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Breast angiosarcoma one year after adenosquamous endometrial cancer – diagnostic pitfalls

Case report

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Abstract: Angiosarcoma of the breast is a rare and very aggressive tumors originated from endothelial cells lining blood vessels.We report a case of a 55-year-old postmenopausal female with a primary breast angiosarcoma diagnosed just a one year after radical hysterectomy and radiation therapy due to endometrial cancer. The patient initially presented with postmenopausal bleeding. Cytology and biopsy of the endometrium were performed and endometrial adenosquamous carcinoma was diagnosed followed by radical hysterectomy and postoperative local radiatiotherapy (50 Gy). One year later patient presented with a great painful tumorous mass in the right breast. Physical examination revealed an oval tumor, located in upper and outer quadrant of the right breast, around 15 cm in diameter. Mammography and ultrasonography were performed. The angiosarcoma of the breast was confirmed by biopsy. The patient underwent radical mastectomy. Histopathology proved the diagnosis of angiosarcoma (high-grade, numerous mitoses over 10/10 HPF, necrosis, ''blood lakes'', infiltrative borders). Differential diagnosis of a breast angiosarcoma should be considered in all painful breast tumours no mather the time and the location of the previous radiation treatment even if benign characteristics of these masses have been detected by mammography and breast ultrasound.

Keywords: *Primary breast tumors • Angiosarcoma • Concomitant malignancies • Radical mastectomy*

1. Introduction

Angiosarcoma of the breast is a rare lesion accounting for 0.04% of all malignant breast tumors [1]. These tumors arise from endothelial cells lining blood vessels and tend to be aggressive with high recurrence rates and a poor prognosis [2]. The neoplastic cells look like the vascular endothelium and are frequently stained with endothelial markers such as CD 31 and CD 34 [3] They are commonly divided into 2 types, primary and secondary angiosarcoma. Primary breast angiosarcomas arise without a recognized associated factor and occur in younger women. Secondary angiosarcomas occur most frequently after breast conservation therapy with radiation therapy; however, the average latency period described in the literature is 5–6 years [4,5]. Nevertheless, clinical presentation of the angiosarcomas has changed, due to the altered treatment principles for breast cancer: in patients treated with radical mastectomy and radiotherapy, the breast angiosarcoma

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occurrence was in the edematous arm and in patients treated by segmental resection, anti-hormonal therapy and radiotherapy, occurrence was in the irradiated field on the thoracic wall [6]. Besides, some new investigations suggest a bidirectional effect between breast and endometrial cancer, not exclusively related to tamoxifen use, creating new perspectives in the early diagnosis of breast angiosarcomas [7].

In this article, we describe the clinical presentation of breast angiosarcoma diagnosed only twelve months after total hysterectomy and radiation therapy due to endometrial adenosquamous cancer. This case presentation is very interesting for two reasons: first, breast angiosarcoma in this patient developed out of field of radiation therapy and much before the expected risk time period for development of the secondary sarcoma and second, it appeared just twelve months after radiation therapy.

2. Case report

We report a case of a 55-year-old postmenopausal female with a primary breast angiosarcoma diagnosed just a year after radical hysterectomy because of endometrial cancer. The patient initially presented with postmenopausal bleeding. Her medical history revealed hypertension and obesity. Family history was unexpectedly negative for malignancies up to the fifth line. Her first period started at the age of 13, and stopped at the age of 52 and she had two pregnancies, 2 vaginal deliveries. Cytology and biopsy of the endometrium were performed and endometrial adenocarcinoma was diagnosed. A radical hysterectomy was performed. Histopathology revealed endometrial adenosquamous cancer (50% of tumor consisted of poor differentiated endometrial cancer, 50% was poor differentiated planocellular cancer, nuclear grade 3). A postoperative local radiotherapy (50 Gy) was performed as a brachytherapy (4 fractions) as well as an external beam radiation therapy (22 fractions). At hospital discharge, a physical breast examination was done and no breast abnormalities were detected. As the patient had had mammography two years before the surgery and it had been without pathological signs, she wasn`t advised to repeat it.

One year later the patient presented with a great painful tumor mass in the right breast. Physical examination revealed an oval tumor, located in upper and outer quadrant of the right breast, with a smooth and elastic consistency, around 15 cm in diameter. There was no suspicious axillary lymphadenopathy. Mammography showed a huge tumor mass in the right breast with high density predominantly localized in the upper and outer quadrant. (Figure 1) Breast sonography revealed a hypoechogenic heterogenous cystic lesion with an intraluminal tumor and a peripheral hypervascularisation. An incisional biopsy was performed, leading to the diagnosis of the angiosarcoma of the breast. Preoperative abdominal sonography and chest radiography were normal. The radical mastectomy was performed (Figure 2). An angiosarcoma (high-grade, numerous mitoses over 10/10 HPF, necrosis, ‘’blood lakes’’, infiltrative borders) was proved by histopathology–immunohistochemistry analysis confirmed the presence of immunoreactivity for factor VIII, CD34, vimentin, reticulin and SMA, and absence of PAS, desmin and alcian-blue staining. (Figure 3). Postoperative period was without complications.

3. Discussion

The first case of angiosarcoma of the breast was described by Schmidt in 1887 [8]. However, the first report of sarcoma after radiotherapy for breast cancer appeared in 1936, [9] and the first case of angiosarcoma arising within the skin of a previously irradiated breast was described in 1981 [10] . Angiosarcomas of the breast are very rare tumors with a poor prognosis, originating from endothelial cells. Angiosarcomas of the breast can develop as a primary or secondary malignancies or they

Figure 1. Mammography: a huge tumor mass in the right breast

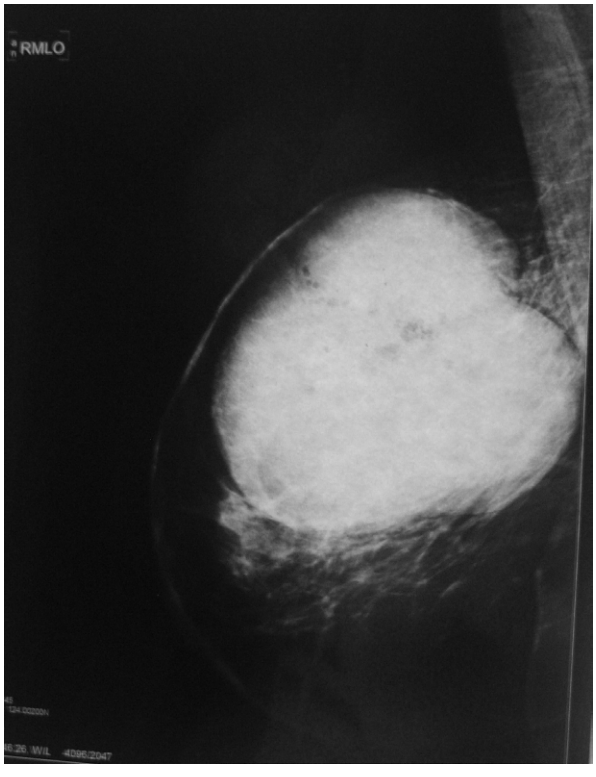


Figure 2. Right breast with tumor after mastectomy

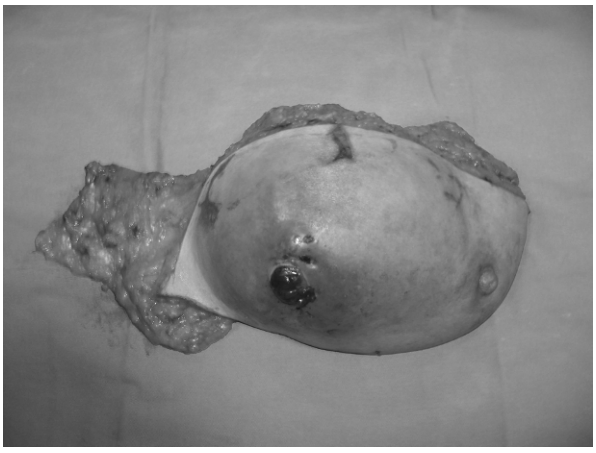
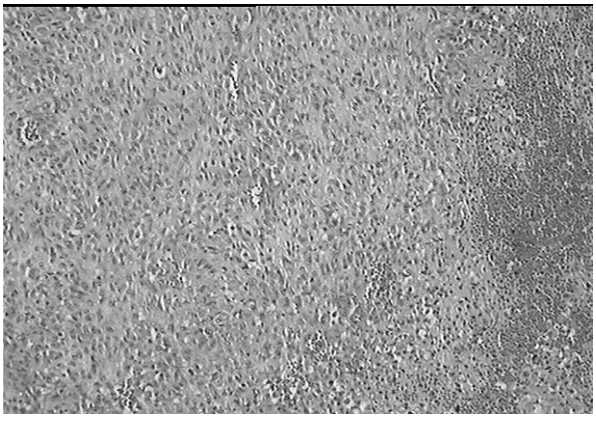


Figure 3. Hystopathology: breast angiosarcoma



can arise due to chronic lymphoedema of the upper extremity following mastectomy and radical dissection or radiotherapy of the axillary lymph nodes [11]. Primary angiosarcoma usually occurs in younger women, and often involves the breast parenchyma. The incidence rate is 0.0005% to 0.05% of all cancers in the breast [12]. Secondary angiosarcoma usually occurs in elderly women with a history of previous breast conserving surgery with whole breast radiation treatment due to the breast cancer. The overall incidence of angiosarcoma of the breast is estimated to be between 0.002% and 0.05% per year [13]. Huang et al., demonstrated that the relative risk of angiosarcoma doubled after breast cancer surgery even if no radiotherapy had been administered. This suggests a possible multifactorial etiology that should be investigated [14]. The criteria established by Cahan et al. [15] are widely used for the diagnosis of radiotherapy-induced sarcoma: a history of radiotherapy, an asymptomatic latency period of several years (5 or more), an occurrence of sarcoma within a previously irradiated field, and a histological confirmation of the sarcomatous nature of the post-irradiation lesion. The case described here doesn't fulfill these criteria. However, these criteria should be supplemented by new risk factors described in up-to-date research of breast angiosarcomas [16,17]. Our patient developed a secondary breast angiosarcoma although the region of the radiation treatment was not adjustment to the breast, rather far away. Besides, the time period between radiation treatment and angiosarcoma development was much shorter than it was reported up today. However, in previous publications, the free interval of 5 years was not respected by some authors and some of them even suggest that the free interval should be shortened to 3 years, but none of them reported time intervals shorter than 36 months [18]. In the literature, the average reported age for the development of the breast angiosarcoma was 71 years and, in the presented case, it was 55 years [7].

In breast angiosarcomas there are no clear clinical findings pointing to the diagnosis. The breast angiosarcoma is not considered as a hormonal tumor and no definite relationships are known between endometrial and sarcoma tumors, although some bidirectional effect between breast and endometrial cancers are pointed out [7]. The patient often presents with a painful palpable mass, as found in our case, while some report a rapidly growing lump. The size of the tumor varies from 4 to 10 cm. The presented case is one of the largest diagnosed breast angiosarcomas up today (15 cm). The presented patient also had intra-lesional hemorrhage, regarded as an important characteristic of the breast angiosarcoma [7]. The mass is usually mobile with no apparent fixation to the skin or chest all, similarly to the presented case. Diagnosis may be challenging due to the lack of typical radiologic characteristics on the mammogram or echosonography. An MRI of the breast is often helpful in identifying a tumor of vascular nature with malignant kinetic features. In the presented case mammography and echosonography did not lead to the diagnosis of the angiosarcoma. The angiosarcoma of the breast tends to metastasize hematogenously, rather than lymphogenously [19]. Distant metastases have been seen in lung, skin, liver, bone, CNS, spleen, ovary and heart, while the nodal metastasis is very low (6%) [20].

Patients with angiosarcomas of the breast usually present with large tumors, and total mastectomy is the procedure of choice, as it was done in the presented case. Typically, tumor cells of these angiosarcomas do not invade the regional lymph nodes, and axillary node dissection is not necessary for most patients. However, in the case of a large tumor located near the axilla and palpable nodes it is often necessary to do an axillary node dissection. The huge tumor size and localization in the upper and outer quadrant were the reasons for the axillary node dissection in the presented case. In

conclusion, we should notice that the differential diagnosis of a breast angiosarcoma should be considered in all painful breast tumors no matter the time and the location of the previous radiation treatment even if benign characteristics of these masses have been detected by mammography and breast ultrasound.

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