Rare disease

Breast angiosarcoma secondary to phyllodes tumour

Sílvia Costa, Susana Alexandra Rodrigues Graça, António Ferreira, Jorge Maciel

Department of General Surgery, Centro Hospitalar Gaia/Espinho, EPE, Gaia, Portugal

Correspondence to Dr Sílvia Costa, sisse.costa@gmail.com

Summary

Angiosarcomas are rare malignant tumours that arise from endothelial cells lining vascular channels, representing 0.04% of malignant neoplasms of the breast. Breast angiosarcomas (BAs) were first described by Schmidt in 1887, and may be primary or secondary to the pre-existing conditions. Primary BAs are more common in young women and present as a palpable mass. Secondary BAs arise in older patients, frequently 5–6 years after radiotherapy, and present as a rash. The authors describe the case of an 83-year-old woman with no history of thoracic radiotherapy or surgery. She had been observed for a breast nodule where biopsy revealed phyllodes tumour. The patient refused surgery and returned 2 years later because of an impressive increase in tumour volume and skin ulceration. She underwent mastectomy with local skin flaps. Histopathological result revealed high-grade angiosarcoma of 15×12 cm. There was follow-up without evidence of recurrence, after radiotherapy.

BACKGROUND

Angiosarcomas are rare malignant tumours that arise from endothelial cells lining vascular channels.^{1–2} The breast is one of the most common sites in the body to develop angiosarcoma.³ Schmidt⁴ described the first case of breast angiosarcoma (BA). BA can be primary (sporadic) or secondary to the pre-existing conditions.

Primary BAs are rare and account for 8% of breast sarcomas,⁵ they occur usually during the third and fourth decades of life, presenting as palpable masses.

Secondary BAs occur most frequently in older women, in average 5–6 years after breast conservation surgery with radiation therapy.⁶ Angiosarcomas are also known to be secondary to chronic lymphoedema (after axillary lymphadenectomy—Stewart-Treves syndrome; or after inguinal lymphadenectomy—Kettle's syndrome), foreign material (graft material and sponges) and environmental carcinogens (arsenic, dioxin and vinyl chloride). Secondary angiosarcomas usually present as a rash, and bluish skin discolouration occurs in up to a third of patients due to the vascular nature of the tumour.^{1–7} In the series by Sher *et al*,⁸ the mean tumour size of the mass at presentation was 5.5 cm.

Mammographically, the appearance is non-specific. An ill-defined, non-calcified mass or focal asymmetry is the most common finding. In the study by Yang *et al*,⁵ 19% of patients had tumours that were not visible mammographically but were visible with sonography and MRI.

Sonography is useful for confirmation of a mass when a palpable abnormality is found. Masses may be circumscribed or ill-defined. Diffuse, abnormal, mixed hyperechoic and hypoechoic regions without a discrete mass were noted in 38% of patients in the series of Yang *et al*.⁵

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.^{5–9} Irregular areas of high T1 signal may be seen in higher-grade lesions (haemorrhage or venous

lakes).¹⁰ MRI is useful in determining tumour extent and in planning surgery.

Surgical complete resection in the form of mastectomy or wide excision remains the cornerstone treatment for both forms of angiosarcoma. The axillary lymph node resection has no role in treatment due to the low incidence of axillary metastasis.⁸ Given the endothelial origin of BAs, angiogenesis inhibition represents a potentially attractive therapeutic modality.¹¹ Thorpe *et al*¹² suggested that monoclonal antibodies with affinity to antigens in tumour vasculature such as endoglin could be applicable in the therapy of this vicious neoplasm. Chemotherapy with docetaxel may reduce local recurrence rate.¹³ Although data are limited, hyperfractionated radiation therapy has resulted in reduced cell repopulation of rapidly growing tumours.¹⁴

Three grades of angiosarcoma are described.² Low-grade (or grade 1) tumours consist of anastomosing vascular channels that invade the surrounding breast tissue. Intermediate-grade tumours have more solid neoplastic vascular growth and an increased mitotic rate. High-grade lesions have gross sarcomatous areas, as well as areas of necrosis, haemorrhage and infarction. Complete excision and careful histological evaluation are needed to accurately determine tumour grade.¹

BAs are usually highly aggressive, with high local recurrence and poor prognosis. The prognosis for patients with angiosarcoma depends on tumour size, presence of residual disease and cellular pleomorphism.^{15–16} According to Nascimento *et al*,¹⁷ grade of the tumour may not be an important prognostic factor. Regional metastasis to axillary lymph nodes is rare. Metastases occur most frequently in bones, lungs and liver.^{1–6}

CASE PRESENTATION

We report the case of an 83-year-old woman with no relevant medical history, no history of thoracic radiotherapy or surgery. There was no family history of breast

Figure 1 Tru-cut biopsy performed 2 years back showing biphasic lesion with an epithelial component without atypia and hypercellular mesenchymal component with some pleomorphism and vessels without morphological deviations (phyllodes tumour).

carcinoma. She had been observed 2 years back for a breast lump whose biopsy revealed fibroepithelial lesion composed of epithelium without atypia in spindle cell stroma with atypia, but without mitotic figures, compatible with phyllodes tumour of uncertain malignant potential (figure 1). The patient refused surgery. However, she returned 2 years later because of dramatic increase of tumour volume (15 cm) and skin ulceration (figure 2). MRI confirmed the presence of a heterogeneous bulky tumour mass with irregular contour heavily T2-weighted and highly vascularised, invading the skin but not the pectoralis major muscle; there were no suspicious changes in the contralateral breast or lymph nodes (figure 3).

She underwent mastectomy with local skin flaps. The histopathological analysis revealed a high-grade angiosarcoma of 15×12 cm in a 2125 g mastectomy, with anastomosing vascular channels alternating with fusocellular areas. The tumour had abundant mitoses and extensive areas of necrosis, with free margins (figure 4). The recovery was uneventful. She was referred to the sarcomas (study group) consult, and radiotherapy was performed.

OUTCOME AND FOLLOW-UP

Follow-up without evidence of recurrence (1 year).

DISCUSSION

Phyllodes tumours are fibroepithelial tumours composed of epithelial elements projecting into a hypercellular

Figure 3 MRI shows a heterogeneous bulky tumour mass with irregular contour, highly vascularised, invading the skin but not the pectoralis major muscle.

Figure 4 High-grade angiosarcoma forming irregular vascular spaces, with marked pleomorphism and evident nucleoli.

stromal in a leaf-like fashion. They were first considered as a kind of breast sarcoma, but their relatively benign behaviour has led them to be considered separately. Phyllodes tumours of breast show variable clinicopathological behaviour ranging from benign to malignant depending on histological features (stromal cellularity, stromal cytologic atypia, infiltration at the tumour's edge and mitotic activity). All forms of phyllodes tumours are regarded as having malignant potential. Pathogenesis of the phyllodes tumour remains an enigma, although recent studies have suggested that the epithelium exerts a field effect that potentiates stromal overgrowth. Malignant change usually occurs within the hyperplastic stromal cells, resulting in sarcomatous lesions. The most common are: fibrosarcoma, liposarcoma and rhabdomyosarcoma.¹⁸

Figure 2 Clinical aspects before and after surgery.

Rarely, chondrosarcoma, osteosarcoma and angiosarcoma can also be encountered.¹⁹

Only two cases of angiosarcoma arising from recurrent phyllodes tumour have been reported in the literature.^{20 21} Both of the reported cases are about young patients (22 and 30 years old), with recurrent phyllodes tumours. Hence, to the best of our knowledge, we are reporting a very rare case of angiosarcoma arising from phyllodes tumour.

Learning points

- Breast angiosarcomas (BAs) are a rare entity, specially arising from phyllodes tumour.
- BAs are usually highly aggressive, with high local recurrence and poor prognosis; surgical complete resection remains the corner-stone treatment, with no indication of axillary lymphadenectomy.
- Owing to its endothelial aetiology, angiogenesis inhibitors drugs represent a promising therapeutic modality. Chemotherapy with docetaxel has been shown to reduce local recurrence. Radiation therapy is indicated, including for secondary BAs.
- With the increasing application of breast conserving surgery, reports of postirradiation BAs are escalating because early recognition of this pathology is crucial to institute early therapy.

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Competing interests None.

Patient consent Obtained.

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