine, adriamycin, cyclophosphamide, and dacarbazine [7].

Metastasis of breast LMS most often occurs in the lungs and bones; however, it may also disseminate to other less common organs. Because LMS is generally very slow growing, development of metastatic disease may occur years after the initial resection [6] similar to our case. In addition, Liang et al describe situations where metastasis to the liver and brain occurred 16 and 20 years after the initial treatment of breast LMS, respectively [3].

The risk of metastasis seems to be unrelated to tumor size [6]. Isolation of circulating tumor cells (CTC) during the early stages of invasive sarcomas may detect the risk of metastatic LMS [2]. Detecting CTC would not have been possible for our patient, as she did not present with invasive disease at the initial time of diagnosis. Because sarcomas exhibit micro-dissemination within the blood for years before clinical metastatic disease develops, it is possible that detecting these CTCs to identify patients at the stage between local and distant metastatic disease will help guide clinical and therapeutic decisions [2].

Chinen et al describe the method to isolate sarcomatous CTC simply by their physical size and not by any cellular marker; isolation by size of tumor cells has a relatively reliable sensitivity since sarcoma cells are documented to be larger than lymphocytes [2]. However, more studies are necessary for a true prognostic value of CTC detection.

Prognosis is generally optimistic compared to the other breast sarcomas [1]. Five year survival rates are 63%, 36%, and 14% for localized, regional, and distant disease respectively. However, because of the prolonged risk of recurrence, long-term follow-up may be indicated [6].

| AUTHOR(S) | JOURNAL | YEAR | NUMBER OF CASES |
|---|---|---|---|
| Norris HJ and Taylor HB | *Cancer* | 1968 | 1 |
| Haagensen CD | *Diseases of the Breast* | 1971 | 1 |
| Mindan P et al | *American Journal of Clinical Pathology* | 1974 | 1 |
| Hernandez FJ | *American Journal of Clinical Pathology* | 1978 | 1* |
| Barnes L and Pietruska M | *Cancer* | 1977 | 1 |
| Degrell I | *Acta Medica Academiae Scientiarum Hungaricae* | 1980 | 1 |
| Chen et al | *Cancer* | 1981 | 1 |
| Gobardhan | *The Netherlands Journal of Surgery* | 1984 | 1 |
| Nielsen BB | *Virchows Arichiv A* | 1984 | 1 |
| Yatsuka K et al | *Japanese Journal of Surgery* | 1984 | 1 |
| Callery CD et al | *Annals of Surgery* | 1985 | 2 |
| Yamashina M | *Japanese Journal of Clinical Oncology* | 1987 | 1 |
| Christensen L et al | *European Journal of Surgical Oncology* | 1988 | 1 |
| Arista-Nasr J et al | *American Journal of Clinical Pathology* | 1989 | 1 |
| Pollard SG et al | *Cancer* | 1990 | 1 |
| Alessi E et al | *The American Journal of Dermatopathology* | 1992 | 1 |
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| Waterworth PD et al | *British Journal of Surgery* | 1992 | 1 |
| Bosciano A et al | *Tumori* | 1994 | 2 |
| Gutman H et al | *Surgery* | 1994 | 2 |
| Levy RD et al | *South African Journal of Surgery* | 1995 | 1 |
| Ugras S et al | *Surgery Today* | 1997 | 1 |
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| Gupta RK et al | *Acta Cytologica* | 2000 | 1 |
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| Boehm D et al | *World Journal of Oncology* | 2010 | 1* |
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| Masannat Y et al | *Case Reports in Medicine* | 2010 | 1* |
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| Fujita N et al | *The Breast* | 2011 | 1 |
| Oktay Y and Fikret A | *Journal of Surgical Case Reports* | 2011 | 1 |

TABLE 1: Patients with primary breast leiomyosarcoma documented in the Literature. *Male patients

## Conclusion

Physicians and surgeons treating breast leiomyosarcoma must be vigilant of potential lung metastases in order to optimize short- and long-term oncologic outcomes.

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