Ulusal Cer Derg 2014; 30: 54-56
DOI: 10.5152/UCD.2014.2450

A case report of primary breast angiosarcoma causing hemorrhagic shock in pregnancy

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ABSTRACT

Angiosarcoma is a rare breast tumor. In contrary to other breast tumors, primary breast angiosarcomas are seen in the third and fourth decades. Clinically, they present as rapidly growing masses. They can also be seen during pregnancy. The aim of this article is to report on a primary breast angiosarcoma case that occured during pregnancy and resulted in hemorrhagic shock.

Key Words: Angiosarcoma, breast cancer, pregnancy, hemorrhagic shock

INTRODUCTION

Angiosarcoma is a rare malignant tumor arising from the vascular endothelium. Unlike other deeper localized sarcomas, it usually occurs in the skin and soft tissue (1). Breast is one of the most frequent locations of angiosarcoma. Primary angiosarcoma can rarely be seen in the uterus, ovary, lung, heart, small intestine, thyroid, orbit and oral cavity (1).

Breast angiosarcoma constitutes approximately 0.04% of all breast cancers and 8% of breast sarcomas (2). Primary breast angiosarcoma is usually seen in the third and fourth decades in contrast to other breast cancers seen in more advanced ages. Especially in young women, it often manifests as a fast growing palpable mass. Six-12% of primary breast angiosarcomas is diagnosed during pregnancy (3).

CASE PRESENTATION

A 27-year old, seven-month pregnant patient was admitted to our outpatient breast clinic. She had previously been evaluated at another clinic 2 months ago for a palpable mass on the left breast and her breast ultrasonography showed a 35.8x18.7 mm in size, well-defined, slightly heterogeneous hypoechoic mass lesion. Two months later, a control breast ultrasound revealed 2.5-fold increase in size of the lesion, with a thick capsule, and posterior acoustic shadowing. On Doppler ultrasound examination, the lesion appeared as significantly hypervascular. A fine-needle aspiration biopsy was performed with high-suspicion of malignancy, and together with the clinical, pathological and radiological findings the lesion was classified as breast angiosarcoma.

On physical examination, she had a large mass on the left breast, causing ulceration of the skin and covering the entire breast. The patient was evaluated in the multidisciplinary breast disease council and mastectomy and medical abortion were recommended. However, the patient refused the recommended treatment.

She re-applied to our clinic in the postpartum period, with new investigations performed in another center. The contrast enhanced chest tomography revealed a 17 cm lobular, spherical, well-defined, heterogeneous mass lesion in the chest that shifted the breast parenchyma to the periphery, showing peripheral contrast enhancement (Figure 1). The nipple was medially dislocated, and the breast skin was thickened due to infiltration by the mass. Destructive lesions compatible with metastasis were detected in the sternum, T11 and T6 anterior vertebral bodies. Subsequent radiologic studies showed metastatic lesions in T3, T6, T11 vertebrae, 3rd rib, the sternum, liver and lungs. The patient with was referred to medical oncology for chemotherapy with a diagnosis of metastatic breast angiosarcoma.

Medical oncology planned 6 cycles of iphosphamide 3400 mg, and 3400 mg mesna treatment in every 21 days. After receiving a course of chemotherapy, seven months after giving birth, she was admitted to the

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Received: 31.10.2013
Accepted: 23.11.2013

Available online at www.ulusalcerrahidergisi.org

emergency department with non-stopping bleeding on the left breast. She was transfused with 20 units of packed red cells and one unit thrombopheresis over 2 days. Due to massive blood transfusion and lack of response to compressive treatment she developed hemorrhagic shock and was emergently operated. Left simple mastectomy was performed. Histopathologic examination showed a 20 cm in diameter, moderately differentiated angiosarcoma (Figure 2). She was stabilized thereafter and was discharged on the 3rd postoperative day.

She later presented to Gynecology clinics with a bleeding lesion on the vulva. The lesion was excised and the histopathological evaluation showed metastatic angiosarcoma. Multiple hemorrhagic intracranial metastases were detected, which were considered inoperable by Neurosurgery. A 10x3gy=30Gy irradiation was performed by Radiation Oncology. She was admitted to our emergency department due to respiratory distress, and was transferred to the intensive care unit with a diagnosis of respiratory failure due to pneumonia. She died on her 4th day in the intensive care unit, 13 months after initial diagnosis.

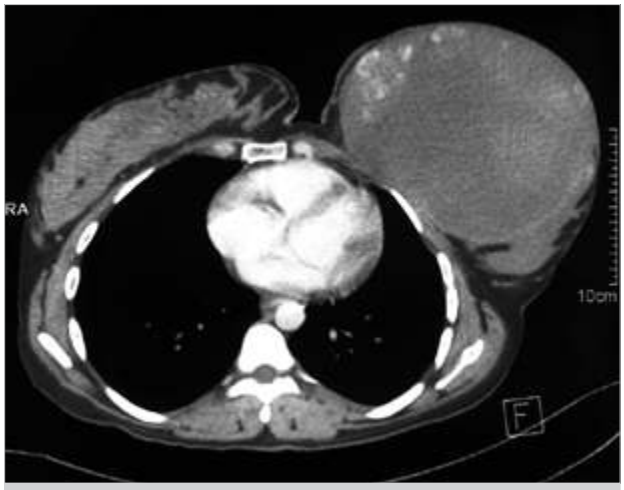

Figure 1. Dynamic contrast thorax CT showing a regular bordered giant mass of 17 cm in size in the left breast, with contrast enhancement in the periphery

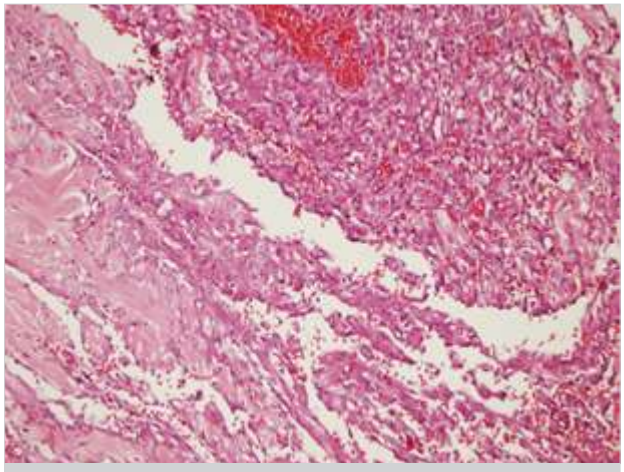

Figure 2. Anastomosing complex vascular channels, endothelial proliferation and focal nuclear atypia

The patient approved the use of her data for scientific publication.

DISCUSSION

Breast angiosarcoma is seen at earlier ages as compared to other breast cancer types (4). The latest studies show an increase in the incidence of breast angiosarcoma due to the increased rate of breast conserving surgery and radiotherapy (5). Risk factors include trauma, radiation, lymphedema, breast implants, Xeroderma pigmentosum, neurofibromatosis and vinyl chloride (6). In our patient, none of these risk factors were present.

Breast angiosarcoma manifests as a painless, fast-growing mass that causes discoloration in the skin. This represents the vascular structure of the tumor. In most cases, the masses are over 4 cm. In this case, the tumor size was 4 cm at the time of diagnosis, it reached 8 cm 2 months after discharge and in the simple mastectomy specimen, and 11 months later the tumor diameter was 20 cm.

Mammography findings are non-specific for diagnosis. Liberman et al. (7) have reported that in 33% of the patients the mass could not be viewed in mammography, usually due to the dense breast tissue in the young patients. Mammography was not planned in our patient since she was young and pregnant. On ultrasound, heterogeneous, hyperechoic , hypervascular mass is monitored (8). In this case, the mass was slightly hypoechoic, heterogeneous and hypervascular on ultrasound. Breast magnetic resonance imaging is more sensitive in the diagnosis of angiosarcoma as compared to other radiological evaluations (8). Angiosarcoma is detected as a large, well-circumscribed, non- calcified mass requiring histopathologic diagnosis (7). Preoperative diagnosis with fine-needle aspiration biopsy or tru-cut biopsy is often difficult. Chan et al. (3), have reported that 37% of biopsies are false negative. Therefore, in case of radiological and pathological incompatibility, repeat biopsy is required. During histological examination immunohistochemical markers, particularly endothelial cell -specific (CD31, CD34) ones should be evaluated (9).

Angiosarcoma of the breast is usually seen during pregnancy and lactation in young fertile women and it shows rapid progression. These findings have led to the assumption that hormones were effective on the formation of the tumor, however, estrogen and progesterone receptors were reported to be negative in most cases (10). Pathological examination of this case was negative for estrogen and progesterone receptors. The rapid advancement of the disease during pregnancy and lactation are thought to be related to the suppressed immune system and placental growth factors, besides hormonal effect (6).

Breast angiosarcoma shows hematogenous spread like other sarcomas. Distant metastases are observed at an early stage. Breast angiosarcoma have been reported to metastasize usually to the lungs, liver, skin, subcutaneous soft tissues, bones, central nervous system, the contra-lateral breast, and ovaries. Unlike other sarcomas and breast cancer, lymph node metastases are rarely seen (11). In this case, lung, liver, bone, skin,

vulva and central nervous system metastases were observed.

Palpable breast masses might be tumors arising from the breast parenchyma as well as nonparenchymal tumors. It is very difficult to diagnose a breast lesion as breast angiosarcoma. Differential diagnosis should be made considering both radiological and histopathological properties. Differential diagnosis includes benign hemangioma, cystosarcoma phylloides, stromal sarcoma, metaplastic carcinoma, squamous cell carcinoma showing sarcomoid property, myoepithelioma, fibromatosis, fibrosarcoma, liposarcoma and proliferative lesions with reactive spindle cells (12). This case was initially accepted as either an atypical fibroadenoma or hemangioma. A fine needle aspiration biopsy was performed due to rapid growth of the lesion, which revealed angiosarcoma.

Breast angiosarcoma has a worse prognosis than other breast cancers. The prognosis of primary breast angiosarcoma varies according to histological grade. Histologically, it is classified in three stages. As grade increases disease recurrence rate increases and prognosis is worsened. 5-year disease-free survival is 76% for grade 1 tumors, whereas this rate is 15% for grade 3 tumors. However, there is no precise correlation (13). Prognostic factors include tumor size, presence of residual tumor, cellular pleomorphism and proliferative index (14). Several studies reported better survival in tumors less than 4 cm, although some other studies indicate there is no correlation between tumor size and survival.

Primary treatment of breast angiosarcoma is surgical resection. Generally mastectomy is preferred, while breast-conserving surgery can be performed in small and grade 1 lesions (4). The role and importance of chemotherapy and radiotherapy in the treatment remain unclear. Adjuvant radiotherapy is used in patients with post-surgical micro-residual disease. Sometimes radiotherapy can be used for palliation of complications due to metastasis (15). Sher et al. (11) showed that there was no significant survival difference between patients receiving adjuvant chemotherapy with anthracyclines, taxanes, gemcitabine and ifosfamide and those without chemotherapy. Studies on chemotherapeutic drugs that provide partial response are still ongoing. With the addition of TNF-alpha and IFN -alpha to adjuvant treatment, a 84% success rate has been shown (6). Nevertheless, further studies are required.

CONCLUSION

Breast angiosarcoma is a rare breast tumor that is seen in young fertile women. It has an aggressive course with distant metastases at an early stage. Thus, surgical procedure should be carried out immediately after diagnosis without further delay. The disease is usually resistant to chemotherapy and radiotherapy. When diagnosed, especially in early stage tumors, surgical treatment is the main and only treatment option.

Informed Consent: Written informed consent was obtained from the patient who participated in this case report.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - İ.A.B., M.V., Z.K.; Supervision - M.V., F.A.; Data Collection and/or Processing - İ.A.B., Z.K., F.K., T.Ö.; Literature Review - İ.A.B., Z.K.; Writer - İ.A.B., Z.K.; Critical Review - F.A., M.V., F.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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