An unexpected diagnosis of breast malignancy

T Richardson, F Cottier

Weaver Vale General Practice, Runcorn, UK

ABSTRACT

Inflammatory breast cancer constitutes 5% of all breast cancer diagnoses. Diagnosis is based on clinical signs including skin changes, erythema and oedema, together with rapid progression and involvement of more than one-third of the affected breast. It is an aggressive tumour with great metastatic potential, metastases being present in 30% of patients at first presentation.

Primary non-Hodgkin's lymphoma of the breast is rare but is well reported. It accounts for 0.5% of all breast malignancies and 1% of all non-Hodgkin's diagnoses. Prognosis of primary breast lymphoma varies depending on the stage of disease with stage IE having a 5-year survival rate of 78–83% and stage IIE having a 5-year survival rate of 20–57%.

We present a rare case of non-Hodgkin's lymphoma mimicking an inflammatory breast cancer. The aim of this case report is to highlight an unusual presentation of non-Hodgkin's lymphoma and the diagnostic difficulties that arise.

KEYWORDS

Non-Hodgkins lymphoma – Inflammatory breast cancer

Accepted 3 April 2017

CORRESPONDENCE TO

Tom Richardson, E: tomrichardson@doctors.org.uk

Introduction

Inflammatory breast cancer is an aggressive form of cancer with high metastatic potential and poor prognosis. We highlight an unusual presentation of non-Hodgkin's lymphoma (NHL) mimicking inflammatory breast cancer and the diagnostic difficulties experienced in both primary and secondary care.

Case history

A 48-year-old woman presented with a small lump in her right axilla first noticed two days prior to consultation when she strained to open a heavy door. The patient subsequently experienced pain down her right arm, axilla and flank. The patient carried out regular self-examination of her breasts and had not noticed any prior breast lump. She had had a mammogram the previous year, which was normal. She was otherwise systemically well and there was no history of weight loss or fever. There was a family history of chronic lymphoid leukaemia, from which her mother suffered. Although, not volunteered at the initial consultation, she reported retrospectively experiencing fatigue and night sweats prior to presentation.

On examination, a small, 3-mm, firm, tender lump was palpable in the right axilla. An initial diagnosis was made of infected sebaceous cyst. This was treated with a one-week course of antibiotics and a full blood count was taken.

Four days later she presented again with an increase in the size of the lump, which was confirmed on examination.

A small second lump was also noted. Breast examination was undertaken at this stage and was normal. The full blood count showed mild lymphocytosis, white cell count $12.1 \times 10^9/l$ and lymphocytes $5.12 \times 10^9/l$. A routine ultrasound of the right axilla was arranged and was carried out one month later.

Ultrasound demonstrated two pathological nodes, 2.5×2 cm and 3×2 cm in size, matted together with increased vascularity, highly likely to be malignant, probably originating from the breast. At this stage, the patient reported no breast lump or skin changes of the breast. She was referred urgently to the breast clinic.

At presentation to the breast clinic two weeks later, a large inflammatory mass occupying over 50% of the volume of the right breast was found. The nodes within the axilla had enlarged to the size of a tennis ball. The initial clinical diagnosis was inflammatory breast cancer, based on the rapid progression of the breast mass, erythema and oedema of the breast. She was told that the prognosis was poor and that she would be referred for palliative chemotherapy. Mammography, fine-needle aspiration cytology and computed tomography (CT) of the chest, abdomen and pelvis were all arranged urgently.

The CT report stated that there was a 12-cm mass situated in the right breast, with an 8×5 cm node in the axilla. Malignant supraclavicular nodes were also present, compressing the brachiocephalic and jugular veins, and malignant nodes were present at the hilum of the lung. There were bilateral metastatic pleural effusions.

Fine-needle aspiration cytology showed large-cell NHL. The NHL was staged as IIA (E). She was subsequently

referred to oncology and commenced a six-cycle regime of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy. Chemotherapy was started two weeks after her appointment at the breast clinic. At this stage, she was told that the aim of treatment was curative rather than palliative.

There was a good response to chemotherapy. No breast lump or nodes were palpable at the end of her treatment. CT displayed residual disease remaining in the breast but all nodal disease had resolved, as had the malignant effusions. She was subsequently referred for radiotherapy with a total dose of 30 Gy over 15 fractions. Following the completion of radiotherapy, further imaging showed complete remission.

The patient remains on four-monthly follow up. She is currently physically well and is starting to return to normal activity.

Discussion

Inflammatory breast cancer is uncommon and has been quoted as accounting for 2.5% of all breast cancers in the United States,¹ while others have quoted up to 5%.² It is an aggressive tumour with great metastatic potential;³ metastases are present in 30% of patients at first presentation.⁴

Diagnosis of inflammatory breast cancer is made on clinical findings.⁵ The World Health Organization describes the clinical symptoms as rapid breast enlargement and skin changes (redness, oedema, orange-peel appearance) that involve more than one-third of the breast. Often the breast does not have a discrete palpable mass but a diffuse firmness is common.⁶ One diagnostic difficulty is that of distinguishing locally advanced breast cancer that has been neglected from a rapidly progressive inflammatory breast cancer. Therefore, an arbitrary figure of a six-month history is required for diagnosis.⁵

Inflammatory breast cancer has no specific histological appearance, although they have been noted to be highly angiogenic, lymphangiogenic and vasculogenic.⁷ Tissue sampling, however, is vital, as sarcomas can present with a similar clinical picture, as well as benign inflammatory or infective conditions.⁵ Within the literature, there are a number of studies that report abscesses presenting as cancer and vice versa,^{8–11} as well as many other diagnoses presenting with the complaint of a 'red breast'.¹²

Radiological imaging is recommended as part of the investigation and staging process but is not part of diagnostic criteria.⁵ Despite this, skin and trabecular thickening may be seen on mammogram, while high-resolution ultrasound may detect an abnormality in up to 90% of inflammatory breast cancers, which will facilitate a targeted biopsy.^{13,14} Magnetic resonance imaging (MRI) will display diffuse breast and pre-pectoral oedema, skin thickening and non-enhancement of mass.^{15,16}

The management of inflammatory breast cancer is almost always initially with systemic chemotherapy. Following chemotherapy, surgery should be considered, although in some patients, surgery may be suitable as a first-line treatment.⁵

Radiotherapy is almost always used as a postoperative adjuvant therapy,¹⁷ while endocrine therapy is indicated postoperatively in all those who are found to have a hormone receptor-positive cancer.^{2,5}

Lymphoma is a solid malignancy of the immune system. Of these, 90% are the non-Hodgkin's type, with the remaining 10% being Hodgkin's type. NHL can be further classified depending on symptoms at diagnosis as well as histological findings.¹⁸ NHL is the sixth most commonly diagnosed cancer in the UK.¹⁹ In 2014, the UK incidence was 13,600 and mortality was 4,800.¹⁹ NHL can equally affect either gender and most are diagnosed after the age of 60 years.^{19,20}

Primary NHL of the breast is rare but well reported. It accounts for 0.5% of all breast malignancies²¹ and 1% of all NHL diagnoses. Prognosis of primary breast lymphoma varies depending on the stage of the disease, with stage IE having a 5-year survival rate of 78–83% and stage IIE having a 5-year survival rate of 20–57%.²²

Diagnosis of NHL of the breast is based on four criteria devised by Wiseman and Liao, who first classified the condition in 1972.²³ These can be summarised as follows:

- > the site of presentation is the breast;
- > a previous history of lymphoma or evidence of widespread disease are absent at diagnosis;
- > lymphoma is demonstrated with close association to breast tissue in the pathologic specimen;
- > ipsilateral lymph nodes may be involved if they develop simultaneously with the primary breast tumour.

Most cases of breast NHL present as painless lumps that typically in the outer upper quadrant of the breast.²⁴ There are, however, a number of reports that are well documented in the literature of NHL of the breast initially presenting as a breast abscess.^{25,26} Although not considered in this case, a breast abscess could have part of the differential diagnosis as the cause of this large inflammatory mass that developed.

Although there is limited evidence, R-CHOP chemotherapy appears to be the most promising regime of treatment,²⁷ while radiotherapy and surgery may also be appropriate as treatment in certain cases.²²

This case displayed a very unusual presentation of NHL. A literature search yielded three papers describing three similar cases.^{28–30} However, these differed in terms of age, presentation and subsequent progression.

Taubman and McKay describe two cases of women aged 74 and 80 years presenting with an axillary lump and pain.²⁸ When patients were examined, they were noted to have signs of inflammatory breast cancer, including erythema, oedema and calor of the breast. Neither patient ever developed a discrete breast mass prior to treatment. The paper suggests that the features of inflammatory breast cancer were due to lymphatic obstruction by the axillary lymphadenopathy.²⁸ Pruthi *et al.* describe a 74-year-old woman presenting with a one-month history of enlarging breast mass, orange-peel skin changes and erythema.²⁹ Seifi *et al.* describe a much younger patient of 45 years who presented

with weight loss, back pain and night sweats.³⁰ On examination, the patient was found to have breast lumps that were shown to be NHL after lumpectomy. This proved to be a particularly aggressive NHL, with spread to the vertebrae, which led to the patient's death after a further four months.³⁰

Our case differs in a number of ways from the above reports. The patient presented at a younger age (apart from the case described by Seifi),³⁰ with a much shorter history and a very small axillary lump. Breast examination remained normal until six weeks after initial presentation. The 12-cm breast mass developed rapidly over a two-week period. Our case would appear to support Taubman and McKay's hypothesis that the appearance of an inflammatory breast cancer may have been due to obstruction of normal lymphatic drainage by axillary lymphadenopathy.²⁸

The diagnostic difficulties of this case led to the patient being misdiagnosed twice; first as having an infected sebaceous cyst and second as having an inflammatory breast cancer. The only stage, however, that led to a delay in the final diagnosis was while the patient awaited an ultrasound scan and the subsequent referral to the breast clinic. Such delays lead to the potential for a malignancy to progress from localised disease to widespread disease significantly impacting on management and prognosis.

Conclusion

This is a rare clinical picture and the misdiagnoses highlight the diagnostic difficulties that both general practitioners and specialists alike face. Clinicians need to be aware of rare presentations, as well as having an awareness of diagnostic difficulty. Clinicians should have a high index of suspicion with prompt referral for investigations and specialist opinion within a reasonable timeframe to ensure that sinister diagnoses are not missed.

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