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Rare breast malignancies and review of literature: A single centres experience

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ABSTRACT

INTRODUCTION: Breast cancer is a heterogeneous condition, with variants which are less common but still very well defined by the World Health Organization (WHO) classification. With the small number of cases each year large trials are difficult to perform. This series aims to discuss the rare breast malignancies encountered within a breast department and the evidence based approached to their management.
METHOD: Literature search of electronic databases via PubMed and the search engines Google/Google Scholar were used. Emphasis on keywords: breast cancer and the type of histology used to limit search. Searches were screened and those articles suitable had full text versions retrieved. The references to all retrieved texts were searched for further relevant studies.
CONCLUSION: Due to the rarity of some of these breast cancers, systematic evaluation of patient with detailed histopathology will aid accurate diagnosis and management. The series hopes to add the existing understanding of this small percentage of cases.

1. Introduction

Breast cancer is the commonest cancer in UK [1] and one-third of all new cases of cancer in women [2] with about 55,000 new diagnoses made annually. A large majority of breast cancers (60%) are invasive ductal carcinoma [3] which is often described as no special type with about 10% being invasive lobular carcinoma. However as a heterogeneous condition, there are other variants which are less common but still very well defined by the World Health Organization (WHO) classification [4]. With the small number of cases each year large trials are difficult to perform.

This series aims to discuss the rare breast malignancies encountered within a breast department and the evidence based approached to their management.

2. Lymphoma of the breast

2.1. Case reports 1

A 68 year old lady was recalled from breast screening for a poorly defined opacity in her left lower breast. Mammogram showed a 2 cm lesion and an FNA was reported as C5 suspicious for lymphoma. She underwent a core biopsy of the breast lump. This suggested a B cell mature follicular lymphoma. Lymphoid cells were B cells expressing CD20 and CD 79a. Reactive T cells CD2, CD3 and DC5 were all positive surrounding the follicles. CD5 restricted to T cells. Lymphoid cells were cyclin D1-negative. Follicular cells expressed CD10, Bcl6 and BCl2. In situ hybridisation studies for kappa and lambda light chains show scattered plasma cells with a polytypic pattern of light chain expression. She underwent bone marrow biopsy, which showed no evidence of marrow infiltration by follicular lymphoma.

Treatment: She went on to have 8 courses of R-CHOP. After her 5th cycle the vincristine was changed to vinblastine to help with neuropathy. An interval CT showed reduction in size of known lesion in the left breast indicating response to treatment. She was maintained on Rituximab on 2 monthly basis for 2 years.

She remained follow up suggesting no recurrence after 2 years of diagnosis Fig. 1.

2.2. Case reports 2

A 76 year old lady presented with a 9 week history of a rapidly enlarging lump on the sternal notch. On examination there was a 3 cm by 3 cm firm lump palpable on the sternum. Breast examination was unremarkable. Mammogram showed no abnormality in the breast but ultrasound of the mass showed a soft tissue lesion. FNA came back as C4 suspicious of lymphoma and core biopsy showed features suggesting of plasmablastic lymphoma. Staging CT scan confirmed the presternal mass was infiltrating the pectoralis major muscles with no definite bony destruction but high attenuation in the marrow implying marrow infiltration. There was

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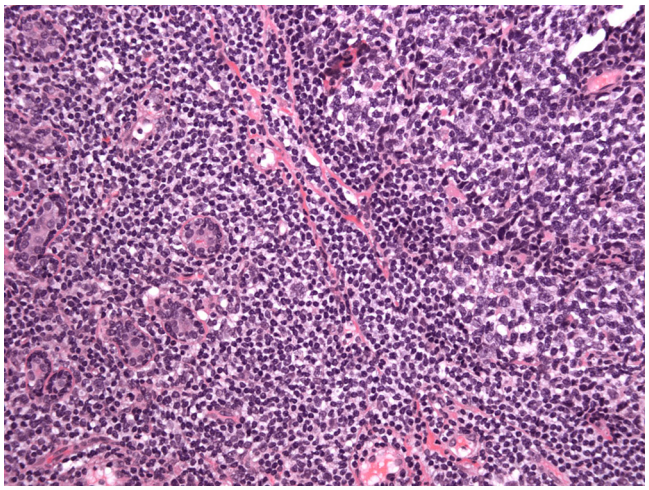

Fig. 1. Immunohistochemistry sample of lymphoma of breast.

no significant lymphadenopathy elsewhere and spleen was normal. Bone marrow aspirate and trephine from the posterior iliac crest had no features to suggest myeloma or marrow infiltration with lymphoma.

A repeat CT 3 months post diagnosis and following chemotherapy showed that the soft tissue mass was completely resolved with no residuum, but there was diffuse ground glass change in both lungs suggesting drug toxicity, intercurrent infection or diffuse lymphoma in the lungs.

2.3. Case reports 3

A 49 year old lady was recalled from screening for an abnormality detected in the left breast. Ultrasound showed a 21 mm mass. FNA was C1 and core biopsy was reported as lymphoid tissue with suspicion of lymphoma B3. Incidentally, she also had a 2 cm by 2 cm firm lump on the right forearm ulnar aspect, firmly adherent to underlying structures. The breast lesion was completely excised for histology. Immunohistochemistry demonstrated expression of the B-cell antigens CD20 and CD79a by the majority of the lymphoid cells, with abundant small reactive T-cells (CD2-positive, CD3-positive, CD5-positive and CD43-positive). There were small numbers of IgD and CD23-positive B-cells consistent with residual mantle zone cells. Larger numbers of Bcl-6-positive cells are identified within the germinal centres but these germinal centre cells are Bcl-2-negative. The Ki67 proliferative fraction is high within the reactive germinal centre fragments. The appearances confirmed B-cell, mature, extra nodal marginal zone lymphoma of mucosal associated lymphoid tissue (MALT). Immunohistochemistry on the wedge biopsy of the lesion on the arm showed expression of the B-cell antigens CD20 and CD79a by the neoplastic cells, in keeping with diffuse large B cell lymphoma which might represent a high grade transformation of the breast lymphoma. Staging CT and PET CT showed involvement of a right axillary node (3.3 cm) and bone marrow examination showed no infiltration.

She has since had 4 cycles of R-CHOP chemotherapy is due for a repeat CT to assess interval progress, with a view to complete 2 further cycles and stop treatment if a final CT and PET show response.

2.4. Review of literature

Malignant lymphomas primarily arising in the breast and in the absence of previously detected lymphoma localizations are termed 'primary breast lymphomas' (PBLs) [5]. PBL accounts for less than 0.5% of breast malignancies [6]. The PBL incidence is 0.04–0.53% of all primary malignant tumours of the breast and 2.2% of extra nodal lymphomas [5]. The most common presentation of PBL is with an incidental breast mass [7,8]. On histology, majority of these are diffuse large B cell lymphoma (DLBCL) with other PBL of low grade histology i.e. follicular lymphoma or extra nodal marginal zone (MALT) lymphoma being rarer [6]. In a series of 37 patients with lymphoma involving the breast at initial presentation, 49% were DLBCL, followed by follicular and MALT representing a combined 38% [7]. Likewise in a Swiss series, 5 out of 7 patient with primary breast lymphoma had DLBCL, one follicular and one a MALT lymphoma [8]. These PBL of low grade histology has been further investigated by the International extra nodal lymphoma study group which studied 60 patients (36 follicular and 24 MALT) [7] most presented with Ann Arbor stage Ie of IIe except for IV_E in 3 patients due to bilateral breast involvement, found on imaging and confirmed on cytology. Only 2 of the 60 presented with B-symptoms [6].

Current treatment of DLBCL following tissue diagnosis is with RCHOP based chemotherapy alone or with radiotherapy. Ganjoo et al. [7] reported a 5 year progression free survival rate of 61% and 5 year overall survival of 82%. In a French series [9] of 19 patients (17 DLBCL, 2 follicular/diffuse grade 3 lymphomas), four patients received local treatment only (resection and local radiotherapy) while the remaining 15 received chemotherapy (CHOP or ACVBP followed by involved field radiotherapy). Three of the four patients treated with local treatment only died of their lymphomas. Among the 11 treated with CHOP, 2 died of their lymphomas. The role of CNS prophylaxis remains unclear as rates of CNS involvements are low. The IELSG series demonstrated a similar behaviour of MALT PBL with primary extra nodal MALT in other locations. However patients with follicular PBL had worse progression-free survival (PFS) and overall survival (OS) compared to limited stage nodal follicular in other locations, suggesting an adverse prognostic role of primary breast localisation [6]. In the Swiss series, of all PBL, five and ten year survivals were 57% and 17%, respectively. In the 3 patients who died, 2 had tumours that was Bcl-2 positive but Bcl-6 negative. All surviving patients have positive Bcl-2 and Bcl-6 immunostaining. This may represent important prognostic factors if proven in a larger study [8].

The role of surgery in this disease should be limited to get a definitive diagnosis [10,11]. While for the staging and the treatment CT scan and chemo radiotherapy are, respectively, mandatory [12,13]. Nowadays, surgical resection plays a therapeutic role only in MALT lymphomas, whereas for large B cell lymphomas has only a diagnostic indication. For such disease, the cornerstone of treatment is systemic chemotherapy [12].

3. Ovarian cancer metastasizing to breast

3.1. Case report

This is an 86 year old lady with known ovarian serous papillary carcinoma of the ovary for which she had undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy and omentectomy a year ago. This was followed by chemotherapy in the form of 6 cycles of Carboplatin. She presented with a lump in her right axilla. On examination there was a 3×3 cm lump in the right axilla. Mammogram showed a 30 mm pathological node and FNA was reported as C5, metastatic in nature. Needle fragment from lymph node revealed poorly differentiated carcinoma. A core biopsy of the node showed features consistent with metastatic poorly differentiated serous papillary carcinoma of ovarian or primary peritoneal origin. Tumour expressed pancytokeratins and cytokeratin 7 but not cytokeratin 20. Staining for CA125 showed