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Angiosarcoma of the Breast; Report of a Case and Literature Review

Angiosarcoma of the breast is a rare tumor that accounts for 0.04 % of all breast neoplasms at the third and fourth decades of life; in contrast with carcinoma, which generally arises later.

Angiosarcoma of the breast usually manifests as a painless, palpable mass without tenderness, with or without bluish-red discoloration of the overlying skin.

Angiosarcoma has a high mortality rate and a very poor prognosis. Mastectomy and chemotherapy are the most likely choices of treatment for a primary angiosarcoma of the breast. Immunotherapy may also play a part in treating this rare type of breast cancer.

This paper presents a case of angiosarcoma of the breast, and relevant data in the literature is also reviewed to discuss the questions on its origin, symptoms, diagnosis and treatment.

Keywords: angiosarcoma, breast, mammography, ultrasonography

Introduction

Malignant breast lesions that arise from strumal tissues are extremely rare, accounting for <1% of all malignant breast tumors. Most mammographically and clinically evident intraparenchymal vascular tumors prove to be malignant angiosarcomas.[1,2] Angiosarcoma is the most common sarcoma to occur in the breast, but is relatively rare.

Angiosarcoma usually presents as a palpable mass, but 17% of cases may present with a bluish discoloration, or bruising of the overlying skin. [2] This malignant tumor occurs primarily in young women.[3] Preoperative diagnosis of angiosarcoma of the breast by aspiration cytology and biopsy is often difficult. Ultrastructural examination and immunostaining for factor VIII-related antigen helps with the diagnosis of angiosarcoma of the breast.

This neoplasm carries a very poor prognosis.[4] Metastases have been reported in the liver, lungs, skin, bones, central nervous system, spleen, ovaries and lymph nodes.[2,5] Angiosarcoma can recur in the breast after conservative surgery or following postoperative radiotherapy.[6] The mean latency is 5-6 years. This tumor tends to grow very quickly and is generally difficult to treat successfully.

Case Report

This is a case report of a primary angiosarcoma of the breast. The patient was a 45-year-old woman who presented to the breast clinic with a mass of ten months' duration in her left breast.

In physical examination, a hard mass was seen in the upper inner quadrane of the left breast. The overlying skin had bluish red discoleration. On palpation, a 4×5×5 cm firm mass with lobulated borders was felt. The mass was not painful nor tender, and it was adherant to the superficial skin.There was no nipple, retraction, skin thickning or axillary lymphadenopathy. The right breast was

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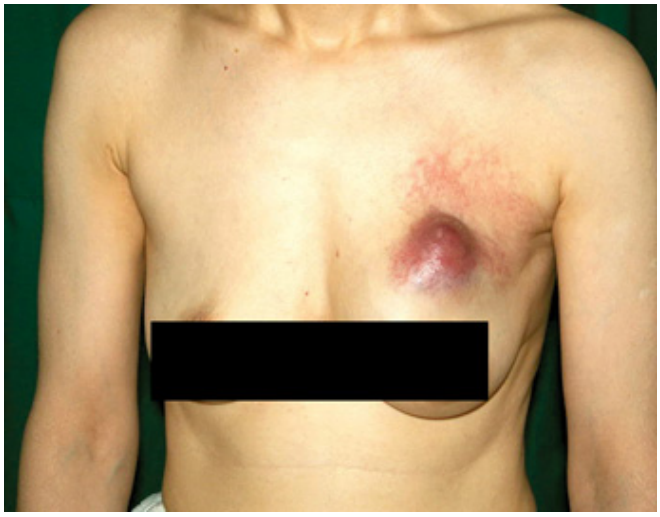

Fig 1. Figure shows a mass in the upper inner quadrane of the left breast which is accompaind by bluish red discoloration in the overlying skin.

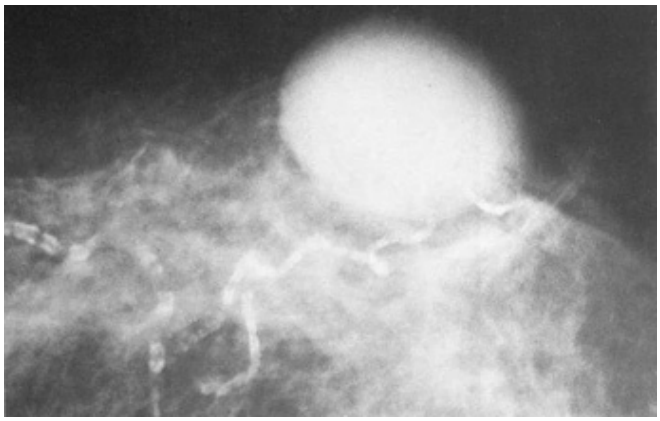

Fig 2. Craniocoudal mammogram shows an uncalcified mass in the breast.

normal in clinical examination.

A mammogram of the left breast was requested, and showed an uncalcified lobulatecl mass, 4 cm in diameter (Figure 2). Ultrasound of the breast showed a hypoechoic mass with lobulated margins, without posterior shadowing (Figure 3). The classification was probably malignant. Tumor markers such as alpha-feto protein and CEA were all within the normal limits.

At surgery, the tumor was completely excised; no metastatic lesion was identified within the sampled lymph nodes. Grossly, the mastectomy specimen showed extensive bruising of the skin and an illdefined mass in the upper inner quadrant of the left breast. The cut surface of the tumor appeared spongy due to the numerous dilated blood filled vascular spaces. Microscopic examination of the mass demonstrated many dilated capillaries including an irregular vascular network with prolifration of atypical endothelial cells, suggestive of an angiogenic tumor. Immuno-histochemically, the neoplastic cells were weakly positive for factor VIII. There were papillary clusters of tumoral cells with sarcomatous spindle cell patterns on histological examination, corresponding with poorly differentiated grade III angiosarcoma (Figure 4).

Chemotherapy was done for the patient after surgery but multiple liver metastases were detected 10 months after the operation and she died of disseminated lung metastases and pulmonary insufficiency.

Discussion:

Angiosarcomas are the most common sarcoma of the breast but are still relatively rare.[7] The neoplasm is of vascular origin.Two hundred and nineteen cases have been described since the first report in 1887. [8]

The frequency of this rare tumor is 0.04 % of primary breast tumors[9] and approximately 8% of breast sarcomas. 10 Stewart reported one angiosarcoma for every 2000-3500 breast cancers.

Angiosarcoma is a lethal neoplasm first described by Schmidh in 1887 and subsequently by Bannamn in 1907. [11] Since then, several reports have been published, ascribing different terms to this malignant condition, such as hemangioendothelioma [11] hemangiosarcoma and hemangioblastoma. [12]

Angiosarcoma occurs in the breast as a primary lesion, but cutaneous angiosarcoma also arise in chronicly lymphoedematous arms after axillary treatment for carcinoma (Stewart-Treves syndrome). Angiosarcoma occurs almost exclusively in the female breast,[13] with only five cases of male breast angiosarcoma reported in the literature.

This tumor usually occurs during the third and fourth decades of life, in contrast with breast carcinoma which generaly arises later. [14] Twelve percent of the cases are found during pregnancy, implying a hormonal effect. [4] However, reported cases with positive estrogen receptors are so rare that the hormonal dependency of angiosarcoma is still unresolved.

Angiosarcoma may have an insidious clinical onest, presenting as a painless often discrete mass that grows rapidly. [2] Some patients complain of a painful mass

with tenderness.

Approximately 2% of patienty may presen with diffuse enlargement of the breast. However, a bluish red discoloration of the overlying skin may enuse. Nipple retraction, discharge, or axillary node enlargement are generally absent. In most reported cases, the tumor size is > 4cm in diameter.[4] Most reports indicate that tumor size does not correlate with survival. The tumor size at discovery can reach 4 cm in diameter. Bilateral tumors have been reported and several cases have been diagnosed in the postmenoposal women.

Due to the paucity of breast imaging techniques, mammgraphy remains the principal imaging approach for which information is available. On mammograms, angiosarcomas appear as an ill-defined mass and lack the spiculation often seen in breast carcinomas. Rarely, the tumor may show a soap bubble appearance with a mean size of about 4.5 cm. They rarely manifest coarse non-branching microcalcifications.[3] In a series of 19 mammary angiosarcomas, 30% were missed on mammography. Sonography usually shows a solid mass that may have well-defined or lobulated margins, with both hypoechoic and hyperechoic appearance. There is often no acoustic shadowing.[1,3] Magnetic resonance imaging (MRI) of angiosarcoma shows a mass with low signal intensity on T1-weighted images, but high signal intensity on heavily T2-weighted images. The latter suggests the presense of vascular channels containing slow-flowing blood. [1,6]

In our patient, the mammographic and sonographic findings were nonspecific, and because of the spontaneons bluish-red discoloration of the skin overlying the mass, angiosarcoma was highly suspected.

Preopreative diagnosis, by aspiration cytology and biopsy, may be difficult. Chen et al. reported that the false negative rate of biopsy was 37%.

The differential diagnoses of this rare malignancy include benign hemangioma, cystosarcoma phyllodes, stromal sarcoma, metaplastic carinoma, fibrosacoma, liposarcoma, and reactive spindle cell prolifrative lesions.

Ultrastructural examination can reveal the vascular nature of angiosarcoma and demonstrate the existence of Weible-Palade bodies and pinocytic vessicles. Immunostaining for factor VIII-related antigen is helpful in the diagnosis of angiosarcoma of the breast.[2]

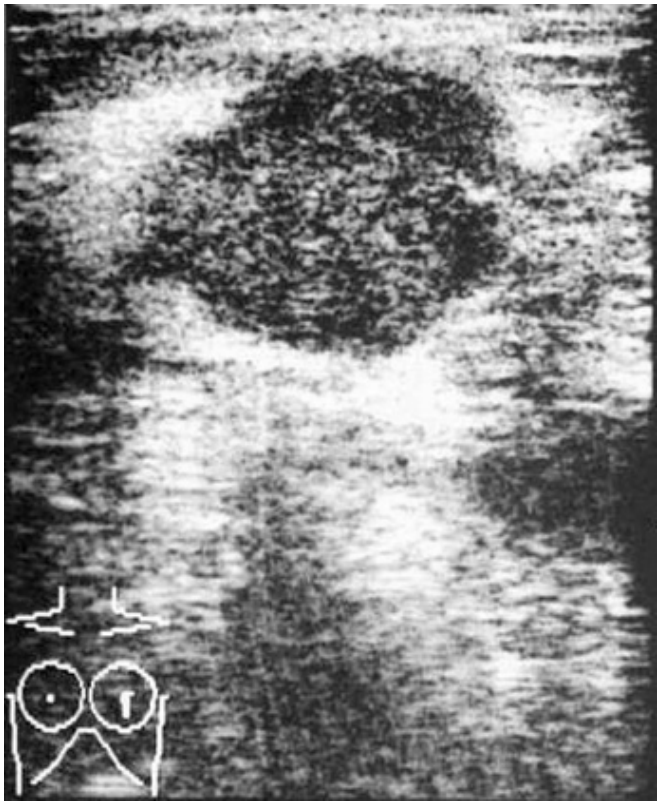

Fig 3. Ultrasound shows a hypoechoic lobulated mass without posterior shadowing.

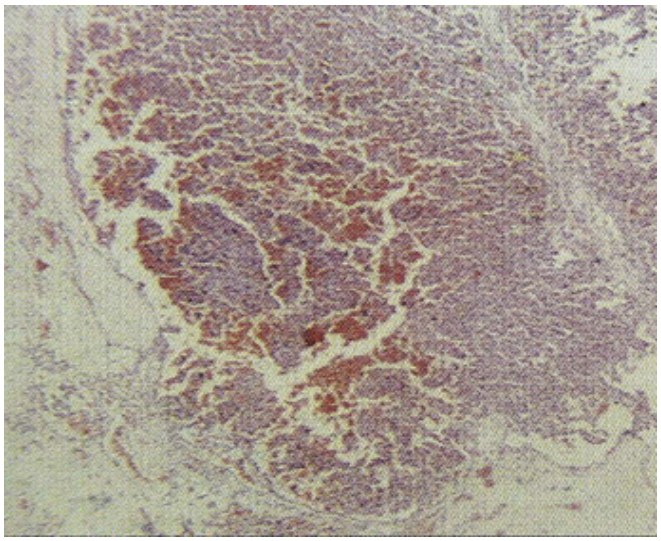

Fig 4. Angiosarcoma of the breast H & E, Low power.

The histologic features of angiosarcoma of the breast are classified into grades I, II and III. Angiosarcomas have a wide range of histological appearances from well-differentiated grade I tumors consisting infiltrating bland vascular channels to poorly differentiated grade III tumors with a sarcomatous spindle cell pattern. Large amounts of blood are often pre-

sent. Papillary clusters of tumors cells, which can be mistaken for ductal carcinoma in situ, may also occur. Poorly differentiated angiosarcomas are not easy to distinguish from poorly differentiated spindle cell carcinoma or other forms of sarcoma on morphology alone and factor VIII immunostaining may be necessary to confirm the diagnosis.

Angiosarcoma of the breast tends to metastasize hematogenously to lungs; similar to other soft tissue sarcomas. It often metastasizes to lungs, liver, bones, skin and the contralateral breast, which are not frequently involved by other type of sarcomas. [4,15,16] Chen et al. reviewed the metastatic sites of primary angiosarcoma of the breast and showed that the lungs, skin, bones, liver, brain and ovaries are the most common sites, in order of frequency.[17] Sondena et al. surveyed the metastatic site of previously reported cases and found that the liver was the most common site followed by lungs, lymph nodes and bones. Angiosarcoma has a high mortality rate, with only 10 to 27 % of patients remaining disease-free after 5 years. [4]

Because angiosarcomas of the breast are very rare, there is no established standard treatment.[2] Mastectomy and chemotherapy are the most likely treatment choices for primary angiosarcoma of the breast. Although some individuals seem to benift from adjuvent chemotherapy, available treatments for patients with disseminated disease is of minimal benefit.[2,4,15] Immunotherapy may also play a part in treating this rare type of breast cancer.

According to recent research published in the Brithish Journal of Plastic Surgery, the prognosis after complete surgical excision may be better than what is generally believed. Recently, an approach to attacking a prolifrative endothelium has been extensively investigated. It was demonstrated that rapidly prolifrating tumor endothelial cells were susceptible to immunotoxins in experimental models. [2,18]

Close interaction between endothelial cells and the blood appears to make the vasculature a practical target for therapy. Specific antibodies conjungated with efficient cytotoxins or radioactive isotopes could be used to target the tumor vessels. Endoglin is an antigen known to be expressed mainly on the surface of endothelial cells.[1,2] Thrope et al. suggested that it may be possible to treat angiosarcoma with anti-endoglin monoclonal antibodies if immunohistochemical staining for endoglin is positive.

As previously mentioned, angiosarcoma has a poor prognosis and is refractory to systemic chemotherapy.[1,2]

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