



# Radiation-induced Stromal Sarcoma of Breast: A Case Report and Literature Review

Amir Shahram Yousefi Kashi <sup>1</sup> and Farzad Taghizadeh-Hesary <sup>2,\*</sup>

<sup>1</sup>Cancer Research Center, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Radiation-Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\*Corresponding author: Department of Radiation-Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: f\_taghizadeh@sbmu.ac.ir

Received 2020 July 08; Revised 2020 July 13; Accepted 2020 July 14.

## Abstract

**Introduction:** Post-irradiation mammary stromal sarcoma (MSS) is a rare condition, and it is worth learning new knowledge from each case.

**Case Presentation:** We present the case report of a 59-year-old female with a medical history of breast cancer, who presented with an axillary mass on the same side. The patient was further evaluated and finally diagnosed with MSS with chondroid differentiation. Thereafter, she underwent neoadjuvant chemotherapy to facilitate the surgical resection of the tumor. However, she experienced local progression and lung metastasis during chemotherapy.

**Conclusions:** MSS with chondroid differentiation was resistant to the standard chemotherapy regimens of sarcoma. Radiotherapy is a potential choice in the case of chemoresistant MSS. Further trials may reveal this notion.

**Keywords:** Breast, Natural History, Radiotherapy, General Surgery

## 1. Introduction

Breast sarcomas are a group of heterogeneous tumors that constitute less than 1% of all primary breast cancers and less than 5% of all soft tissue sarcomas (1). Mammary stromal sarcoma (MSS) accounts for 0.03% of all primary breast malignancies among Iranian patients (2-4). It may contain heterogenous metaplastic components (e.g. muscle, bone, or cartilage) (5). A difficulty is considered in the management of MSS with chondroid differentiation, especially due to the undefined natural history. To our knowledge, no study has yielded the natural history of MSS with chondroid differentiation. This gap in the literature has hampered its management. In this case report, we try to give an example to shed light on the natural history of MSS with chondroid components.

## 2. Case Presentation

A 59-year-old female presented to our hospital with a chief complaint of armpit lump. Physical examination showed a large well-movable mass in her right axilla (Figure 1).

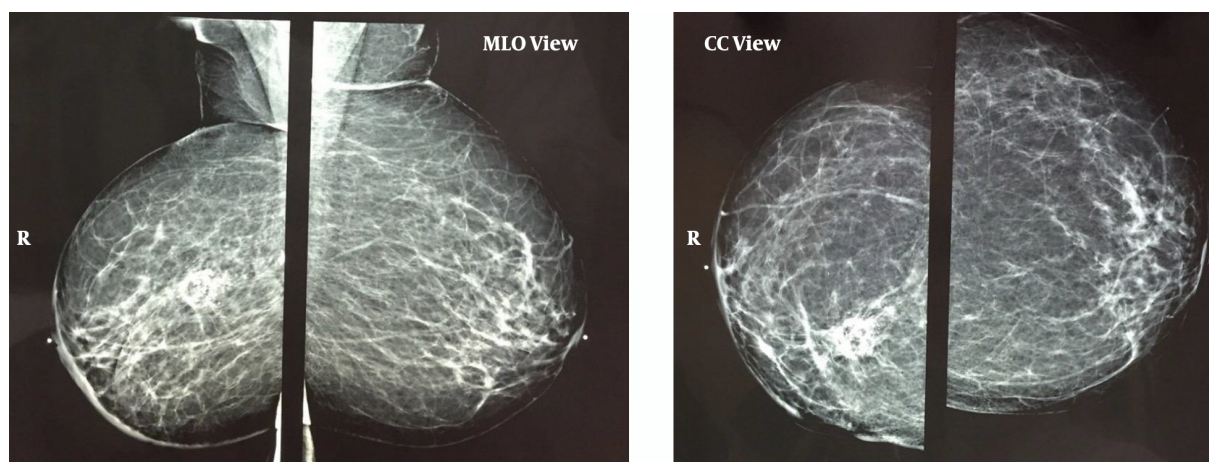
The physical examination of her breast was unremarkable. Her medical history was significant for right breast invasive ductal carcinoma, the status of post lumpectomy,



Figure 1. The right axillary mass.

chemotherapy, and radiotherapy of 5 years ago. Mammography demonstrated post-irradiation changes in the right breast (Figure 2).

Based on ultrasonography (US), a lobulated heterogeneous hypoechoic soft tissue mass measuring  $10 \times 7 \times 5.3$  cm in the axillary tail of the right breast posterior to the pectoralis muscle was detected. She underwent US-guided fine-needle aspiration of the axillary mass. In the cytopathology report, no atypical cell was detected. Based



**Figure 2.** Post-breast-conserving therapy scar is seen in the right breast, which contains central lucency and calcification due to fat necrosis. Diffuse Right breast skin and trabecular thickening accompanied by post-surgical distortion in the breast and axilla are visible. Axillary mass is not demonstrated in the mammogram. MLO, mediolateral-oblique; CC, cranial-caudal.

on hematoxylin and eosin (H & E) stain of the core needle biopsy, the primary diagnosis was metaplastic breast carcinoma with chondroid differentiation. For confirmation of diagnosis, Immunohistochemical (IHC) staining was performed. The tumor tissue was positive for CD10 and vimentin, while it was negative for cytokeratin AE1/AE3, cytokeratin CAM 5.2, P63, CD34, epithelial membrane antigen (EMA), S100, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). The KI67 was positive in 5% of tumor cells. The final diagnosis was reported as CD10<sup>+</sup> MSS with chondroid differentiation, possibly secondary to prior radiotherapy. No distant metastasis was detected in the initial staging workup. Because of the large tumor size, preoperative chemotherapy with doxorubicin plus ifosfamide (AI) regimen was planned. However, the tumor significantly progressed during chemotherapy courses, both local and systemic. Metastatic workup demonstrated 2 right-sided pulmonary nodules measuring 7 mm and 5 mm and mild right pleural effusion favoring metastatic involvement. The case was presented at the Tumor Board of Shohada-e Tajrish General Hospital. Due to the extension of the tumor, the surgical resection of the growing retro pectoral mass was unavailable. Considering the long interval from prior radiotherapy (RT), the palliative radiation of the chest wall mass was planned for her (6). Informed consent was taken from the patient.

### 3. Discussion

Radiation-induced sarcoma (RIS) is a well-known treatment complication that constitutes about 3% of all sarco-

mas (7). RIS was initially described in the early 1900s by Perthes et al. Later, the diagnostic criteria of RIS were introduced by Cahan et al. (8) as the lesions of different histology that are located at the RT field with a latency period of more than 4 years. In 2010, the sarcoma group of Memorial Sloan Kettering Cancer Center (MSKCC) modified this definition and declared that RIS may occur as soon as 6 months after RT (9). Over the past decades, the incidence of RIS has significantly risen (10). This may be due to an increase in the survival of irradiated patients by more effective systemic therapies, more utilization of RT (e.g. with the increased rate of breast-conserving surgery), and the increased use of modern RT techniques (e.g. intensity-modulated radiation therapy) (11). Studies have shown the poor prognosis of RIS in comparison with primary sarcomas. The RIS is relatively higher grade, larger, and deeper in location. Furthermore, prior RT impairs effective surgery and RT that further mitigates the prognosis (9). The MSS is a rare entity among Iranian females that accounts for 0.03% of breast cancers (2). It may be developed de novo or arise secondary to RT (12). In 1962, Berg et al. (13) defined the pathologic features of MSS. According to the 2013 World Health Organization classification of tumors, stromal sarcoma is categorized as the tumors with uncertain differentiation (14). Microscopically, MSS is characterized by spindle cells with nuclear atypia, brisk stromal mitotic activity, and IHC positivity for vimentin and CD10, and negativity for CD34 (15, 16). Histologically, its differential diagnosis is cystosarcoma phyllodes and metaplastic carcinoma. It can be differentiated from the former and later by sparing the lobular component and IHC characteristics, respectively (17). Because of the rarity of this disease, the therapeutic ap-

proach remains controversial. Similar to other sarcomas, surgery is the only potentially curative modality. Considering limited lymphatic involvement, wide local excision or mastectomy without lymphadenectomy is the most accepted surgical approach for MSS. The primary goal is resection of the tumor with negative margins (18). In the case of inoperable tumors, other modalities (e.g. chemotherapy or RT) can potentially facilitate the resection. However, the tumor of our case was resistant to the AI regimen. This case report can provide a clue to try alternative choices as neoadjuvant chemotherapy for MSS with chondroid components. Future studies can reveal this notion. Followings are learning points of this case report:

- 1) MSS is an extremely rare entity; so, the mainstay of therapy remains a major dilemma.
- 2) MSS has an aggressive natural history that intends to spread either locally or distant.
- 3) MSS with chondroid differentiation was resistant to the standard chemotherapy of sarcoma (i.e. AI regimen).
- 4) Radiotherapy is a potential choice in the case of chemoresistant MSS.

## Footnotes

**Authors' Contribution:** ASYK provided the data and supervised the manuscript. FTH designed and wrote the manuscript. ASYK and FTH revised the manuscript. All authors read and approved the final manuscript.

**Conflict of Interests:** The authors declare that they have no conflict of interest.

**Funding/Support:** Not applicable.

**Informed Consent:** Informed consent was taken from the patient.

## References

1. May DS, Stroup NE. The incidence of sarcomas of the breast among women in the United States, 1973-1986. *Plast Reconstr Surg.* 1991;**87**(1):193-4. doi: [10.1097/00006534-199101000-00045](https://doi.org/10.1097/00006534-199101000-00045). [PubMed: [1984266](https://pubmed.ncbi.nlm.nih.gov/1984266/)].
2. Jazayeri SB, Saadat S, Ramezani R, Kaviani A. Incidence of primary breast cancer in Iran: Ten-year national cancer registry data report. *Cancer Epidemiol.* 2015;**39**(4):519-27. doi: [10.1016/j.canep.2015.04.016](https://doi.org/10.1016/j.canep.2015.04.016). [PubMed: [26070507](https://pubmed.ncbi.nlm.nih.gov/26070507/)].
3. Keramati A, Shandiz FH, Taghizadeh-Hesary F, Gharib M. Metaplastic breast carcinoma with osseous remnant post standard treatment of invasive ductal carcinoma: case report and review of literature. *Eur J Oncol Invalid date Invalid date.* 2018;**23**:52-6.
4. Akbari H, Hesary F, Nikoukar L. Distribution of Breast Cancer Biomarkers by Age in Iran. *J Anal Oncol.* 2017;**6**(1):7-13. doi: [10.6000/1927-7229.2017.06.01.2](https://doi.org/10.6000/1927-7229.2017.06.01.2).
5. Tang PH, Petrelli M, Robeck PJ. Stromal sarcoma of breast: a light and electron microscopic study. *Cancer.* 1979;**43**(1):209-17. doi: [10.1002/1097-0142\(197901\)43:1<209::aid-cnrcr2820430132>3.0.co;2-q](https://doi.org/10.1002/1097-0142(197901)43:1<209::aid-cnrcr2820430132>3.0.co;2-q). [PubMed: [761163](https://pubmed.ncbi.nlm.nih.gov/761163/)].
6. Houshyari M, Kashi AS, Varaki SS, Rakhsha A, Blookat ER. Regional lymph node radiotherapy in breast cancer: single anterior supraclavicular field vs. two anterior and posterior opposed supraclavicular fields. *Electron Physician.* 2015;**7**(2):1032-8. doi: [10.14666/2015.1032-1038](https://doi.org/10.14666/2015.1032-1038). [PubMed: [26120411](https://pubmed.ncbi.nlm.nih.gov/26120411/)]. [PubMed Central: [PMC4477762](https://pubmed.ncbi.nlm.nih.gov/PMC4477762/)].
7. Penel N, Grosjean J, Robin YM, Vanseymortier L, Clisat S, Adenis A. Frequency of certain established risk factors in soft tissue sarcomas in adults: a prospective descriptive study of 658 cases. *Sarcoma.* 2008;**2008**:459386. doi: [10.1155/2008/459386](https://doi.org/10.1155/2008/459386). [PubMed: [18497869](https://pubmed.ncbi.nlm.nih.gov/18497869/)]. [PubMed Central: [PMC2386887](https://pubmed.ncbi.nlm.nih.gov/PMC2386887/)].
8. Cahan WG, Woodard HQ, Higinbotham NL, Stewart FW, Coley BL. Sarcoma arising in irradiated bone: report of eleven cases. 1948. *Cancer.* 1998;**82**(1):8-34. doi: [10.1002/\(sici\)1097-0142\(19980101\)82:1<8::aid-cnrcr3>3.0.co;2-w](https://doi.org/10.1002/(sici)1097-0142(19980101)82:1<8::aid-cnrcr3>3.0.co;2-w). [PubMed: [9428476](https://pubmed.ncbi.nlm.nih.gov/9428476/)].
9. Gladly RA, Qin LX, Moraco N, Edgar MA, Antonescu CR, Alektiar KM, et al. Do radiation-associated soft tissue sarcomas have the same prognosis as sporadic soft tissue sarcomas? *J Clin Oncol.* 2010;**28**(12):2064-9. doi: [10.1200/JCO.2009.25.1728](https://doi.org/10.1200/JCO.2009.25.1728). [PubMed: [20308666](https://pubmed.ncbi.nlm.nih.gov/20308666/)]. [PubMed Central: [PMC3651600](https://pubmed.ncbi.nlm.nih.gov/PMC3651600/)].
10. Salminen SH, Sampo MM, Bohling TO, Tuomikoski L, Tarkkanen M, Blomqvist CP. Radiation-associated sarcoma after breast cancer in a nationwide population: Increasing risk of angiosarcoma. *Cancer Med.* 2018;**7**(9):4825-35. doi: [10.1002/cam4.1698](https://doi.org/10.1002/cam4.1698). [PubMed: [30044058](https://pubmed.ncbi.nlm.nih.gov/30044058/)]. [PubMed Central: [PMC6143936](https://pubmed.ncbi.nlm.nih.gov/PMC6143936/)].
11. Hall EJ. Intensity-modulated radiation therapy, protons, and the risk of second cancers. *Int J Radiat Oncol Biol Phys.* 2006;**65**(1):1-7. doi: [10.1016/j.ijrobp.2006.01.027](https://doi.org/10.1016/j.ijrobp.2006.01.027). [PubMed: [16618572](https://pubmed.ncbi.nlm.nih.gov/16618572/)].
12. Blanchard DK, Reynolds C, Grant CS, Farley DR, Donohue JH. Radiation-induced breast sarcoma. *Am J Surg.* 2002;**184**(4):356-8. doi: [10.1016/s0002-9610\(02\)00943-1](https://doi.org/10.1016/s0002-9610(02)00943-1). [PubMed: [12383902](https://pubmed.ncbi.nlm.nih.gov/12383902/)].
13. Berg JW, Decrosse JJ, Fracchia AA, Farrow J. Stromal sarcomas of the breast. A unified approach to connective tissue sarcomas other than cystosarcoma phyllodes. *Cancer.* 1962;**15**:418-24. doi: [10.1002/1097-0142\(196203/04\)15:2<418::aid-cnrcr2820150226>3.0.co;2-v](https://doi.org/10.1002/1097-0142(196203/04)15:2<418::aid-cnrcr2820150226>3.0.co;2-v). [PubMed: [13867580](https://pubmed.ncbi.nlm.nih.gov/13867580/)].
14. World Health Organization. *WHO Classification of Tumours of Soft Tissue and Bone IARC WHO Classification of Tumours.* Lyons, France: World Health Organization; 2013.
15. Kumar S, Sharma J, Ralli M, Singh G, Kalyan S, Sen R. Primary Stromal Sarcoma of Breast: A Rare Entity. *Iran J Pathol.* 2016;**11**(5):469-73. [PubMed: [28974969](https://pubmed.ncbi.nlm.nih.gov/28974969/)]. [PubMed Central: [PMC5604113](https://pubmed.ncbi.nlm.nih.gov/PMC5604113/)].
16. Yang GZ, Li J, Jin H, Ding HY. Is mammary not otherwise specified-type sarcoma with CD10 expression a distinct entity? A rare case report with immunohistochemical and ultrastructural study. *Diagn Pathol.* 2013;**8**:14. doi: [10.1186/1746-1596-8-14](https://doi.org/10.1186/1746-1596-8-14). [PubMed: [23356903](https://pubmed.ncbi.nlm.nih.gov/23356903/)]. [PubMed Central: [PMC3564823](https://pubmed.ncbi.nlm.nih.gov/PMC3564823/)].
17. Arora S, Rana D, Pujani M, Chauhan V. Malignant Spindle Cell Tumor Breast-a Diagnostic Dilemma. *Indian J Surg Oncol.* 2018;**9**(3):387-90. doi: [10.1007/s13193-018-0750-x](https://doi.org/10.1007/s13193-018-0750-x). [PubMed: [30288003](https://pubmed.ncbi.nlm.nih.gov/30288003/)]. [PubMed Central: [PMC6154355](https://pubmed.ncbi.nlm.nih.gov/PMC6154355/)].
18. Zelek L, Llombart-Cussac A, Terrier P, Pivot X, Guinebreteiere JM, Le Pecoux C, et al. Prognostic factors in primary breast sarcomas: a series of patients with long-term follow-up. *J Clin Oncol.* 2003;**21**(13):2583-8. doi: [10.1200/JCO.2003.06.080](https://doi.org/10.1200/JCO.2003.06.080). [PubMed: [12829679](https://pubmed.ncbi.nlm.nih.gov/12829679/)].