



Radiation-induced angiosarcoma of the breast: a case report

Chafik Rhoul, MD^{a,b,*}, Ayoub Kharkhach, MD^{a,b}, Houssam Aabdi, MD^{a,b}, Abderrahman Atmani, MD^{a,b}, Mohammed Mhand, MD^{a,b}, Noura Seghrouchni, MD^{a,c}, Bennani Amal^{a,c}, Tarik Bouhout^{a,b}, Badr Serji^{a,b}, Tijani El Harroudi^{a,b}

Introduction: Breast angiosarcoma is a rare, aggressive tumour affecting adult women. It can occur in two forms, primary form and secondary forms or radiation-induced breast angiosarcoma affecting patients with history of breast or chest radiotherapy.

Case presentation: The authors report a new case of breast angiosarcoma in 52-year-old women, with history of invasive ductal carcinoma, and reporting a discoloration of her breast skin. The patient did undergo a mastectomy of right breast and adjuvant chemotherapy.

Conclusion/discussion: Surgery with total excision associated or not to adjuvant chemotherapy remains the treatment of choice in breast angiosarcoma.

Keywords: breast angiosarcoma, breast cancer, breast surgery, breast radiation, case report

Introduction

Angiosarcoma (AS) is a high grade malignant and a rare tumour, that ordinary originates from the endothelial cells of blood or lymphatic vessels^[1]. AS can affect any organ, nevertheless the skin remains the most affected area^[2]. Breast AS represents less than 1% of the mamillary neoplasm^[3]. They can occur spontaneously and then are called primary AS or secondary to breast or chest irradiation therapy which are called secondary AS or radiation-induced breast AS (RIAS)^[4].

Case report

We report a new case of breast AS, in 52-year-old women, who has received a conserving surgery with axillar lymph node dissection back in 2015 to her invasive high grade ductal carcinoma with adjuvant combination therapy of chemotherapy and radiotherapy. The chemotherapy regimen received consisted of 6 cycles of Doxorubicin: 100 mg/m² and 1000 mg/m² of

HIGHLIGHTS

- The breast angiosarcoma is a rare, aggressive tumour affecting adult women.
- This case report may help more to diagnosis this skin tumour.
- The treatment consists on mastectomy associated or not to chemotherapy.

Endoxanes plus 125 mg/m² of Docetaxel. The patient underwent for irradiation therapy of her right breast with 50 Gray plus 12.5 Gray as boosting charge. Three years later, the patient did notice discoloration of her right breast skin with palpable nodule of the same breast (Fig. 1). A surgical biopsy was performed of her skin lesion showed an AS in the histopathological examination (Fig. 2). Although, the computed tomography scan findings did not find any second location of the AS. The patient underwent for right mastectomy without reconstructive surgery and adjuvant chemotherapy with no postoperative course was uneventful. Currently, 9 months after her breast surgery and chemotherapy, the patient is in a good health with no evidence of disease. This case has been reported following the SCARE criteria^[5].

Discussion

Epidemiology

Breast AS are an aggressive and rare tumour^[1]. Primary forms, which occur spontaneously represents less than 0.04% of all malignant breast neoplasm, it is observed in women without a history of breast irradiation during their third or fourth decades^[3]. The secondary form represents less than 0.05% of all malignant tumours of the breast, it is observed in elderly women who have benefited from mammary radiotherapy^[3]. The

^aFaculty of Medicine and Pharmacy, Mohammed Ist university, ^bDepartment of Oncological Surgery, Regional oncology Center and ^cDepartment of Pathology, Mohammed VI University Hospital Oujda Morocco

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Mohammed I University Oujda Faculty of Medicine and Pharmacy Oujda, Oujda, Morocco Tel.: +212681123099 fax. +33751387513. E-mail address: rhoulc@gmail.com (C. Rhoul).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Annals of Medicine & Surgery (2023) 85:5047–5050

Received 25 September 2022; Accepted 31 July 2023

Published online 4 September 2023

<http://dx.doi.org/10.1097/MS9.0000000000001141>



Figure 1. The appearance of the tumour with blackish-purple cutaneous lesion.

incidence of RIAS may vary from 0.14 to 0.5% in women who have received surgical treatment associated with radiotherapy^[3].

Diagnosis

The clinical presentation of AS is diverse, it can form as a single or multiples nodules, as a papules or vesicles lesions, however, one third of the patients present only a tumour. Therefore, the discoloration of the breast skin or the appearance of a tumour within radiation field should be alarming sign must lead to a biopsy for histological proof^[6]. Generally, the primary form of AS is like a nodule, nevertheless, for the secondary form it is a violaceous skin spot^[7]. With regard to breast imaging, mammography and/or MRI have a limited place for positive diagnosis, but MRI is lightly more efficient in the detection of AS^[8-10].

Histology

RIAS and AS have similar histological features^[11,12]. It is a poorly limited invasive tumour infiltrating the dermis and often the subcutaneous tissue^[13]. It contains an irregular and anastomotic vascular network, with increased sized endothelial cells containing a rare cytoplasm showing different degrees of nuclear atypia^[13,14]. AS is classified into three grade, low, intermediate and high grade^[3], depending on cytological atypia, the number of mitoses, endothelial proliferation and the presence of necrosis or haemorrhage^[4,10].

Immunohistochemistry has an interest in undifferentiated forms or when histological diagnosis is not clear^[15]. The AS express, especially, the following endothelial markers, CD31,

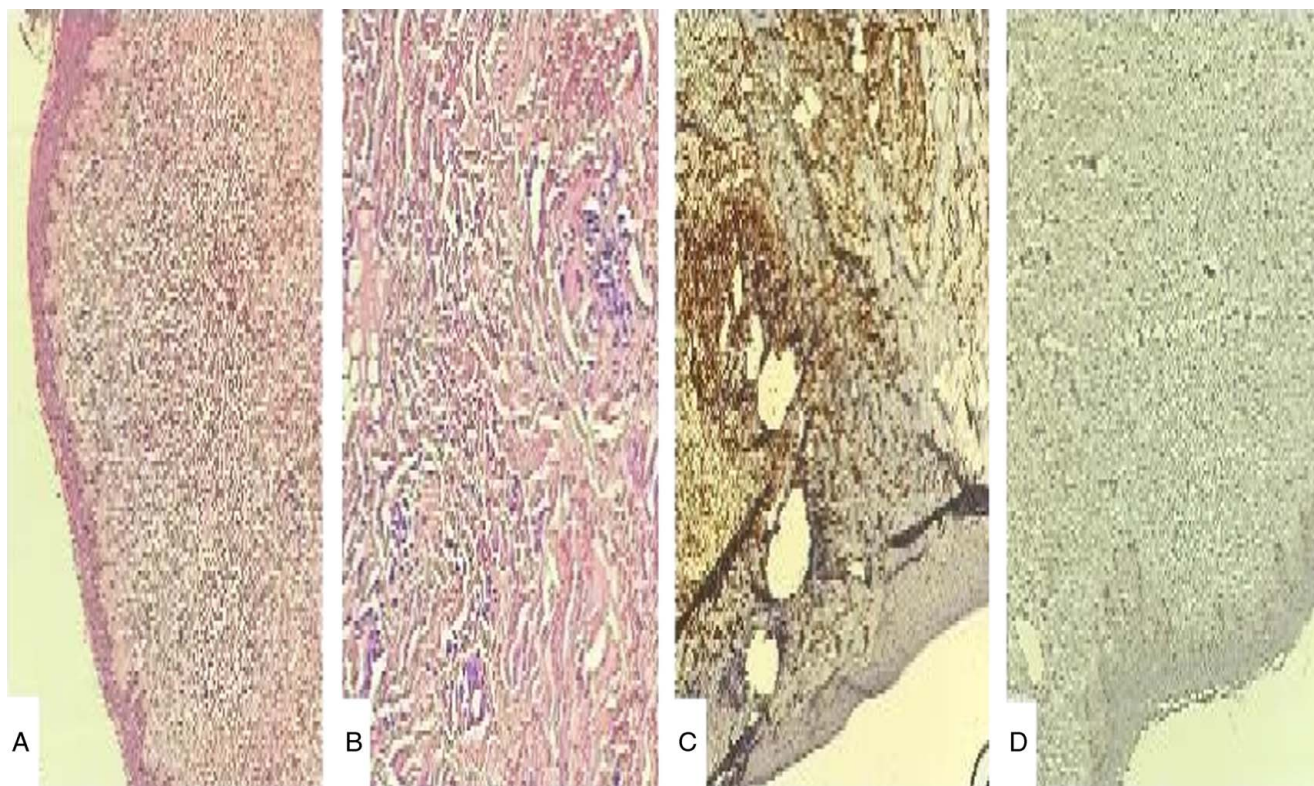


Figure 2. Microphotography showing: (A) The dermis contains ill-defined tumour composed of angulated and irregular vascular spaces associated to blood lakes. (B) Vessels are lined by atypical, multilayering and hobnailing endothelial cells. (C) Tumour shows strong and diffuse membranous CD31 positivity. (D) CK expression is absent.

CD34, FLI1 and ERG^[15]. ERG, an ETS family transcription factor, is considered the most sensitive and specific marker for endothelial differentiation^[15]. Some lymphatic markers including D2-40, PROX-1 and VEGFR-33, can be observed in certain cutaneous AS^[16,17].

Treatment

As far as the treatment is concerned, there is no agreement for its modalities^[18]. The main treatment consists of surgery, with local excision to mastectomy^[2]. A mastectomy with negative margins is recommended^[2]. The recurrence rate remains high, although with negative margins, it can vary from 54 to 92%^[19]. Lymphadenectomy is not systematically recommended because the lymph nodes are rarely touched^[3]. The excision of lymph nodes associated with radiotherapy is recommended when the tumour is extensive and near to draining nodes^[20].

The indication of radiotherapy is controversial, especially in patients who have developed RIAS^[21].

Nevertheless, after a conserving surgical treatment of breast the adjuvant radiotherapy must be indicated given the low risk of the occurrence of a RIAS after breast irradiation^[22].

The role of chemotherapy has not been clearly defined. Several studies have shown an important role of taxanes and anthracyclines in the treatment of ASs with a response rate from 20 to 60%^[23]. Neo-adjuvant chemotherapy is indicated if there is a surgical delay for any reason, to reduce the progression of tumoral cells^[24].

Prevention

Clinical suspicion is the major key to the diagnosis of post-radiation AS^[25]. During breast cancer observation, especially in patients who have received conserving surgical treatment and radiotherapy, any skin lesion in the irradiated area should draw the practitioner's attention and lead to a biopsy for histological examination.

Conclusion

RIAS remains a rare malignant affection, which must be known by any practitioner. Its diagnosis is based on a biopsy with histopathological examination. Surgery remains the treatment of choice with total excision associated or not with adjuvant chemotherapy.

Ethical approval

Not applicable, no ethical approval was needed for this work.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Source of funding

This work was not funded or supported by any organization.

Author contribution

All authors have contributed equally in writing this paper.

Conflicts of interest disclosure

All authors have no conflict of interest to declare.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Dr. Rhoul Chafik.

Data availability statement

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

- [1] Abraham JA, Hornicek FJ, Kaufman AM, *et al.* Treatment and outcome of 82 patients with angiosarcoma. *Ann Surg Oncol* 2007;14:1953–67.
- [2] Farran Y, Padilla O, Chambers K, *et al.* Atypical presentation of radiation associated breast angiosarcoma: a case report and review of literature. *Am J Case Rep* 2017;18:1347–50.
- [3] Virgilio E, Lombardi M, Stefano DD, *et al.* Angiosarcoma of the Breast: A Rare and Dismal Complication of Breast Surgery Associated with Radiation. *Am Surg* 2017;83:e71–3.
- [4] Shah S, Rosa M. Radiation-Associated Angiosarcoma of the Breast: Clinical and Pathologic Features. *Arch Pathol Lab Med* 2016;140:477–81.
- [5] Agha RA, Franchi T, Sohrab C, *et al.* The SCARE 2020 guideline: updating consensus Surgical Case Report (SCARE) guidelines. *Int J Surg* 2020;84:226–30.
- [6] Seinen JM, Styring E, Verstappen V, *et al.* Radiation-associated angiosarcoma after breast cancer: high recurrence rate and poor survival despite surgical treatment with R0 resection. *Ann Surg Oncol* 2012;19:2700–6.
- [7] Scow JS, Reynolds CA, Degnim AC, *et al.* Primary and secondary angiosarcoma of the breast: the Mayo Clinic experience. *J Surg Oncol* 2010;101:401–7.
- [8] West JG, Qureshi A, West JE, *et al.* Risk of angiosarcoma following breast conservation: a clinical alert. *Breast J* 2005;11:115–23.
- [9] Hodgson NC, Bowen-Wells C, Moffat F, *et al.* Angiosarcomas of the breast: a review of 70 cases. *Am J Clin Oncol* 2007;30:570–3.
- [10] Iqbal FM, Ahmed B, Vidya R. Double-edged sword of radiotherapy: a cause of secondary angiosarcoma after breast conservation therapy. *BMJ Case Rep* 2016;2016:bcr2016215310.
- [11] Mentzel T, Schildhaus HU, Palmedo G, *et al.* Postradiation cutaneous angiosarcoma after treatment of breast carcinoma is characterized by MYC amplification in contrast to atypical vascular lesions after radiotherapy and control cases: clinicopathological, immunohistochemical and molecular analysis of 66 cases. *Mod Pathol* 2012;25:75–85.
- [12] Laé M, Lebel A, Hamel-Viard F, *et al.* Can c-myc amplification reliably discriminate postradiation from primary angiosarcoma of the breast. *Cancer Radiother* 2015;19:168–74.
- [13] Cuperus E, Leguit R, Albrechts M, *et al.* Post radiation skin tumors: basal cell carcinomas, squamous cell carcinomas and angiosarcomas. A review of this late effect of radiotherapy. *Eur J Dermatol* 2013;23:749–57.

- [14] Zalaudek I, Gomez-Moyano E, Landi C, *et al.* Clinical, dermoscopic and histopathological features of spontaneous scalp or face and radiotherapy-induced angiosarcoma. *Australas J Dermatol* 2013;54:201–7.
- [15] Ronchi A, Cozzolino I, Zito Marino F, *et al.* Primary and secondary cutaneous angiosarcoma: Distinctive clinical, pathological and molecular features. *Ann Diagn Pathol* 2020;48:151597.
- [16] Kahn HJ, Bailey D, Marks A. Monoclonal antibody D2-40, a new marker of lymphatic endothelium, reacts with Kaposi's sarcoma and a subset of angiosarcomas. *Mod Pathol* 2002;15:434–40.
- [17] Miettinen M, Wang ZF. Prox1 transcription factor as a marker for vascular tumor evaluation of 314 vascular endothelial and 1086 non-vascular tumors. *Am J Surg Pathol* 2012;36:351–9.
- [18] Bonito FJP, de Almeida Cerejeira D, Dahlstedt-Ferreira C, *et al.* Radiation-induced angiosarcoma of the breast: A review. *Breast J* 2020;26:458–63.
- [19] Uryvaev A, Moskovitz M, Abdach-Bortnyak R, *et al.* Post-irradiation angiosarcoma of the breast: clinical presentation and outcome in a series of six cases. *Breast Cancer Res Treat* 2015;153:3–8.
- [20] Monroe AT, Feigenberg SJ, Mendenhall NP. Angiosarcoma after breast-conserving therapy. *Cancer* 2003;97:1832–40.
- [21] Gutkin PM, Ganjoo KN, Lohman M, *et al.* Angiosarcoma of the Breast: Management and Outcomes. *Am J Clin Oncol* 2020;43:820–5.
- [22] Kunkel T, Mylonas I, Mayr D, *et al.* Recurrence of secondary angiosarcoma in a patient with post-radiated breast for breast cancer. *Arch Gynecol Obstet* 2008;278:497–501.
- [23] Skubitz KM, Haddad PA. Paclitaxel and pegylated-liposomal doxorubicin are both active in angiosarcoma. *Cancer* 2005;104:361–6.
- [24] Li GZ, Fairweather M, Wang J, *et al.* Cutaneous Radiation-associated Breast Angiosarcoma: Radicality of Surgery Impacts Survival. *Ann Surg* 2017;265:814–20.
- [25] Wijnmaalen A, van Ooijen B, van Geel BN, *et al.* Angiosarcoma of the breast following lumpectomy, axillary lymph node dissection, and radiotherapy for primary breast cancer: three case reports and a review of the literature. *Int J Radiat Oncol Biol Phys* 1993;26:135–9.