

Mammary angiosarcoma in two patients at either end of the age spectrum

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Angiosarcoma of the breast is rare and has a poor prognosis due to its aggressive nature. This is a report of two patients with mammary angiosarcomas, each with different clinical presentations, and at either end of the age spectrum. One is an 18-year-old woman who presented with a rapidly enlarging breast mass, and the other a 72-year-old woman whose breast mass was found during screening mammography. The radiological features of mammary angiosarcoma are summarised in this report.

Introduction

Angiosarcoma of the breast is a rare malignant neoplasm characterised by rapidly proliferating, extensively infiltrating, anaplastic cells derived from blood vessels lining irregular blood-filled spaces. This rare tumour accounts for 0.04% of primary mammary tumours¹ and approximately 8% of mammary sarcomas.² The annual incidence is 5.8 per 10 million women.³ Because angiosarcomas are aggressive, tending to recur locally and metastasise widely, they are difficult to treat and the prognosis is dismal. The 5-year survival rate varies from only 8 to 50%.⁴ Mammary angiosarcomas tend to metastasise haematogenously, rather than lymphogenously. Metastases to the lungs, skin, subcutaneous tissue, liver, bone, central nervous system, spleen, ovary, omentum, and adrenal gland have been described.^{5,6} This is a report of two patients with mammary angiosarcomas, with different clinical presentations and at either end of the age spectrum.

Case reports

Case 1

In February 2006, an 18-year-old, nulliparous woman presented to a private clinic with a self-discovered left breast lump, noted since the end of 2005. An ultrasound scan of both breasts was performed and she was told that she had a benign lesion. Nonetheless, it was suggested she underwent a fine-needle aspiration, which yielded haemorrhagic aspirate only.

A few months later, in July 2006, she noted that the lump was enlarging rapidly so sought another medical opinion at the surgical unit of a regional hospital in Hong Kong. A physical examination found that the left breast was diffusely swollen. No discrete palpable mass was found. The breast was soft and non-tender and there was no associated discolouration of the skin, nipple discharge, or axillary lymphadenopathy.

An ultrasound scan of the breasts (Fig 1) found a 7.2 cm x 3.6 cm x 7.6 cm (width x depth x height) heterogeneously hypoechoic mass with cystic components occupying most of the central upper portion of the left breast. Its margin was infiltrative and poorly defined. Increased intralesional vascularity was demonstrated by a Doppler study. No enlarged lymph nodes could be seen in the axillae. The right breast was normal.

A Tru-Cut biopsy was taken from the left breast lesion under ultrasound guidance. Sections showed several cores of a vascular lesion consisting of variably sized vascular spaces. The conclusion was that this was a vascular tumour, and its malignant potential could not be accurately assessed without an excisional biopsy.

In October 2006, an excisional biopsy of the left breast lesion was performed. At operation a large, vascular, haemorrhagic tumour, occupying most of the left breast, was found. The underlying muscles were not involved. Because there was neither a well-defined margin nor any demarcation between tumour and normal breast tissue, a left subtotal mastectomy was performed.

The surgical specimen consisted of a dark haemorrhagic tumour with a central haemorrhagic cavity. In the periphery, the tumour consisted of anastomosing and intercommunicating vascular channels lined by one or two layers of endothelial cells with

Key words

Breast neoplasms; Hemangiosarcoma;
Neoplasm metastasis

Hong Kong Med J 2010;16:141-4

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年齡相距甚遠的兩名乳腺血管肉瘤患者

乳腺血管肉瘤很罕見，其侵略性對預後是不利的。本文報告兩名年齡相距甚遠的乳腺血管肉瘤患者，分別出現不同的臨床症狀。其中一名18歲患者的乳房有快速變大的腫瘤，另一名72歲患者於定期乳房篩檢時發現乳房有腫瘤。本文並總結乳腺血管肉瘤的影像學特徵。

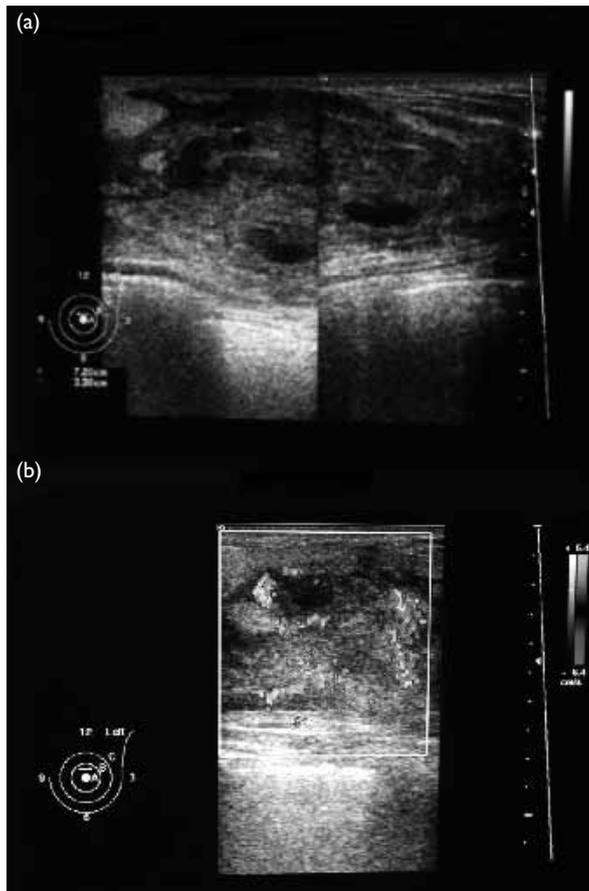


FIG 1. (a) Ultrasound images of the left breast lesion of case 1: an ill-defined mixed hypoechoic lesion with an internal cystic component measuring about 7.5 cm is seen. (b) Doppler ultrasound of the left breast lesion demonstrates a highly vascular tumour

rare mitoses. At the centre, it was more cellular, with solid spindle areas exhibiting mild cellular atypia. It showed diffuse infiltration between the fat lobules, around and into the mammary lobule with destruction of the ducts and lobules. Overall, the histological picture was consistent with mammary angiosarcoma, of a moderate nuclear grade. The superficial and superior margins were focally involved.

In view of the margin involvement, a radical mastectomy was performed in early November 2006. Clear margins were achieved and four axillary lymph nodes were sampled. These were all free of metastases. During the same session, a total reconstruction of the left breast with a pedicle transverse rectus abdominis myocutaneous flap was performed by plastic surgeons.

Her postoperative course was uneventful. She had an F-18-deoxyglucose positron emission tomographic (FDG-PET) scan that was negative and underwent a course of adjuvant radiation therapy. To date, 27 months after mastectomy, this patient has not shown any signs of recurrence or of metastases. She is still being followed up regularly.

Case 2

A healthy 72-year-old woman, who had attended a well woman clinic in Hong Kong for screening mammographies every 2 years since 2004, was noted to have a developing mass during her third screening mammography in July 2008.

The mass was about 0.5 cm in size, situated in the lower outer quadrant of her left breast (Figs 2a, 2b) and was of intermediate density with a lobulated margin. There was no associated architectural distortion or microcalcification cluster. The overlying skin was not thickened and there was no axillary lymphadenopathy. A supplementary ultrasound scan was performed but the lesion could not be localised.

About 1 month later, a stereotactically guided core needle biopsy of the left breast mass was performed with a 14-Gauge needle. The preliminary

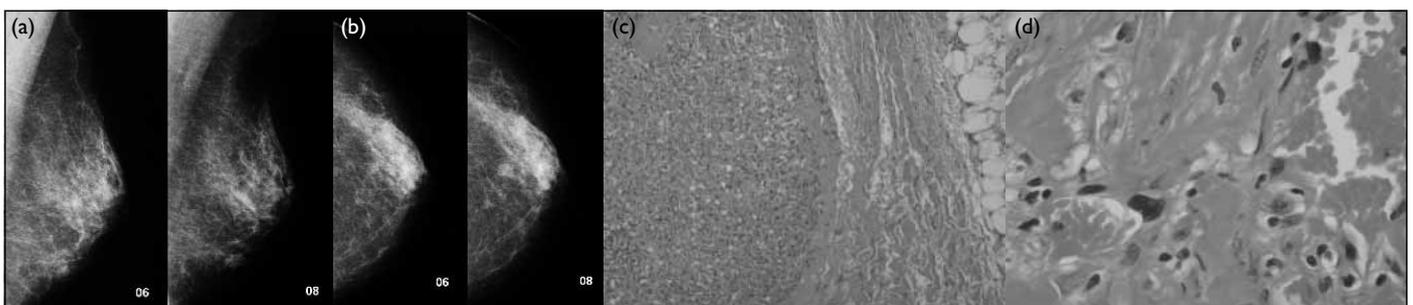


FIG 2. Left mammograms in (a) mediolateral oblique and (b) craniocaudal views in 2006 and 2008. There is an interval tumour noted in the lower outer quadrant of left breast. It is of intermediate density and has a lobular outline. There is no associated calcification or architectural distortion. (c) The mammary vascular tumour (H&E, x 100). (d) Atypical endothelial cells (H&E, x 400)

pathology report described it as a well-differentiated angiosarcoma, type I.

Removal of the lesion was arranged soon after the biopsy result was known. Radio-guided occult lesion localisation was done under mammographic guidance and 0.35 mCi of Tc-99m sulphur colloid was injected into the mass. The patient was then transferred to the operating suite where a wide local excision, guided by a gamma-detecting probe, was performed, aiming to achieve a 2-cm tumour-free margin.

Pathological examination of the surgical specimen revealed a 0.7-cm vascular lesion composed of inter-anastomosing vascular channels (Fig 2c). The vascular channels were dilated and congested with blood. The lining endothelial cells were atypical, displaying mild nuclear pleomorphism and hyperchromatism (Fig 2d). Mitotic figures were inconspicuous. The features were those of a well-differentiated angiosarcoma, type I. The tumour was close to the superior and inferior soft tissue margins (0.3 cm and 0.2 cm clearance, respectively).

This patient has been referred to an oncology unit for further care and is waiting for an FDG-PET scan. The decision to have either a total mastectomy or adjuvant radiotherapy is yet to be made.

Discussion

Primary mammary angiosarcoma tends to affect younger women, in the third and fourth decades of life,⁷ in contrast to mammary carcinoma which generally arises later, in women aged between 55 and 69 years.⁸ Liberman et al⁹ reported that the 29 women in their series had a mean age of 42 years at the time of diagnosis, whereas in Yang et al's series of 24 patients,¹⁰ the mean age was 40 years. This young age at diagnosis means this group falls below the recommended age for mammographic screening. This may explain why most patients (as in our first case) with mammary angiosarcoma present with symptoms and tend to have large tumours.

Mammary angiosarcomas are rarely clinically occult. A typical clinical manifestation is painless breast enlargement or palpable masses. Occasional skin discolouration is found. Only three of the 29 patients in Yang et al's series¹⁰ had their tumours detected by screening. In our second case, the 72-year-old woman was diagnosed by routine mammographic surveillance. It was the advanced age of onset of the disease that permitted the detection of her tumour at an early, asymptomatic stage while it was still small, permitting wide local excision of the lesion.

When patients present with a breast mass or enlargement, the baseline imaging investigation is a mammogram. Breast angiosarcomas often have

non-specific radiographic features, and may even be mammographically occult. Liberman et al⁹ found that the mammograms appeared completely normal in 33% (7 out of 21) of cases of primary angiosarcoma. There are several possible reasons why, despite the large tumour size, some angiosarcomas are not readily detected by mammography. Angiosarcomas tend to ramify between the fat lobules, around and into the mammary glands, and are often deeply embedded in the breast tissue with vague tumour margins. The tumour is composed of dilated anastomosing vascular channels of low cellular density, so is often isodense and easily obscured by the dense breast parenchyma characteristic of young women. Moreover, angiosarcomas are rarely calcified and lack associated architectural distortion or spiculation.

In Yang et al's series,¹⁰ all (3/16) mammographically occult tumours were visible on ultrasound scans, suggesting the importance of supplementary ultrasonography for diagnosing symptomatic tumours. On the other hand, the authors observed that 54% (7/13) of the masses in their series were hyperechoic or mixed hyper- and hypo-echoic on ultrasound scans unlike breast carcinomas, which are very rarely hyperechoic. This may reflect the vascular nature of angiosarcomas and the multiple interfaces of the vascular channels and thus should alert the radiologist to a possible diagnosis of angiosarcoma. Nonetheless, the clinical and sonographic features of mammary angiosarcomas may often be non-specific and may mimic benign lesions, leading to diagnostic difficulty, as demonstrated by our first case. Although neither of our patients had magnetic resonance imaging, this is a powerful tool for detecting breast lesions, with high contrast resolution and sensitivity.¹¹ It is invaluable in demonstrating the extent of an aggressive breast mass and possibly confirming the vascular and aggressive nature of a mammary angiosarcoma. In Yang et al's series,¹⁰ magnetic resonance images of nine tumours were available. All showed large lobular masses that were heterogeneously hypointense on T1-weighted images and heterogeneously hyperintense on T2-weighted images. Areas of haemorrhage and cystic cavities representing venous lakes were common. Intense initial heterogeneous enhancements with washout kinetics were observed. These observations suggest a high Breast Imaging Reporting and Data System category and confirm the aggressive nature of the tumour.

Making a preoperative diagnosis of mammary angiosarcoma with aspiration cytology and biopsy is often difficult. Chen et al⁵ reported that in 37% (32/87) of their cases, the malignant nature of the lesion was not recognised in the initial biopsy specimens. As in case 1, the fine-needle aspiration obtained a haemorrhagic aspirate only and the Tru-Cut biopsy could only indicate a vascular tumour whose

malignant potential could not be accurately assessed without excisional biopsy. This makes preoperative diagnosis and surgical planning difficult.

Angiosarcomas are divided into three types histologically. Type I (well-differentiated) lesions show well-formed vascular channels with one to two layers of endothelial cells. Papillary growth and endothelial tufting are minimal to absent. Mitoses are rare. Haemorrhage, necrosis, and pleomorphism are not generally present. Type II (moderately differentiated) tumours are characterised by irregular vascular channels with papillary growth and endothelial tufting. There may be focal solid areas composed of spindled cells. Mitoses are present, but necrosis is usually absent. Type III (poorly differentiated) lesions consist of predominantly solid areas of malignant polygonal or spindled cells. Few well-developed vascular channels are present but may be difficult to identify. Mitotic figures, haemorrhage, necrosis, and pleomorphism are common findings.

Because the prognosis is closely related to the type of angiosarcoma, the lesion should be extensively sampled and thoroughly studied microscopically to establish the tumour type. Sometimes an incisional or excisional biopsy is inevitable. According to Rosen et al,⁶ the estimated probabilities of disease-free survival 5 years after initial treatment are: type I: 76%, type II: 70%, and type III: 15%. The median length of disease-free survival is also related to tumour type (type I: >15 years, type II: >12 years, and type III: 15 months). The pre-treatment duration of the lesion and the primary tumour size are not significantly related to the risk of recurrence or to survival. On the other hand, Liberman et al⁹ found that patients whose lesions were classified pathologically as 'higher grade' were

significantly ($P<0.05$) more likely to have abnormal mammograms and to develop recurrent disease.

Because breast angiosarcomas are very rare, there is no established standard treatment.¹² Almost all authors advocate aggressive surgical resection as the treatment of choice. Axillary lymph node dissection is unnecessary since metastasis to the nodes is rare. Adjuvant chemotherapy has shown some success as a means of limiting recurrence in type III lesions, but has not been proven effective for type I or II tumours.

Conclusion

Mammary angiosarcomas, although rare, are aggressive lesions associated with a poor prognosis. They tend to occur in younger patients who may present with a painless rapidly enlarging breast mass. Mammograms may be deceptively normal. Therefore, ultrasound is an important supplementary tool able to reveal a hypervascular mass, often with hyperechoic components. Magnetic resonance imaging should be considered, as it is useful for local staging and confirming the vascular and aggressive nature of the lesions. An early and adequate tissue biopsy to confirm the diagnosis is needed to facilitate early treatment. Careful pathological evaluation is crucial for predicting the clinical outcome, risk of recurrence, and survival.

Acknowledgement

The authors thank Dr KLMak (Consultant, Department of Pathology, Kwong Wah Hospital) for invaluable advice and support.

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