CASE REPORT

Growing concern following compression mammography

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SUMMARY

A patient without clinical symptoms had a mammogram in October 2008. The procedure caused intense persistent pain, swelling and development of a haematoma following mediolateral left breast compression. Three months later, a 9×11 cm mass developed within the same region. Core biopsies showed a necrotizing high-grade ductal carcinoma, with a high mitotic index. Owing to its extensive size, the patient began chemotherapy followed by trastuzumab and later radiotherapy to obtain clear margins for a subsequent mastectomy. The mastectomy in October 2009 revealed an inflammatory carcinoma, with 2 of 3 nodes infiltrated by the tumour. The stage IIIC tumour, oestrogen and progesterone receptor negative, was highly HER2 positive. A recurrence led to further chemotherapy in February 2011. In July 2011, another recurrence was removed from the mastectomy scar. She died of progressive disease in 2012. In this article, we discuss the potential influence of compression on the natural history of the tumour.

your breath; it will be over in a minute'. However, the patient found the pain unbearable. By the time she got to the parking lot, she could feel swelling and a lump forming on the outside of her breast. At home, her breast became swollen and throbbing with a reddish bruise forming on the surface.

Throughout the weekend, she took aspirin for pain and just 'laid still as it was too painful to do anything'. Her pain persisted, and following a call to the screening clinic, staff advised her to take paracetamol. At the earliest opportunity, she also saw her personal physician who reported: 'contusion, ecchymosis, and haematoma?' The mammographic report indicated a lesion in the upper outer quadrant of the left breast with associated calcifications, indicating a low suspicion finding (figure 1). Her physician ordered a diagnostic mammogram; however, fearing further compression of her painful breast, she went on a holiday to recuperate. Her pain intensity increased, and the patient had trouble sleeping and eating, so she returned in early December for further follow-up.

BACKGROUND

This was the second case reported to us of a haematoma following screening mammography. Both patients were middle aged and had not taken any medication to increase their bleeding risk. They were advised that prolonged pain was not a cause for concern and that the use of analgesics would remedy the pain. There was no consideration that there could be a more serious underlying problem. This second case motivated us to write this report, particularly because it was followed-up by the development of an aggressive malignancy.

CASE PRESENTATION

A 60-year-old woman underwent a screening mammogram on a Friday in October 2008. The patient performed monthly breast self-examinations which were normal and the pre-examination report filled out by the patient indicated nothing unusual. Physical examination by a technician also indicated nothing abnormal. She had no family history of breast cancer and no personal or family history of coagulation disorders. No medications had been taken that would predispose her to bleeding.

The mammogram involved craniocaudal and mediolateral views. During the left breast mediolateral compression, the patient indicated that she was experiencing significant pain and told the technician: 'I think we need to stop, this is really hurting me, and my arm is killing me, and something is really wrong'. The technician advised her, 'Hold

INVESTIGATIONS

Another appointment with her physician indicated 'painful left shoulder, frozen shoulder, no nodes, mass in upper left quadrant, larger, need biopsy, cancer? left upper quadrant'. The physician arranged for a referral to a trauma surgeon with expertise in breast surgery in early January, stating that he advised her to have follow-up diagnostic mammogram, but the patient declined and went on a holiday to recuperate. On her return, he noted that the mass was still tender, but larger and her shoulder was frozen. The surgeon noted extensive bruising, concluding that the mass was a haematoma due to its sudden onset and the fact that it was softer and more fluctuant than that would be expected for cancer. Upon needle aspiration, 'old blood-type fluid' was removed, and he concluded that the mass was an organised left haematoma. She was referred for ultrasound-guided drainage; however, the procedure revealed a necrotizing high-grade infiltrating ductal carcinoma (January 2009) at the site of the suspicious finding noted on the previous mammogram.

DIFFERENTIAL DIAGNOSIS

The enlarged mass that followed the patient attending mammography could have arisen for several reasons. It could have been a malignancy, inflammation from injury or a haematoma; however, the fact that the swelling developed so rapidly following the compression and that it was somewhat fluctuant would suggest a haematoma in this case.

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Figure 1 Left breast cranial caudal image.

TREATMENT

In 1 February, the left breast mass was reported to be 9×11 cm in size by physical examination. Owing to the large size and extensive area of redness of the rapidly growing tumour, chemotherapy was initiated to reduce the size and to obtain clear margins for a subsequent mastectomy. The stage IIIC tumour was oestrogen and progesterone receptor negative, but highly HER2 positive with a high mitotic index. The patient began doxorubicin, cyclophosphamide and docetaxel for eight cycles followed by trastuzumab. In July 2009, she suffered another injury when a dog jumped on her and injured her left breast. This led to pain and swelling at the tumour site and it was not determined at that time whether this additional trauma was a haematoma, bruising or a tumour recurrence. She then discontinued the chemotherapy and was advised to begin a course of 28 radiation treatments. A mastectomy in October 2009 revealed a 5 cm inflammatory carcinoma with 'multiple microscopic foci of infiltrating ductal carcinoma within the intervening stroma'. Two of three nodes were infiltrated by the tumour. In January 2011, she developed new lesions at the site of her mastectomy scar, which were confirmed to be malignant. The following month she was put on trastuzumab and vinorelbine, which led to the complete disappearance of lesions. During the course of her radiotherapy and chemotherapy, it was consistently reported that she tolerated her treatments well.

OUTCOME AND FOLLOW-UP

While continuing on vinorelbine and trastuzumab, a tumour recurrence was removed from the mastectomy scar in July 2011. She was subsequently found to have metastatic disease and opted for no active treatment. The patient died in 2012 of progressive disease.

DISCUSSION

In this case, the patient's legitimate concerns were not appropriately addressed at the onset, and we question how common postmammography pain is discounted. While mammography can routinely detect lesions between 1 and 1.5 cm and

compression may aid in visualisation of suspicious masses, little consideration is given to the consequences of compression other than effects on image clarity or screening compliance. Mammography compression (involving forces up to 200 N or 45 lbs) can be associated with mild to severe pain.^{1–4} Studies using a visual analogue scale have reported mammography pain in the range of 74–93%.⁴ Women with higher pain sensitivity, such as those with dense breasts,⁴ are often advised to take analgesics or tranquilisers to endure the procedure more comfortably. Yet, pain is also a biological warning sign for tissue damage; therefore, routinely blinding potential injury with analgesics is a questionable practice.^{1 2}

Mammographic compression can cause cutaneous bruising⁵ and has led to the rupture of breast implants,⁶ cystic masses,^{7 8} and as reported by Cawson and Malara,⁹ may result in haematoma. As regular mammographic screening may only occur annually or biennially, the lesion may not be detected until the subsequent mammogram, as in the report by Cawson and Malara,⁹ or it may heal without treatment and without subsequent detection. Alternatively, pain resulting from compression may deter women from further screening, which may uncover the injury. Although in the present case (and the one we previously encountered), there was no predisposition to bleeding; she did subsequently use aspirin briefly following the injury, which could have led to further bleeding. A report by Chetlen *et al*¹⁰ on haematoma formation following breast core needle biopsy observed its occurrence twice as frequently in women taking antithrombotic therapy. In the present case, the rapid development of swelling immediately following the injury should have led to a suspicion of haematoma rather than routine postmammography pain.

Another uncertainty relates the effect of compression on occult malignancies (ie, dormant or slow growing tumours), particularly those expressing HER2 positivity (epidermal growth factor receptor) as in the present patient. Musolino *et al*¹¹ observed that interval tumours (those discovered between screenings), in addition to having a higher histologic grade, proliferation rate and oestrogen receptor negative status, were three to four times more likely to be HER2 positive than screen detected. Tagliabue *et al*¹² demonstrated that wound fluid and postsurgical serum samples contained growth factors that induced proliferation of surgically removed HER2-positive breast carcinoma cells. Notably, carcinomas that overexpressed HER2 showed a consistently higher induced growth rate. This corresponds to animal studies by Stuelten *et al*^{13 14} who orthotopically injected metastatic mouse breast cells into the mammary fat pads of BALB/c mice. Nine days later, a wound was created locally above the fat pads or remotely above the scapula. A significant increase in tumour size was observed in animals with local injuries, but not those with wounds distant from the tumour site. Tumour growth was also augmented by the local injection of wound fluid. Abramovitch *et al*^{15 16} likewise demonstrated that proximal wounds promoted tumour growth and vascularisation in nude mice, whereas remote incisions did not. Proximal injection of wound-derived growth factors was correspondingly able to accelerate tumour doubling time.¹⁵ The authors concluded that such wound fluid may trigger 'the angiogenic switch of avascular, dormant microtumours'. Thus, tumours expressing these surface receptors may be more sensitive to growth factors associated with wounding.¹⁷ Can compression to occult tumours alter their natural history—inducing greater hormone independence while increasing growth factor dependence? This would explain heightened aggressiveness of interval tumours relative to screen-detected cancers.^{18 19}

The question arises whether this patient, with no palpable cancer at mammography, but a significant compressive injury, would have naturally developed a 9×11 cm aggressive inflammatory carcinoma 3 months later. The patient's tumour was highly positive for HER2. Haematoma formation, with abundant growth factor release, in the vicinity of inflammatory tumours may be particularly positioned to induce rapid tumour growth.^{1 17} This could also explain several anomalies related to interval tumours: why these tumours suddenly appear when not clearly apparent on a previous mammographic screening; why these tumours tend to be hormone independent, but HER2 positive; and why such tumours are more aggressive than screen-detected cancers.^{18 19}

Breast cancer remains the only malignancy diagnosed by examining it in an unnaturally flattened appearance. In light of the case presented here, a future goal should be to promote screening and diagnostic methods that avoid compression, detecting abnormalities of the breast in its natural three-dimensional shape. New technologies for breast cancer detection that avoid compression such as 3D imaging methods are emerging and should be encouraged.

Learning points

- ▶ Pain from screening mammography may occur in up to three-quarters of women and can be a biological warning sign for tissue damage; screening methods that avoid compression such as 3D ultrasound and 3D tomography should be pursued.
- ▶ Mammographic compression has been associated with cutaneous bruising, haematoma, rupture of breast implants and cystic masses.
- ▶ Prolonged pain and haematoma after mammography should be carefully monitored and evaluated because it affects the quality of life of the patients and sometimes may conceal a malignant process.
- ▶ Interval cancers are often larger and more aggressive than screen-detected cancers.
- ▶ Further studies should be undertaken to understand the effects of injury on tumour development.

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