

Primary Undifferentiated Pleomorphic Sarcoma of the Breast in a Male Patient: A Case Report and a Review of the Literature

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Abstract

Male breast cancer is a rare disease, accounting for less than 1% of all breast cancers. Like soft tissue sarcomas, breast sarcomas are a heterogeneous group of several subtypes: osteosarcoma, liposarcoma, fibrosarcoma, leiomyosarcoma, angiosarcoma, rhabdomyosarcoma, pleomorphic sarcoma, and sarcomas of uncertain differentiation. Undifferentiated pleomorphic sarcoma constitutes less than 5% of all sarcomas in adults. It is most frequently located in the extremities but has also been reported in the retroperitoneum and the abdomen. However, Localization in the breast is extremely rare, especially in patients with no history of radiation. In this report, we describe an unusual case of undifferentiated pleomorphic sarcoma of the breast in 60-years-old men who presented a tumor measuring over 4 cm with pain in the left breast. He noticed the mass 3 months previously. Breast ultrasound revealed a left tumor. The patient underwent total mastectomy without axillary lymph node dissection. Based on examination of the excised tumor, the initial pathologic diagnosis was atypical spindle-shaped cells with uncertain malignant potential. Histological findings with immunomarkers led to the final diagnosis of undifferentiated pleomorphic sarcoma. Following the simple mastectomy, the patient was given adjuvant hypofractionated radiotherapy. The follow up at 42 months was uneventful. This case highlights a rare and interesting variant of primary breast sarcoma presenting in a male patient. A review of the available literature with evaluation of the etiology, prognostic factors and treatment modalities of pleomorphic sarcoma of the breast are discussed.

Keywords: Undifferentiated pleomorphic sarcoma; Breast sarcoma; Male breast cancer

Introduction

The most common malignant tumor of the breast is adenocarcinoma 93.7%, Sarcomas account for less than 1% of all primary breast malignancies [1]. Undifferentiated pleomorphic sarcoma previously known as malignant fibrous histiocytoma (MFH), is a mesenchymal malignancy originates from the connective tissues of glands and composed of fibroblast and histiocyte like cells, mixed with pleomorphic giant and inflammatory cells [2] that shows no definable line of differentiation [3-5]. Breast sarcomas are commonly seen after radiotherapy. However, primary UPS has been rarely reported to involve the breast [6,7]. Owing to rarity of this entity, the exact treatment guidelines and prognostic variables are yet to be determined [8]. We believe that reporting such cases would contribute to establish treatment protocols of this rare tumor.

Case Presentation

We report a case of primary breast undifferentiated pleomorphic sarcoma (malignant fibrous histiocytoma) in 60-year-old men. He presented to our department to receive the postoperative radiotherapy. He had no known disease, no family history of malignancy and no prior history of radiation therapy. The patient had felt the lump about 3 months before. On physical examination there was a mass measuring 4 cm in diameter detected underneath the nipple and areola of the left breast, there was no palpable axillary nodes and the right breast appeared normal. Breast ultrasound (Figure 1) indicated a strong suspicion of malignancy and all laboratory findings, cancer marker CA15-3, chest X ray, ultrasonography of abdomen, revealed no abnormalities. The patient underwent total mastectomy without axillary lymph node dissection. Intraoperative frozen section analysis suggested spindle cell proliferation with R0 resection. The histological report macroscopically showed a breast tissue specimen measuring 10 × 7.5 × 5.5 cm, partially covered with skin measuring 9 × 6 cm. The cut surface revealed a whitish, fibrotic nodular tumor measuring 4.2 cm in greatest diameter. After fixation and inclusion in paraffin, microscopic

examination of the section of specimen showed marked pleomorphism admixed with bizarre giant cells, spindle cells, and zones of necrosis and myxoid features (Figures 2 and 3). The surgical margins were negative.



Figure 1: Breast ultrasound revealed a hypoechoic lesion with ill-defined borders measuring 42 × 32 × 30 mm, spiculated margins, posterior acoustic shadowing and microcalcifications.

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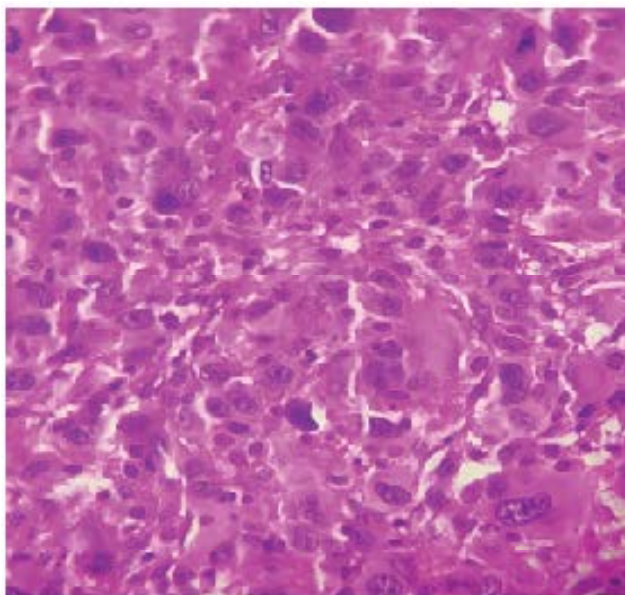


Figure 2: Low-power microphotograph showing obvious pleomorphic spindled cells.

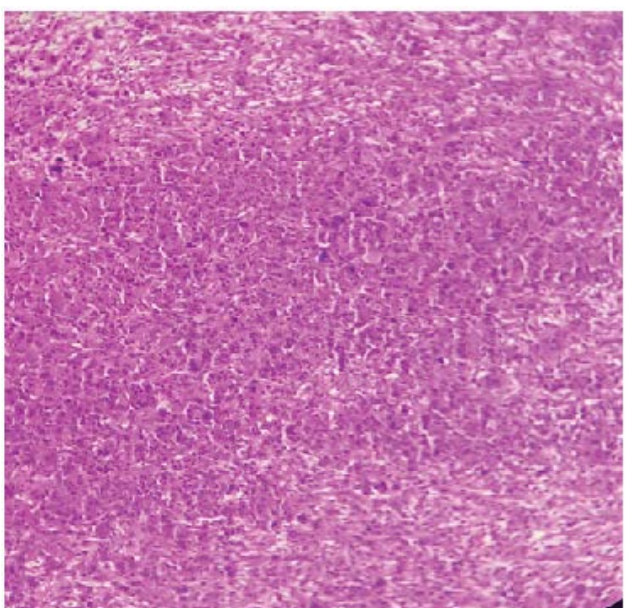


Figure 3: Marked nuclear atypia and mitotic activity.

Immunohistochemistry showed that the tumor was focally positive for smooth muscle actin with a Ki proliferative index of 70%. Cytokeratin, AE1/AE3, EMA, p63, PS100, SOX10, CD34, Desmin, Caldesmon, transgelin and MDM2 were all negative.

Based on histological features and immunohistochemical study, diagnosis of undifferentiated pleomorphic sarcoma was made. After surgery the patient underwent hypofractionated radiotherapy at a dose of 42 Gy to the chest wall with fractions of 2.8 Gy in 15 fractions with 2 tangential wedged elds by using 6 MV photons of a linear

accelerator. Radiotherapy proceeded without incident, except for a mild radiodermatitis. No adjuvant systemic therapy was suggested to the patient. The follow-up of the patient was performed every 3 months for the 1st year, every 4 months for the 2nd year, and 6 months thereafter. Physical examination was performed at every visit, and CT of thorax was obtained yearly. The patient remained disease free, and no evidence of local or systemic disease was detected after 42 months of follow-up.

Discussion

Male breast cancer is uncommon and represents less than 1% of all breast cancers, the overall incidence of male breast cancer continues to increase [9]. Primary sarcoma in the breast is extremely rare account for less than 1% of all breast malignancies and commonly seen after radiotherapy [10]. The risks of developing breast sarcoma are largely unknown. Some authors showed a significant correlation between external beam radiation of the breast or chest wall and the occurrence of sarcoma [11]. Angiosarcoma is the most common sarcoma type of breast, while undifferentiated pleomorphic sarcoma seems to be one of the rarer types [7,12]. The concept of undifferentiated pleomorphic sarcoma was first introduced in 1963 has undergone significant change over the past five decades [4,13].

This tumor is exceptional in male. Indeed, only 6 cases have been described in the literature [14-16]. Undifferentiated pleomorphic sarcomas often grow rapidly and then may be painful. Imaging methods and macroscopy may be shown well-circumscribed masses with heterogeneous composition. Further, they can be identified as pale fibrous and fleshy areas admixed with zones of (cystic) necrosis, hemorrhage, or myxoid features [17]. Microscopically, lesions exhibit cells showing marked pleomorphism admixed with bizarre giant cells, spindle cells, and variable foamy cells [18]. A storiform growth pattern and variable chronic inflammatory cells are also common [17].

Neither the symptoms nor the physical findings of undifferentiated pleomorphic sarcoma of the breast present any characteristic pattern that would easily suggest the diagnosis. Immunohistochemistry may be useful to distinguish primary breast sarcomas from non-mesenchymal malignant tumours and to delineate the level of differentiation of primary breast sarcomas [19]. Desmin, vimentin, smooth muscle antigen, CK, leukocyte common antigen, CD34, HMB-45, SMA, EMA, and S-100 protein should all be analysed in sarcoma patients.

As all soft tissue sarcomas, surgical ablation should always be the first treatment modality of breast sarcomas to insure an excellent local control. Mastectomy was regarded as the first-choice technique, in contrast, some studies have demonstrated no significant advantage to mastectomy in comparison to wide local excision. The role of axillary lymph node dissection is not well defined [20-22], it has been generally considered unnecessary for undifferentiated pleomorphic sarcoma of the breast, since these tumours rarely spread through the lymphatic system [23,24].

Commonly mastectomy without lymphadenectomy is the reference technique as used in our case report. Clear excision margin and larger tumour size are the two most important factors that determine the local recurrence as well as distant metastasis. A tumour size less than 5 cm is associated with a better overall survival. In the absence of prospective and randomized trials, the role of chemotherapy for breast sarcoma remains unclear [25,26] while hormonotherapy has been reported without known benefit [27,28].

In contrast to surgical ablation, there is widespread disagreement for the benefits of radiotherapy. Whilst some authors [29,30] did not

find any benefit for adjuvant radiotherapy, some authors suggest that postoperative radiation may play an important role in reducing local recurrence and improves the disease-free survival [31]. Radiotherapy should be considered for breast sarcomas >5 cm, especially if high-grade, and for patients with positive margins in whom resection is not feasible. However, RT cannot compensate for inadequate surgery, and reexcision to ensure clean margins is strongly encouraged in these cases.

The radiotherapy of a breast sarcoma must assure primarily an efficient target coverage with high prescribed doses to provide a better local control because even after radical surgery, local failures are common [32,33]. According to the recommendation on the management by the ESMO Clinical Practice Guidelines, the postoperative radiation therapy should be administered with the best technique available, at a dose of 50-60 Gy, with fractions of 1.8-2 Gy, possibly with boosts up to 66-68 Gy, depending on the presentation and quality of surgery [34,35].

Also, for the post-mastectomy irradiation, newer strategies such as IMRT and VMAT compared to the conventional radiotherapy, offer some improvement on target coverage, better protection of organs at risk, dose homogeneity, and conformity for this particular case of breast sarcoma [36-38]. The benefit of adjuvant RT for primary (*de novo*) breast sarcomas has not been proven in randomized trials. However, the high rate of local recurrence after surgery alone (up to one-third in some series [23-40]) provides the rationale for postoperative radiation therapy. The prognosis of undifferentiated pleomorphic sarcoma in the breast remains poor because the disease is very aggressive, fast-growing with 44% of local recurrence and 42% of the cases develop distant metastasis [39-41]. Overall 5-year survival of patients with undifferentiated pleomorphic sarcoma has been roughly 50%.

Conclusion

Undifferentiated pleomorphic sarcoma is a challenging tumor whether in terms of diagnosis or treatment. The biological differences from other primary breast tumors necessitate a corresponding difference in approach to diagnostic and management strategies. The therapeutic recommendations are difficult to establish with evolving techniques and limited patient numbers. However, the relatively poor prognosis associated with breast sarcoma has motivated many clinicians to treat patients aggressively with a multidisciplinary team approach necessitating surgeons, pathologists, radiotherapists, and medical oncologists to improve overall survival.

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