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# Angiosarcoma of the breast: a case report

## *Angiosarcoma della mammella: caso clinico*

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**Summary**

**Angiosarcoma of the breast is a rare and highly aggressive vascular cancer. Here we describe a case of a 36-year-old woman with angiosarcoma of the left breast who presented with breast enlargement and a bluish red discoloration in the overlying skin. The mammographic and sonographic findings were aspecific and due to the color doppler findings and the discoloration of the overlying skin, an angiosarcoma was suspected. A biopsy of the area identified at the color doppler sonography was performed and the histological examination showed the presence of a low-grade angiosarcoma. Systemic examinations (CT, total body bone scintigraphy) showed no evidence of metastasis. A left modified radical mastectomy was performed and pathological examination confirmed the presence of a grade I angiosarcoma. Immunohistochemistry showed that the neoplastic cells were positive for factor VIII, CD 31 and CD 34 confirming the tumor vascular origin. The patient presents no evidence of disease 3 years after surgery. Eur. J. Oncol., 14 (4), 217-221, 2009**

*Key words:* **angiosarcoma, breast, mammography, color doppler sonography**

**Riassunto**

**L'angiosarcoma mammario è una rara neoplasia vascolare altamente aggressiva. Nel presente lavoro si descrive il caso clinico di un angiosarcoma mammario sinistro riscontrato in donna di 36 anni che presentava aumento volumetrico della mammella associato a reticolo cromatico bluastro della cute sovrastante. I reperti ecografici e mammografici risultavano non diagnostici, mentre i reperti dell'eco-color-doppler e l'aspetto cutaneo erano suggestivi per un'angiosarcoma. La biopsia effettuata nell'area interessata dall'eco-color-doppler evidenziava un'angiosarcoma di basso grado di malignità (grado I), mentre la valutazione clinico-strumentale (TAC, scintigrafia ossea total body) non rilevava ripetizioni a distanza. Alla paziente veniva praticata mastectomia radicale modificata sinistra e l'esame istologico confermava la presenza di un angiosarcoma di grado I. L'immunoistochimica dimostrava la positività delle cellule neoplastiche per fattore VIII, CD31 e CD34. A distanza di 3 anni dall'intervento chirurgico la paziente a tutt'oggi è libera da malattia. Eur. J. Oncol., 14 (4), 217-221, 2009**

*Parole chiave:* **angiosarcoma, mammella, mammografia, eco color doppler**

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**Abbreviations**

CT: computed tomography
CEA: Carcinoembryonic antigen
TPA: Tissue Polypeptide Antigen
AFP: alpha-fetoprotein
CA15.3: carbohydrate antigen 15.3
CA19.9: carbohydrate antigen 19.9
MRI: Magnetic risonance imaging

## Introduction

Angiosarcoma of the breast is a highly malignant vascular neoplasm, that accounts for only 0.04% of primary mammary tumors and approximately 8% of mammary sarcomas (1-3).

According to their cause angiosarcomas can be divided in primary, with no evident origin, that affect a younger age group of 20-40 years and secondary, occuring most frequently after breast conservation surgery or following postoperative radiotherapy (4).

The rarity of this tumor and its non specific clinical and radiological presentation could explain because there is often a delay in the diagnosis of this disease.

We report herein the history of a 36-year-old woman who suffered from primary angiosarcoma of the left breast.

## Case report

The patient was a 36-year-old woman with a chief complaint of left breast enlargement of six months duration associated with soft tissue thickening and redness in the overlying skin at the upper quadrants of the left breast. She was referred to her primary care physician who suspected an inflammatory mastitis, and gave her an anti-inflammatory therapy for three months. Still persisting symptoms, the patient was admitted to our clinic in May 2007.

She had no relevant medical history and denied history of trauma. Physical examination revealed swollen, dense tissue in the upper outer and inner quadrants of the left breast, associated with *peau d'orange* and a bluish red discoloration in the overlying skin. The tissue was not painful and it was adherent to the superficial skin. No axillary lymphadenopathy was shown. The right breast was normal at the clinical examination.

Tumor markers such as CEA, TPA, CA 15.3, AFP, CA 19.9 were included within the normal ranges. A mammography of both breasts (Fig. 1) was requested and showed ill-defined, asymmetric dense tissue without focal mass or suspicious calcifications with thickening of the cutaneous profile in the upper quadrants of the left breast. Sonography of the left breast (Fig. 2) showed diffuse, abnormal, mixed hyperechogenic and hypoechogenic regions with involvement of the subcutaneous tissue. Color doppler sonography (Fig. 3) in the upper quadrants of the left breast revealed an area with prominent vascularity in the upper quadrants.

Due to a high suspicion of a malignancy at physical examination and on radiological images, 14-gauge core-needle biopsy samples from the area identified at the color doppler sonography were taken and the pathological examination demonstrated the

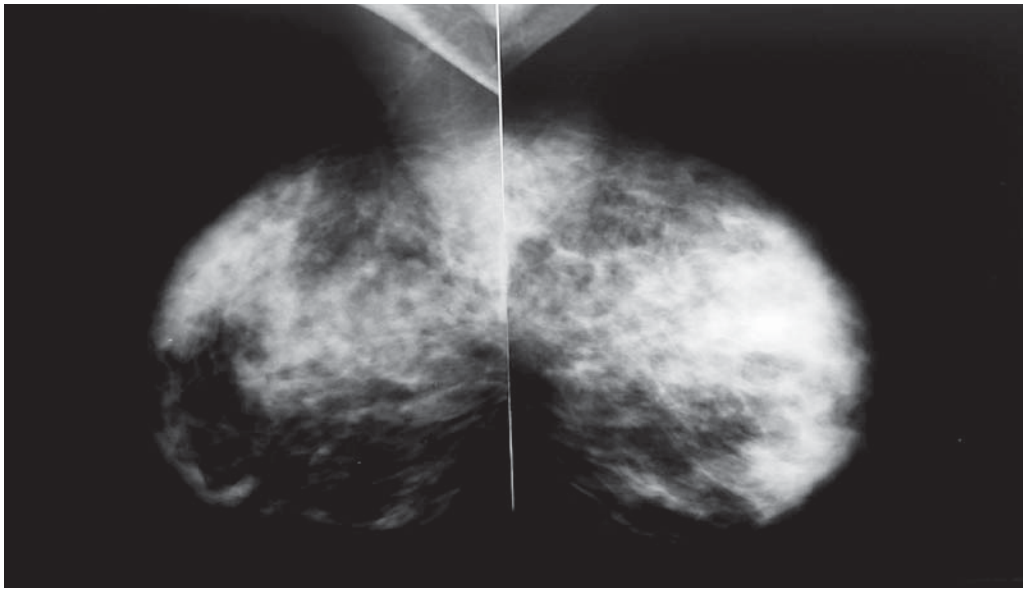

**Fig. 1.** Mammography show ill-defined, asymmetric dense tissue with thickening of the cutaneous profile in the upper quadrants of the left breast.

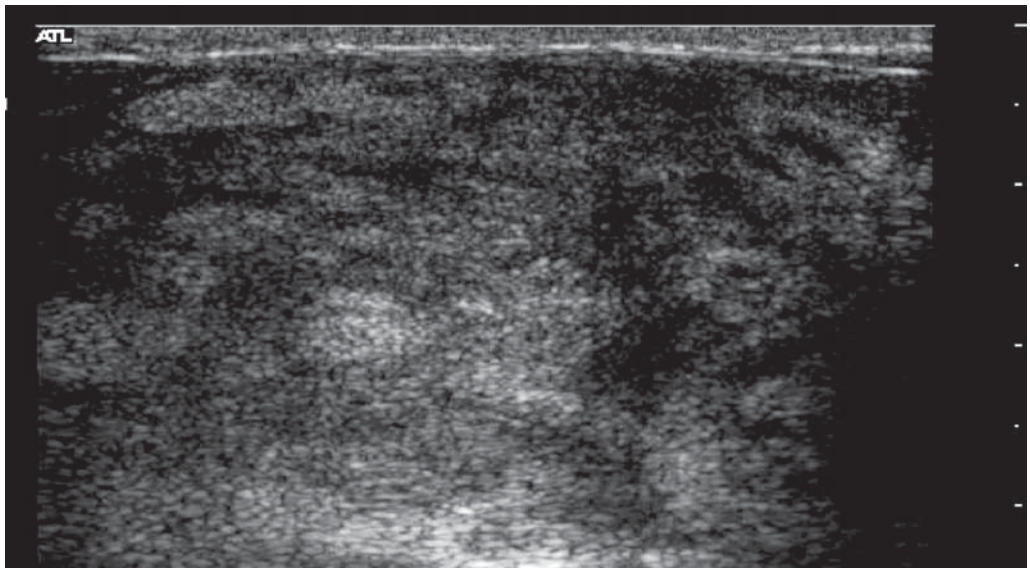


**Fig. 2.** Sonography of the left breast shows diffuse, abnormal, mixed hyperechogenic and hypoechogenic regions with involvement of the subcutaneous tissue.

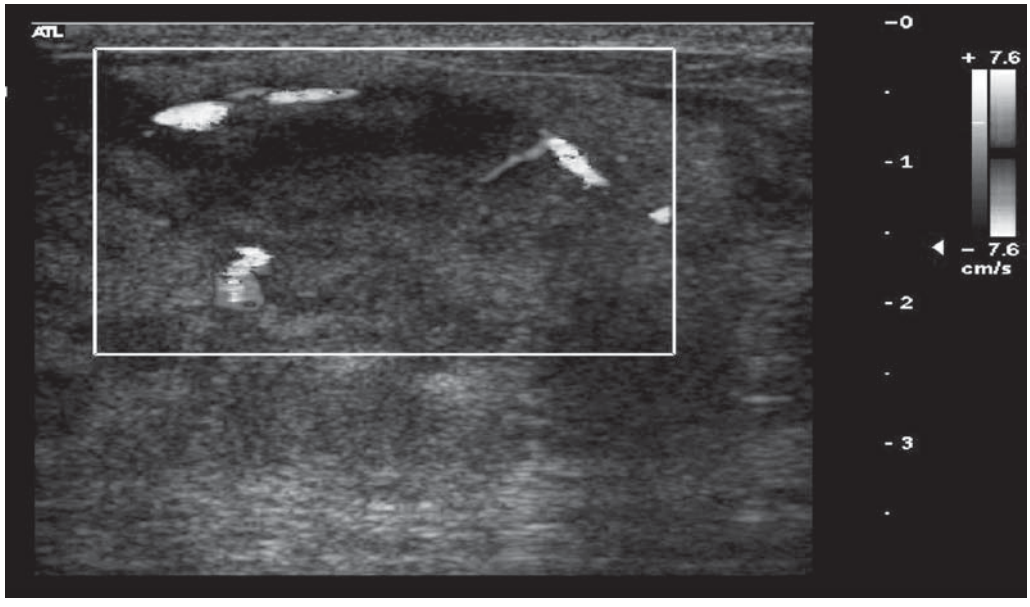


**Fig. 3.** Color doppler sonography revealed an area with prominent vascularity in the upper quadrants of the left breast.

presence of a low-grade angiosarcoma. Staging investigations including CT chest and abdomen, and total body bone scintigraphy showed no evidence of metastasis. Subsequently, she underwent a modified radical mastectomy of the left breast and omolateral axillary node dissection was performed. Grossly, the tumor measured 6 x 4 cm and the cut surface was ill-defined and appeared spongy due to the numerous dilated blood filled vascular spaces. Microscopic examination of the mammary tumor demonstrated well-formed anastomosing vascular channels invading the mammary fat and glandular parenchyma, prominent and iperchromatic nuclei of endothelial cells, corresponding with grade I angiosarcoma. Immunohistochemically, the neoplastic cells were positive for factor VIII, CD31 and CD34, but negative for keratin and estrogen receptor. All lymph-nodes were negative for tumor. The patient did not receive any adjuvant treatment, because there is no indication in low grade angiosarcoma. Three years after surgery, the patient is still without signs of local recurrence or distal metastases.

## Discussion

Angiosarcoma of the breast is a rare malignant neoplasm that arises from endothelial cells lining vascular channels and with a frequency of 0.04% of primary breast tumors and approximately 8% of primary breast sarcomas (1-3). This disease has a relatively higher occurrence among young people.

A primary and a secondary type are known. Primary angiosarcoma of the breast arises in young

women, usually during the 3rd and 4th decade of life. Twelve percent of the cases are found during pregnancy, but no evidence supports the hypothesis that these tumors are hormone-dependent. No risk factors for developing this type of tumor are known.

Secondary angiosarcomas are usually found in older women and they are associated with some risk factors. Two types of secondary angiosarcoma are shown: lymphedema-associated cutaneous angiosarcoma and post-irradiation angiosarcoma (5). Lymphedema-associated cutaneous angiosarcoma (Stewart-Treves syndrome) arises in lymphedematous region and the chest wall after mastectomy and axillary lymph-node dissection (6, 7). Post-irradiation type generally occurs after breast-conservating therapy and radiation therapy. Cahan *et al* (8) described the diagnostic criteria for radiation-induced sarcomas, which include a previous history of radiation therapy (between 25 and 40 Gy) with a latency period of at least 3-5 years, development of sarcoma within the field of previous irradiation and the secondary sarcoma should be histologically different from the primary neoplasm. These criteria were later modified by Arlen *et al* (9) to include tissue adjacent to the radiated field and a shorter latency period of 3-4 years (10).

However, the distinction between primary and secondary angiosarcoma may not be important because clinical behaviour and outcome of both types are very similar (11). Our case can be categorized as primary angiosarcoma.

The clinical manifestations of primary angiosarcomas are usually non specific, commonly being a palpable painless mass with rapid growth or diffuse enlargement of the breast, like our case. Similarly to our case, a bluish red discoloration of the overlying skin occurs in 17-35% of patients (12) and is thought to be attributable to the vascular nature of this lesion. Nipple retraction or axillary node enlargement are generally absent. In the majority of the cases in literature, the tumor size is >4 cm in diameter. Indeed, in our case the tumor size was 6 x 4 cm.

Radiologic findings are often aspecific, and angiosarcoma may be disregarded. On mammograms, angiosarcoma appears as an ill-defined, non calcified mass. Sometimes only skin thickening is observed (13). Liberman *et al* (12) reported that 33% of angiosarcomas in their series were not mammographically detected. Ultrasound is also nonspecific and usually shows diffuse, abnormal, mixed hyperechogenic and hypoechogenic regions or a solid mass with both hypoechoic and hyperechoic appearance. Color doppler evaluation represents a useful adjunct to sonography and in the case of angiosarcoma shows hypervascularity (3). In our patient, the mammographic and sonographic findings were aspecific, and because of color doppler findings and of spontaneous bluish red discoloration of the skin overlying the mass, angiosarcoma was suspected. Although we did not perform MRI in our case, it should be mentioned, because it is being used more and more as a promising imaging modality for breast disease and it is useful in determining the tumor extent and in planning surgery. MRI of angiosarcoma shows a heterogeneous mass with low signal intensity on T1-weighted images, but signal intensity is high in images that are heavily T2-weighted (14).

Preoperative diagnosis of angiosarcoma of the breast, through aspiration cytology and biopsy, is often difficult. Chenet *et al* reported that the false negative rate of biopsy was 37%, but in our case the core-biopsy had confirmed the suspicion of angiosarcoma.

The histologic features of angiosarcoma of the breast are classified into Grades I, II and III (15). Grade I angiosarcoma shows vessels lined by a single layer of relatively flat endothelial cells, normal mitotic figures, no necrosis and no papillary projections. Grade II shows numerous tufts of endothelial cells projecting into the vascular lumen and focal papillary projection. Grade III shows a focus of growth of spindle and polygonal cells. Necrosis and blood lakes were present only in Grade III tumors. The resected specimen from our patient's mammary tumor demonstrated well-formed anastomosing vascular channels that invade the mammary fat and glandular parenchyma and prominent and iperchromatic nuclei of endothelial cells. These features are compatible with those of Grade I, and the prognosis was better than the other grades.

Immunohistochemical staining allows tumors of vascular origin to be differentiated from other types of neoplasms. Vascular-associated immunohistochemical markers used in the literature are factor VIII-related antigen, CD34, desmin, and vimentin (11, 16, 17). CD31 seems to be the most sensitive and specific for endothelial differentiation (11). To our case, the neoplastic cells were positive for factor VIII, CD31 and CD34, confirming the tumor vascular origin.

Because of early development of local recurrence and metastases after treatment, the prognosis is

extremely poor. This lesion tends to hematogenously metastasize similarly to other soft tissue sarcomas, rather than lymphogenously (14). Chen *et al* (18) reviewed the metastatic sites of primary angiosarcoma of the breast and showed that the most common sites were lung, skin, subcutaneous tissue, bone, liver, brain and ovaries. Angiosarcoma has a high mortality rate, with only 10 to 27% of patients remaining disease-free after 5 years.

Surgical resection with mastectomy is the treatment of first choice for both forms of angiosarcoma. For small, Grade I primary lesions, breast conservation therapy may be indicated. Although irradiation may seem to be a contradiction for a possibly radiation-induced tumor, surgery may be accompanied by hyperfractioned radiation therapy in patients with high-grade sarcoma in order to prevent recurrence. The effect of chemotherapy has not yet been established, but this therapeutic modality should certainly be considered for patients with high-risk localized breast angiosarcoma, and adriamycin, cisplatin, ifofosfamide and paclitaxel chemotherapy regimens appear to be highly active (19). Hyperthermia and anti-angiogenesis therapy (20-22), are considered experimental treatments and are available only in a clinical trial at this time, but may be a new approach to angiosarcoma treatment.

The prognosis of angiosarcoma is extremely poor and it is thought to depend on the histologic grade. Patients with a higher-grade lesion are more prone to develop a recurrence and have a lower survival rate (12) than those with a lower-grade lesion (11). Tumor size is also thought to be linked to the patient's prognosis. Furthermore, low-grade angiosarcoma may become high-grade angiosarcoma (11). To date, 3 years after mastectomy, our patient shows no signs of recurrence or of metastases.

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