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# Radiation-associated angiosarcoma after breast cancer: a case report and literature review

Su spinduliniu gydymu susijusi angiosarkoma po krūties vėžio gydymo: klinikinio atvejo aprašymas ir literatūros apžvalga

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#### Introduction

Angiosarcoma after breast cancer conservative treatment is extremely rare pathology and its early diagnostic is complicated. Due to rarity of this patology, there is still no standard approach for treatment. The aim of this article is to present a clinical case of radiation-associated angiosarcoma (RAAS) after breast cancer conservative treatment and review the latest literature sources.

#### **Case report**

This case report presents 66-year-old white postmenopausal women diagnosed with left breast cancer stage I (pT1cN0M0). Breast preserving operation was performed and patient received adjuvant radiotherapy (50 Gy). After 5 years of the follow-up, RAAS of the irradiated left breast was diagnosed. The clinical features of this rare occurrence of RAAS are presented and possible treatment options are discussed. Treatment of patient was performed in National Cancer Institute.

#### **Conclussions**

Early diagnostic, multidisciplinary approach, aggressive R0 surgical treatment and additional doses of radiotherapy – allows us to more successfully treat this rare pathological state. Scientific trials to delineate proper indications for RAAS treatment of the breast are needed.

Key words: angiosarcoma, breast cancer, radiation-associated breast angiosarcoma

# Įžanga

Straipsnio tikslas – aprašyti retą klinikinį su spinduliniu gydymu susijusį angiosarkomos atvejį po krūties tausojančios operacijos ir spindulinio vėžio gydymo, taip pat apžvelgti naujausius literatūros šaltinius.

# Klinikinis atvejis

Straipsnyje aprašomas klinikinis 66 metų moters atvejis. Jai buvo diagnozuotas kairės krūties I stadijos vėžys (pT1cN0M0). 2011 metais atlikta krūtį tausojanti operacija ir taikytas pooperacinės radioterapijos kursas (50 Gy). 2016 metais, po 5 metų nuo pirminio kairės krūties vėžio sudėtinio gydymo, šioje krūtyje nustatyta su spinduliniu gydymu susijusi angiosarkoma. Mes aptariame šios retos angiosarkomos klinikinį atvejį ir galimus gydymo metodus. Ligonė buvo gydoma Nacionaliniame vėžio institute.

#### Išvados

Ankstyva diagnostika, daugiadalykis aptarimas, agresyvus R0 chirurginis gydymas ir adjuvantinio spindulinio gydymo dozės leidžia sėkmingiau gydyti šia retą patologinę būklę. Reikalingi papildomi moksliniai tyrimai, kurie padėtų nustatyti su spinduliniu gydymu susijusios angiosarkomos gydymo indikacijas.

Reikšminiai žodžiai: angiosarkoma, krūties vėžys, su spinduliniu gydymu susijusi angiosarkoma

### Introduction

Angiosarcoma (AS) of breast is a very aggressive malignant tumor of the vascular endothelium [1]. Overall, less than 1% of all soft tissue sarcomas are angiosarcomas and primary AS of the breast represents only 1 in 1700-2000 primary breast cancers [4]. Primary AS developes in patiens who have never had any history or treatment of breast cancer, and may occur in younger women, usually in the 20 to 40 years range. Secondary radiation-associated angiosarcoma (RAAS) developes in a woman who underwent irradiaton for conservative treatment of a primary breast cancer. A secondary angiosarcoma of the breast is associated with two presumed aetiologic factors: chronic lymphedema after a mastectomy with lymph node dissection (Stewart-Treves syndrome) and radiotherapy. The average time between radiation therapy and AS development is 6 years, although several reports indicate this may occur as early as 1-2 years or as late as 41 years after treatment [1]. Because of RAAS rarity and difficulties in radiologic and clinical simptoms, the early diagnosis of RAAS is complicated, and the overall survival and local recurrence results are poor.

# Case report

This case report presents 66-years-old white postmeno-pausal women diagnosed and treated breast cancer pT1cN0M0 stage in National Cancer Institute, Vilnius, Lithuania. On 4th of June 2011 breast preserving operation (quadrantectomy, ipsilateral axillary lymph node dissection) was performed. Pathologic examination revealed invasive ductal carcinoma grade 2 (G2),

Er – positive 8/8 according Allred, Pr – positive 6/8 according Allred, Her2 1+ negative, R0 resection. Lymph nodes were uninvolved pathologically. Patient received adjuvant radiotherapy (50 Gy) and hormotherapy (tamoxifen 20 mg per day). Follow-up. Annual breast digital mammograms and ultrasound were normal. On May 20th 2016 the patient visited NCI out-patient clinic with a complaints of a rapidly growing new masses in the operated and irradiated left breast. Breast physical exam: the breast was enlarged with erythematous infiltrated area, painless 12 cm × 5 cm and various size multiple cutaneous lesions; pink or red discoloration of the skin. Right breast – without palpable pathologic masses. Axillary and regional lymph nodes – without pathologic changes (Fig. 1).

The radiologic examination of this patient included: breast ultrasonography, digital mammography.



**Figure 1.** Left breast with various size multiples cutaneous lesions; pink or red discoloration of the skin

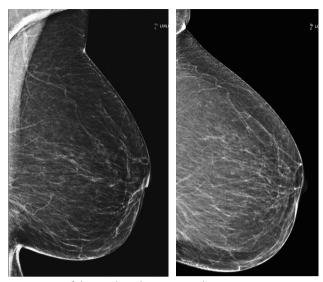
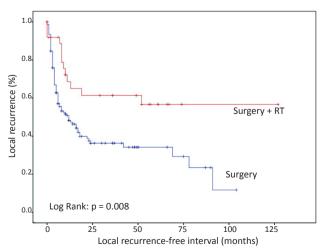


Figure 2. Left breast digital mammograhy

Digital mammography revealed postoperative changes in the left breast Bi-Rads-II, ACR I. No pathological changes as compared with previous mammograms. Breast ultrasonography revealed no pathological changes, axillary and regional lymph nodes were not enlarged. Core biopsy of palpated tumor – possible angiosarcoma due to radiation therapy.

Multidisciplinary team recommended operation, starting with simple mastectomy, in case of invasion to pectoralis major muscle – radical mastectomy by Halsted.



**Figure 3.** Local control, surgery versus surgery + radiotherapy [4]

In June 2016 simple mastectomy, removing widely breast, irradiated and indurated tissues (28 cm  $\times$  15 cm  $\times$  3 cm) was performed. Post-operative period without complications.

Final pathological examination revealed breast angiosarcoma low grade G1 (associated with local radiotherapy) R0. Final diagnosis: Carcinoma of the right breast pT1cN0M0 stage I (2011). Angiosarcoma of the right breast G1 (2016).

Multidisciplinary team recommended to discuss adjuvant doses of radiotherapy.

#### Discussion

The risk of a second cancer malignancy among persons who have had a cancer previously is increasing. Implementing the use of conservation therapy for breast cancer patients, number of reports on RAAS had increased. However, the small difference in the risk of subsequent sarcoma for breast cancer patients receiving radiotherapy does not supersede the benefit of radiotherapy after breast preserving surgery [1, 4, 6].

The reported median latency period between radiation and diagnosis of radiation-associated sarcomas RAAS is 6–7 years. Although several reports indicate this may occur as early as 1–2 years or as late as 41 years after treatment [2, 3, 5].

Retrospective analysis of 332 163 Finnish cancer patients showed the cumulative incidence of AS at 15 years post diagnosis – 0.9 per 1,000 for cases receiving radiation (SE=0.2) and 0.1 per 1,000 for cases not receiving radiation (SE<0.1). 5 year results of the overal survival of RAAS were poor 27–35% [2]. Depla AL er al. in a systematic review of 74 articles analyzed data of RAAS 222 patients. In these patients, the 5-year overal survival was 43%. Surgery with radiotherapy had a better 5-year local recurrence-free interval LRFI of 57% compared to 34% for surgery alone (p=0.008). [4].

In our case report we presented and summarized very reare pathological condition – RAAS after 5 years of combined primary breast cancer treatment.

Generally, the prognosis for angiosarcoma of the breast is rather poor. But in our case for low grade G1 angiosarcoma, after performed wide agressive surgery (R0) and additional radiotherapy – the results are more optimistic.

# **Conclusions**

- In any patients with discoloration that does not disappear – punch or core biopsy should be performed.
- 2. Surgery R0 is considered to be the treatment of choice, but the outcome is poor because of high local recurrence rates.
- 3. The achievement of R0 margins is probably of major importance for improving the patient outcome.
- 4. Adjuvant radiotherapy doses probably decrease the risk of local recurrence.

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