Primary Angiosarcoma of breast- A case report with review of literature

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ABSTRACT

Angiosarcoma is rare, accounting for less than 1% of all malignant mammary lesions. The prognosis is usually poor due to high rates of local recurrence and early development of metastases. We report a 40 year old woman with a highly vascular mass on radiology, she presented with bony metastases at presentation. Core biopsy of the breast mass performed twice showed only haemorrhage and necrosis. Due to biopsy she developed ulceration and presented with nipple discharge. Frozen section done from the base of the ulcer was haemorrhagic and inflammatory. Cytology of nipple discharge too showed inflammation & haemorrhage. Finally mastectomy was done and histopathology showed angiosarcoma of intermediate grade. Immunohistochemically the tumor showed positivity for CD31, multifocal substantial positivity for CD34, FLi-1 diffusely positive and negative for cytokeratin. Ki 67 proliferation index – upto 60-70% in foci, IHC confirmed Angiosarcoma intermediate to high grade. Angiosarcoma is a rare tumor which is difficult to diagnose on core biopsy of breast. A highly vascular breast mass should always be considered malignant until proven otherwise. Surgical treatment seems to be the best course of action.

Key words: Angiosarcoma, breast, CD31, FLi-1.

CASE REPORT

40 years female, presented with breast lump from 6 months which rapidly enlarging since 3 months. There is no history of breast surgery or irradiation. On examination, 8x8 cm mass in central quadrant was firm, non tender, not attached to skin or deep structures and there was no evidence of nipple retraction, skin thickening or axillary lymphnodes. USG showed ill defined irregular large heterogenous hypoechoic mass in breast with significant internal vascularity highly suggestive of vascular mass. Core needle biopsy of the mass showed only haemorrhage and necrosis; so a repeat biopsy was done and this report too was inconclusive. Repeated biopsy of the vascular mass created ulcer at site and presented with nipple discharge.
Cytology of nipple discharge gave similar findings of inflammatory cells and haemorrhage. Frozen section from the base of ulcer was done, no conclusive findings obtained from it except for haemorrhage. Finally total mastectomy was done as the mass was highly vascular. Histopathology and IHC confirmed the diagnosis of angiosarcoma-intermediate to high grade.

**Gross**
Received left mastectomy specimen, skin covered breast measuring 13x12x8cm. Nipple and areola were normal, ulcer of size 3x3.5cm seen with necrotic base and punched out edges. Ulcer located in upper central quadrant. On cut the area beneath the ulcer showed vascular haemorrhagic tumor of size 6x6x8cm, cut section spongy & haemorrhagic in appearance. (Fig 1)

**Microscopy**
Sections show tumor tissue consisting of plenty of anastomosing vascular channels lined by atypical endothelial cells. Also shows plump and oval cells which are highly pleomorphic hyperchromatic nuclei arranged around vascular channels. Extensive areas of haemorrhage & necrosis noted. At places show papillary projections within vascular lumina. (fig 2) The cut margins and the base are free from tumor. No lymph nodes identified in axillary tail. Diagnosis of Angiosarcoma of intermediate grade was given on histology which was confirmed by IHC.

![Fig 1](image1.jpg) **Fig 1** Gross showing mastectomy specimen; cut surface; the tumor is spongy and haemorrhagic.

![Fig 2A](image2A.jpg) **Fig 2A** papillary projections within lumina with large areas of haemorrhage (H&E 10X)

![Fig 2B](image2B.jpg) **Fig 2B** tumor arranged in sheets with haemorrhage (H&E 40X)
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Fig 2C: Tumor tissue consisting of vascular channels lined by atypical endothelial cells (H & E-40X)

Immunohistochemically the tumor showed positivity for CD31, multifocal substantial positivity for CD34, FLi-1 diffusely positive and negative for cytokeratin. Ki 67 proliferation index – up to 60-70% in foci (fig 3), IHC confirmed angiosarcoma intermediate to high grade.

Fig 3A: Immunohistochemistry CD 34 positivity

Fig 3B: IHC showing CD31 positivity

Fig 3C: IHC showing Ki 67 proliferation (60-70%)

Fig 3D: IHC showing FLi-1 positivity
DISCUSSION

Mammary sarcomas are a heterogeneous group of malignant neoplasms that arise from the mammary stroma. Angiosarcomas, one of the most common forms of mammary sarcoma, are developed from endothelial lining of the blood vessels. The first case of Angiosarcoma was reported by Schmidt in 1887. Mammary angiosarcomas can be subdivided into 1) Primary de novo forms in breast parenchyma; 2) Secondary in skin and soft tissues of arm following ipsilateral radical mastectomy and subsequent lymphoedema-The Stewart Treves syndrome (ST syndrome); 3) Secondarily in skin and breast parenchyma or both following conservation treatment and radiotherapy; 4) Secondary in skin and breast parenchyma or both following conservation treatment and radiotherapy.

Angiosarcomas, as with other sarcomas of breast are rare and their incidence is about 0.05% of all primary malignancies of organ. In the present paper as our case concerned we will limit our discussion to primary angiosarcoma of breast. Primary angiosarcomas usually occur in young women (20-50 years). Between 6 and 12% of primary breast angiosarcomas are diagnosed during pregnancy or shortly after, suggesting hormonal effect. However currently no cases or very few cases show positive estrogen receptors, so it is impossible to establish a link between angiosarcomas and hormonal dependency. In the present case, estrogen and progesterone receptors are negative. Hence role of estrogen dependency in angiosarcoma has yet to be proven and is a topic for future research.

In most of the cases reported the patient presents with rapidly enlarging breast mass with more than 4 cm size. For this reason, distant metastases are frequent. The present case showed distant bony metastases at the time of diagnoses. The tumor may present with blue or purple discoloration of skin, nipple and areola were normal. Pre op diagnosis either by FNA or core needle biopsy is difficult. Chen et al reported a percutaneous biopsy false negative rate of 37%. In the present case too FNA and biopsy were inconclusive.

Pathologically, these tumors are subdivided into three groups according to classification given by Donnel et al. Group I angiosarcoma shows dilated, sinusoid like vessels surrounding a duct in the breast. The vessels are lined by flat endothelial cells. No mitoses identified. Group II shows numerous small buds or tufts of endothelial cells. High grade angiosarcomas may contain low or intermediate grade elements, especially at the periphery of the tumor. These elements have deceptively benign appearance and are well differentiated, which explains why majority of core biopsies are negative. Differential diagnosis of this rare tumor include: benign haemangioma, phyllodes sarcoma, stromal sarcoma, metaplastic carcinoma, fibrosarcoma, liposarcoma, squamous cell carcinoma with sarcomatoid features, myoepithelioma, fibromatosis, reactive spindle cell proliferative lesion and high grade mammary carcinoma especially in small biopsy specimens containing only solid areas. Immunohistochemical stains for epithelial markers (pancytokeratin), endothelial markers (CD31, CD34), FLi 1 and other sarcoma markers help in making accurate diagnosis.

Surgery is the main mode of treatment for primary angiosarcoma of the breast and consists of simple mastectomy. Axillary lymph node dissection is not needed as the spread is haematogenous. Chemotherapy and radiotherapy may be used as an adjuvant treatment. Angiosarcomas have poor prognosis, however prognosis depends upon tumor grade, tumor size at diagnosis, and margin status at surgery. According to Rosen’s study, the 5 years disease free survival rate for low grade tumors can be as...
high as 76% and up to 70% for intermediate grade tumors. Whereas 5 years survival rate for high grade tumors is about 15%.

CONCLUSION
A large vascular mass in the breast should be considered as malignant, until proven otherwise. Surgery is the main modality of treatment and consists of total mastectomy. Primary angiosarcoma has poor prognosis, with poor long term survival. Early and precise diagnosis is an important prognostic marker.

REFERENCES