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Case Report

Breast Angiosarcoma with a Preoperative Diagnosis of Late Recurrence of Breast Cancer: A Case Report

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Keywords
Angiosarcoma · Late recurrence · Breast cancer · Mammary tumor · Surgery

Abstract
Angiosarcoma is a malignant mesenchymal tumor characterized by the presence of vascular endothelial cells. Although rare, angiosarcoma developing in the mammary glands has a poor prognosis. We report a case of breast angiosarcoma with a preoperative diagnosis of late recurrence of breast cancer. A 78-year-old woman noticed a tumor in her right breast and visited our hospital. The patient had undergone breast-conserving surgery and axillary lymph node dissection from the right breast 12 years before the visit. The tumor was diagnosed as T4bN0M0, stage IIIB. Anastrozole was administered as postoperative adjuvant therapy for 5 years; the patient also received 50-Gy whole-breast radiation therapy after surgery. Physical examination during her visit revealed an elevated lesion with blue purpura around the nipple in the right breast. We performed breast ultrasound and detected a well-defined 19.6 × 16.4 × 10.7 mm hypoechoic tumor in the left subareolar area. The patient underwent core needle biopsy (CNB). Based on the CNB specimen findings, she was suspected to experience late local recurrence after surgery. Therefore, she underwent total mastectomy after breast-conserving surgery. A dark-red tumor sized 18 × 12 mm was found in a specimen from the nipple. The pathological diagnosis of the specimen revealed short spindle-shaped tumor cells with strong nuclear pleomorphism and a significant interstitial fibrosis. Immunohistochemistry using D2-40 and CD31 antibodies showed irregular luminal proliferation at the anastomosis, infiltration into the surrounding tissue, and massive necrosis, thereby leading to the diagnosis of breast angiosarcoma. We have reported a case of breast angiosarcoma with a preoperative diagnosis of late recurrence of breast cancer.

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Background

Angiosarcoma is a malignant mesenchymal tumor characterized by the presence of vascular endothelial cells. Although rare [1, 2], angiosarcoma developing in the mammary glands has a poor prognosis [3–6]. By using imaging techniques and cytodiagnosis, it has not been possible to characterize angiosarcoma; moreover, tissue biopsy seldom yields an accurate diagnosis of angiosarcoma [7]. We report a case of breast angiosarcoma with a preoperative diagnosis of late recurrence of breast cancer.

Case Presentation

A 78-year-old woman noticed a tumor in her right breast and visited our hospital. She had undergone breast-conserving surgery and axillary lymph node dissection from the right breast 12 years before the visit. The tumor was diagnosed as T4bN0M0, stage IIIB, invasive ductal carcinoma, estrogen receptor (ER) positive, progesterone receptor (PgR) positive, and human epidermal growth factor receptor (HER) 2 negative; the surgical margin was negative. The nuclear atypia score, mitotic count, and nuclear grade were 3. Anastrozole was administered as postoperative adjuvant therapy for 5 years; the patient also received 50-Gy whole-breast radiation therapy after surgery. After completing the adjuvant therapy, she underwent regular follow-up at other hospitals without recurrence. She had no history or family history of addiction.

Physical examination during her visit revealed an elevated lesion with blue purpura around the nipple in the right breast (Fig. 1a). We performed breast ultrasound and detected a well-defined 19.6 × 16.4 × 10.7 mm hypoechoic tumor in the left subareolar area (Fig. 1b, c). Therefore, the patient underwent core needle biopsy (CNB). Following hematoxylin and eosin staining of the CNB specimen, we detected a high-grade necrosis and a high nuclear-cytoplasmic ratio in the tumor cells (Fig. 2a, b). Immunohistochemical analysis revealed the CNB specimen to be cytokeratin (CK) 7, CK20, gross cystic disease fluid protein (GCDFP), ER, PgR and HER2 negative; expression of Ki-67 was high (Fig. 2c). These pathological findings suggested the presence of a poorly differentiated breast tumor. Computed tomography scans did not show any lymph node or distant metastases. Based on these findings, the patient was suspected to experience late local recurrence after surgery. Therefore, she underwent total mastectomy after breast-conserving surgery. A dark-red tumor sized 18.0 × 12.0 mm was found in a specimen from the nipple (Fig. 3a). The pathological diagnosis of the specimen revealed short spindle-shaped tumor cells with strong nuclear pleomorphism and a significant interstitial fibrosis (Fig. 3b). Immunohistochemistry was performed, and the tumor cells were found to be vimentin positive and AE1/AE3, CK7, CK20, GCDFP, ER, PgR and HER2 negative; expression of Ki-67 was high. Immunohistochemistry using D2-40 and CD31 antibodies showed irregular luminal proliferation at the anastomosis (Fig. 3c), infiltration into the surrounding tissue, and massive necrosis, thereby leading to the diagnosis of breast angiosarcoma. During the postoperative follow-up period, when no treatment was provided, recurrence was not observed for 6 months after the surgery.

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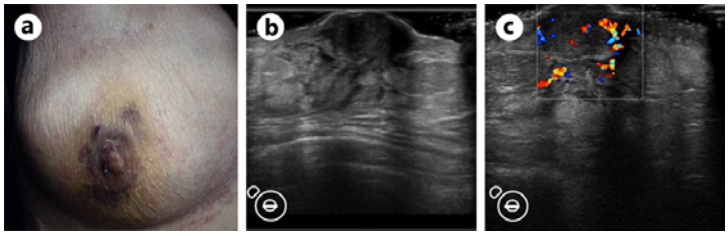

Fig. 1. Physical and ultrasonography findings. **a** Physical examination during the patient's visit revealed an elevated lesion with blue purpura around the nipple in the right breast. **b** We performed breast ultrasound and detected a well-defined 19.6 × 16.4 × 10.7 mm hypoechoic tumor in the left subareolar area. **c** Blood flow rich.

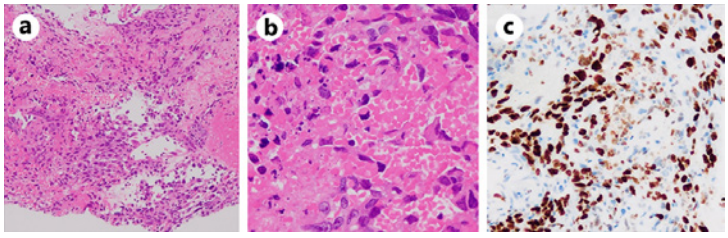

Fig. 2. Pathological findings of the core needle biopsy (CNB) specimen. **a**, **b** Following hematoxylin and eosin staining of the CNB specimen, we detected a high-grade necrosis and a high nuclear-cytoplasmic ratio in the tumor cells (**a** ×100; **b** ×400). **c** Immunohistochemical analysis revealed the CNB specimen to be cytokeratin (CK) 7, CK20, gross cystic disease fluid protein, estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 negative; expression of Ki-67 was high (**c** ×200).

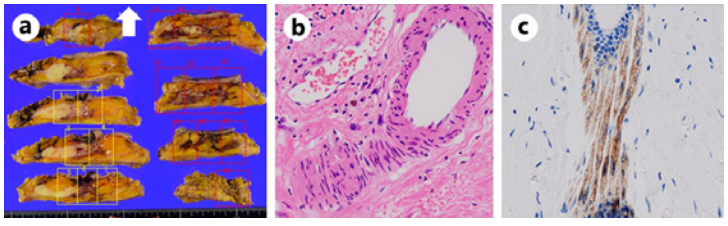

Fig. 3. Macro- and microscopic diagnosis of the resected specimen. **a** A dark-red tumor sized 18.0 × 12.0 mm was found in a specimen from the nipple. **b** The pathological diagnosis of the specimen revealed short spindle-shaped tumor cells with strong nuclear pleomorphism and a significant interstitial fibrosis (×200). Immunohistochemistry was performed, and the tumor cells were found to be vimentin positive and AE1/AE3, cytokeratin (CK) 7, CK20, gross cystic disease fluid protein, estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 negative; expression of Ki-67 was high. **c** Immunohistochemistry using D2-40 (×200) and CD31 antibodies showed irregular luminal proliferation at the anastomosis.

Discussion and Conclusion

Angiosarcoma, a malignant tumor that originates from the vascular endothelium, is roughly classified into primary and secondary angiosarcoma. Primary angiosarcomas are rare malignancies that form silent tumors in the breast parenchyma. The incidence of primary angiosarcoma is about 0.05% [1]. On the other hand, secondary angiosarcomas develop in different areas, including the skin, chest wall, and mammary glands after receiving radiation

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therapy for breast cancer. The incidence of secondary angiosarcoma is rising due to the increased use of preservation surgery for the treatment of breast cancer. It has been reported that secondary angiosarcomas usually develop 4–10 years (average, 7 years) after radiation therapy [2]. The patient in our study developed secondary angiosarcoma about 12 years after irradiation following breast-conserving surgery.

Regarding physical findings, the tumor is usually soft, with good mobility, and sometimes has a blue skin or purpura. By using imaging techniques, it has not been possible to characterize angiosarcoma [8, 9]; however, the presence of angiosarcoma has been reported to show a low-intensity signal in T1-weighted magnetic resonance images and a high-intensity signal in T2-weighted images, as well as high-contrast enhancement from the early to the later stages of dynamic study [8, 10–12].

Histologically, irregular vascular lumens supported by low- or high-grade tumors proliferate in the mammary tissue and infiltrate into the surrounding adipose tissue [13, 14]. Because grades vary between patients, it may be difficult to provide a definitive diagnosis from a small biopsy specimen [9]. In other words, in patients with high-grade tumors, it is difficult to differentiate angiosarcoma from carcinoma or other types of sarcoma due to the presence of solid tumors, necrosis, or mitotic figures in tumor cells. In patients with low-grade tumors, it is difficult to differentiate angiosarcoma from benign hemangioma or pseudoangiomatous stromal hyperplasia. Based on the pathological findings of the CNB specimen, the patient in this study was strongly suspected to have a poorly differentiated breast tumor rather than a high-grade tumor. However, surgical specimens from the patient showed proliferation of high-grade tumor cells with massive necrosis; additionally, after performing immunohistochemistry, the tumor cells were vimentin positive and AE1/AE3 negative. Therefore, the patient was suspected to have malignant mesenchymal tumors. Furthermore, immunohistochemistry for D2-40 and CD31 showed irregular luminal proliferation at the anastomosis, leading to the diagnosis of angiosarcoma.

Surgical resection is the first choice of treatment for breast cancer [15]. Because the possibility of lymph node metastasis is low in patients with angiosarcoma, axillary lymph node dissection may not be required, unless lymph node metastasis is detected [16]. Based on the high incidence of local recurrence and significant reduction in disease-free survival rate in patients with positive surgical margins, surgery achieving a negative surgical margin is desirable [15, 17]. While some studies reported that immunotherapy (interleukin-2) and chemotherapy (anthracyclines and taxanes) were effective for angiosarcoma treatment [5, 18], no optimal therapeutic strategy has been established yet.

Angiosarcoma has been reported to have a poor prognosis (5-year disease-free survival rate, 44%; survival rate, 61%) [3]. Tumor diameter (>5 cm) and tissue grade (high grade) have been identified as prognostic factors for angiosarcoma [3]. In this study, the patient had a small (tumor diameter, 1.8 cm) but high-grade tumor. Therefore, she requires a detailed follow-up in the future to reduce the risk of recurrence.

We reported a case of breast angiosarcoma with a preoperative diagnosis of late recurrence of breast cancer. A deeper understanding of the disease and a comprehensive differential diagnosis are required for effective treatment.

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Statement of Ethics

Written ethical approval for the publication on the present case report (including images) was obtained from the patient.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest to disclose.

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No funding was received for this article and the authors have no conflicts of interest directly relevant to this report.

Author Contributions

All authors were involved in the preparation of this manuscript. R.K. collected the data and wrote the manuscript. S.K., Y.A., T.M., S.I., and W.G. performed the operation and designed the study. S.K. and K.H. summarized the data and revised the manuscript. S.T., Y.K., and M. Ohsawa performed the pathological diagnosis. K.H. and M. Ohira made substantial contributions to the study design, performed the operation, and revised the manuscript. All authors read and approved the final manuscript.

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