Sarcomas of the Breast with a Spotlight on Angiosarcoma and Cystosarcoma Phyllodes

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KEYWORDS

• Sarcoma • Breast • Angiosarcoma • Cystosarcoma • Phyllodes

KEY POINTS

- Breast sarcomas are a distinct tumor group and should be treated differently than breast carcinomas.
- Angiosarcomas as a subgroup are aggressive neoplasms and one of the more common subgroups identified in breast sarcomas.
- Cystosarcoma phyllodes, often not included in sarcoma reviews, are a unique tumor group and should be approached in a similar fashion to breast sarcomas.

INTRODUCTION

Breast sarcomas are a diverse group of neoplasms arising from the nonepithelial components of the breast. Because of the heterogeneity of the histologic subtypes, it is always difficult to lump them into one overarching consensus review. They comprise less than 1% of breast cancer and less than 5% of all sarcomas.[1,2] Annual incidence has been estimated at approximately 45 new cases per 10 million women.[3] There is mounting concern that this will increase over time given the common use of adjuvant radiation for breast carcinoma. Despite the diversity of subtypes, it is important to separate breast sarcomas out as a unique tumor group in an effort to highlight the divergent clinical course from breast carcinoma and encourage the importance of referring patients to a multidisciplinary sarcoma team when logistically feasible.

SUBTYPES AND RISK FACTORS

By and large, all histologic subtypes of sarcoma have the possibility of arising in the breast. Some of the more common subtypes include undifferentiated pleomorphic

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high-grade sarcoma, myxofibrosarcoma, angiosarcoma, and spindle cell sarcoma. Other subtypes (leiomyosarcoma, Ewing, rhabdomyosarcoma, synovial sarcoma, chondrosarcoma, and extraosseous osteosarcoma) have also been reported in smaller case series or case reports; however, these are exceedingly rare.[4,5] In general, with the exception of cystosarcoma phyllodes and primary or secondary breast angiosarcoma, when encountering a soft tissue sarcoma in the breast, the first course of action should be to exclude the possibility of another primary source that has metastasized to the breast.[6]

The two most commonly described risk factors for breast sarcoma include radiation, typically as a treatment for a previous malignancy (ie, mantle radiation for Hodgkin disease or breast carcinoma) and lymphedema (Steward-Treves syndrome).[7] Cahan and colleagues[8] in 1948 defined the criteria for postradiation sarcoma. The requirements are (1) evidence of an initial distinct malignant tumor different from the subsequent sarcoma, (2) development of the second malignant tumor in an irradiated field, (3) long interval between irradiation and development of sarcoma, and (4) histological confirmation of sarcoma. Occupational exposure to vinyl chlorides has been linked to hepatic angiosarcoma,[9] and artificial breast implants have been implicated but are controversial.[10,11] TP53 mutation can predispose to sarcomas in general, with some occurring in the breast.[12] Despite the possible causes, most breast sarcomas present without any obvious predisposing factor.

Radiation-associated sarcomas of the breast can develop after a wide range of time intervals, with a cumulative incidence of 0.3% at 15 years after radiation treatment reported in a case series of patients diagnosed between 1973 and 1997.[13] Whether this will decrease over time with improvement in radiation techniques and with dose reductions, or conversely, increase, as radiation is used more frequently and operations become more conservative, remains to be seen. Various subtypes have been reported in postradiation breast sarcomas, but angiosarcoma seems to be one of the most common. The median time to occurrence after radiation ranges from 5 to 8 years with a wide range of 1 to 16 years reported.[13–15] The risk increases with higher dose of radiation, exposure during childhood, concurrent dose of chemotherapy, and preexisting genetic conditions, such as BRCA-1 mutation.[16–18]

DIAGNOSIS AND STAGING

Diagnosis of breast sarcomas is made histologically by a percutaneous biopsy. Core biopsy is generally preferred to fine-needle aspiration, which will typically yield insufficient material.[19] Punch biopsies may be sufficient for radiation-associated angiosarcoma, which is typically a cutaneous sarcoma. For local staging, breast mammography, ultrasound, and breast MRI are most commonly used. In mammography, microcalcifications are not seen as frequently as in breast carcinomas; therefore, MRI may be a better modality.[20]

The 10-year overall survival of breast sarcomas was 62% in one series[21]; the 5- and 10-year relapse-free survival was 47% and 42% in another series whereby patients did not have distant metastases at presentation.[22] It is difficult to lump such a heterogeneous tumor group together and derive any meaningful data with regard to overall survival. But in various retrospective case series and reports, characteristics like histology, margin status, size, depth of tumor, and grade seem to be the overall driving prognostic factors.[5,21,23,24]

TREATMENT

The treatment paradigm for breast sarcoma has mirrored that of its soft tissue counterparts with the main objective being surgical resection with wide margins. This