Case Report
Primary angiosarcoma of the breast: a case report

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Received September 6, 2018; Accepted September 27, 2018; Epub February 1, 2019; Published February 15, 2019

Abstract: Background: Primary angiosarcoma of the breast is extremely rare, accounting for less than 0.05% of all primary malignancies of the breast. Here, we report here a case of primary angiosarcoma with full description of radiology and histology, including electron microscopic findings. Case presentation: A 39-year-old woman complained of a diffuse hard mass in her right breast. She did not have any history of radiation exposure. Ultrasonography revealed a 7 cm sized mass with an irregular anechoic cystic portion replacing the entire right breast. Modified radical mastectomy was performed. The diagnosis of intermediate grade angiosarcoma was made by microscopic examination, immunohistochemical staining, and electron microscopic examination. The patient underwent four cycles of adriamycin-ifosfamide chemotherapy and received radiation therapy. Multiple bone metastases occurred 9 months after surgery and palliative treatment was given. Follow up was lost at post-operative 22 months. Conclusions: We report a rare case of intermediate grade primary angiosarcoma with detailed radiological and histological findings. Despite postoperative chemoradiation therapy, multiple metastases suggest that intermediate grade may have a more aggressive behavior.

Keywords: Breast neoplasms, malignant, sarcoma, angiosarcoma

Background
Angiosarcoma of the breast occurs in two different settings, primary or with prior radiation therapy. Primary angiosarcoma of the breast is a malignant vascular neoplasm arising in the breast parenchyma without previous radiation history, in contrast to postradiation angiosarcoma, which is a well-known complication of radiation therapy for breast cancer [1, 2]. Primary angiosarcoma of the breast is extremely rare, accounting for less than 0.05% of all primary malignancies of the breast [3]. It occurs sporadically in young women and usually presents as painless and rapidly growing palpable masses [4, 5]. Here, we report a primary angiosarcoma of the breast with the findings of radiologic, microscopic, and electron microscopic features.

Case presentation
A 39-year-old female patient presented with a diffuse hard mass and fullness in the right breast. She was told by a local hospital that there was a 2.5 cm sized mass in her right breast one year ago but refused further evaluation or treatment. She did not have any history of radiation exposure. The mammogram showed asymmetrically increased density in the right breast (Figure 1A). Ultrasonography revealed a 7 cm heterogeneous hypoechoic mass with an irregular anechoic cystic portion replacing the entire right breast (Figure 1B). Core needle biopsy revealed a mesenchymal tumor with anastomosing vascular channels and papillary proliferation. Immunohistochemical staining of CD34 and factor VIII confirmed the endothelial origin, and the histologic features suggested the possibility of an intermediate grade angiosarcoma. Additional radiologic examination including MRI and PET-CT was performed. The axial contrast enhanced T1 weighted image displayed a 7.9×3.6×3.3 cm, irregularly shaped, heterogeneously enhancing lesion with relatively smooth margin that occupied the entire breast (Figure 1C). The mass showed diffuse FDG uptake with a maximum SUV of 1.5 on PET-CT (Figure 1D). Modified radical mastectomy was performed. On gross examination, a 8.0×4.5 cm partially circumscribed hemorrhag-
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A 8.0×4.5 cm partially circumscribed mass with a brick brown to pink color and hemorrhagic cut surface is noted within the breast parenchyma. On cut section, the mass had a brick brown to pink color with a soft consistency and hemorrhagic cut surface (Figure 2). Microscopically, the tumor was composed of anastomosing vascular channels with hyperchromatic endothelial cells. Endothelial tufting, papillary formations, and blood lakes were present. Necrosis was absent, and mitotic index was 1-2/10HPF (Figure 3A-D). Immunohistochemistry was performed once again on the mastectomy specimen, and the tumor cells were positive for vimentin, CD34 and factor VIII-related antigen, confirming the diagnosis of an intermediate grade angiosarcoma (Figure 4A and 4B). Electron microscopy was performed, and the vascular lumens were lined by plump cells with cytoplasmic processes. The cytoplasmic processes were joined by intercellular junctions. Weibel-Palade bodies were noted within the endothelial cytoplasm (Figure 5). Sixteen lymph nodes were retrieved from axillary dissection, and lymph node metastasis was absent. The patient underwent four cycles of adriamycin-ifosfamide chemotherapy and received radiation therapy with a total amount of 5940cGy. Follow-up mammography and ultrasonography at 6 months postoperative showed no evidence of tumor recurrence. However, bone scan at 9 months postoperative discovered newly developed multiple bone metastases in the right rib and left ilium. Palliative chemotherapy and radiation therapy was performed. Patient was lost to follow-up 22 months after surgery.

Discussion and conclusions

Primary breast sarcomas excluding phyllodes tumors are rare and account for less than 0.1% of all breast malignancy [4]. Major histologic subtypes of breast sarcoma are angiosarcoma, malignant fibrous histiocytoma and fibrosarcoma [6]. Angiosarcomas of the breast are divided in two categories according to their etiology; de novo development (primary) or post-radiation therapy related (secondary). Primary angiosarcoma has a median age of 42 years, while secondary angiosarcoma occurs in older women with a median age of 72 years [7].

The MRI of angiosarcoma shows a heterogeneous mass with low signal intensity on T1-weighted images and hyperintensity on T2-weighted images [5, 8]. Enhancement of the mass depends on the tumor grade. Low grade angiosarcomas show progressive enhance-
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Histologically, angiosarcoma displays heterogeneous appearances including well-formed anastomosing vascular channels, endothelial tufting and papillary formations, solid and spindle cell foci, presence of hyperchromatic endothelial cells, and necrosis. Histologic grading is performed with Rosen's 3-tiered grading system based on morphology [9, 10]. The presenting case revealed anastomosing vascular channels with hyperchromatic endothelial cells invading the breast parenchyma, endothelial tufting, papillary formations, and blood lakes. However, necrosis was absent and mitoses were rare with an index of 1-2/10HPF, which was compatible for an intermediate grade angiosarcoma. Although the histologic grade was intermediate, multiple bone metastasis occurred 9 months after surgery. Despite palliative chemoradiation therapy, the disease progressed during the 22 months of follow up and had a poor outcome. Rosen et al. reported that disease-free survival 5 years after treatment are 76%, 70%, and 15% for low-, intermediate-, and high-grade angiosarcomas, respectively, and that intermediate-grade angiosarcomas behave more like low-grade angiosarcomas [10]. However, Adem et al. reported that overall survival was associated with tumor size, but did not significantly differ between low- and high-grade lesions [4]. Recently, Nascimento et al. studied 49 cases of primary angiosarcoma of the breast and reported that there were no correlation between histological grade and patient outcome [1]. In this present case, the tumor was an intermediate grade but multiple metastases occurred in spite of postoperative chemoradiation therapy, suggesting that intermediate

Figure 3. Microscopic findings. A. Anastomosing vasculature of the tumor. B. Focal areas of blood lakes. C. Papillary proliferation of the tumor cells. D. The lining cells of the anastomosing vessels are slightly plump and hyperchromatic with mild nuclear pleomorphism.

Figure 4. Immunohistochemistry. The lining cells of the anastomosing vascular channel are positive for CD34 (A) and Factor VIII (B).
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Figure 5. Electron microscopic findings. Vascular lumen (L) with lining cells. The vascular lining cells have cytoplasmic processes (arrow) and intercellular junctions (open arrow & inset a). Weibel-Palade bodies (circle & inset b) are noted within the endothelial cytoplasm.

In conclusion, we report a primary angiosarcoma replacing the entire right breast with detailed radiological and histological findings. The patient was treated by surgery and postoperative chemoradiation therapy but developed metastasis 9 months after surgery.

Acknowledgements

This study has been approved by the Institutional Review Board at The Catholic University of Korea (KC17ZESI0630), and was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT and Future Planning (NRF-2017R1D1A1B03034165).

Disclosure of conflict of interest

None.

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References


grade may have a more aggressive behavior. However, angiosarcoma of the breast is rare, and the clinical data in literature are limited with mostly descriptive studies of a small sample size or retrospective studies based on review of databases such as Surveillance, Epidemiology, and End Result Program (SEER) or Florida Cancer Data System (FCDS) [3, 4, 11-13]. Further studies on a larger scale are needed to validate histologic grade as a prognostic factor.

Primary angiosarcoma tends to spread hematogenously and shows a high propensity for metastasis including bone, lung, and liver. Complete surgical resection of the tumor with negative margins is the mainstay of treatment for breast sarcomas [6, 14]. Lymph node metastasis is very rare in breast sarcomas and radical dissection of axillary lymph nodes should only be performed in histologically proven isolated nodal disease or to relieve symptoms [6, 15]. Systemic adjuvant chemotherapy may be offered, since angiosarcoma is a potentially chemosensitive disease with a response rate of 48% to anthracycline- and gemcitabine-based chemotherapy in the metastatic setting [7]. The role of radiation therapy is controversial. Adjuvant radiation therapy for primary breast angiosarcomas has not been proven in randomized trials [6, 11].
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