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Case Report

A Waiting Game: The Use of Neoadjuvant Endocrine Therapy as a Bridge to Surgery

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Introduction

Breast cancer is the most common cancer in the UK, with 53,696 new diagnoses in 2013. Despite increased awareness of breast cancer, approximately 5% of patients still present to the clinical services with stage IV disease [1].Hormone therapy has been used for many years in treatment of breast cancer. In the 1960's it was discovered that hormonal deprivation or blockade could slow down or stop the growth of breast tumours [2]. After the discovery of hormonal assays, hormonal blockade became a routine part of the armament for Estrogen Receptor (ER) and Progesterone Receptor (PR) positive breast cancer. In selected.patient groups, Hormone therapy has been advocated as a viable treatment when patients are unsuitable for surgery due to either comorbidities or patient choice. Neoadjuvant hormonal therapy can be utilised as a bridging therapy in some cases, to delineate patients with good prognostic tumour biology, resulting in down sizing of the tumour and rendering the patient eligible for surgical resection.

Case Report

We report here a case of a 76-year old lady that presented tothe emergency department in August 2013 with a large fungating left breast mass. It had been present for 2 years, gradually increasing in size, however she only presented at this point due to an area of ulceration on the infero-lateral side, which was bleeding (Image 1). Despite the large size of the mass it was the bleeding which caused the patient concern enough to seek medical attention.

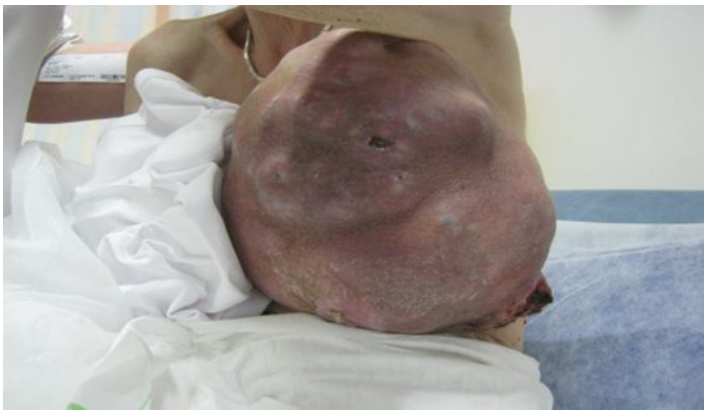

Figure 1: Large fungating left breast mass

She had no significant medical history to this point. Examination revealed a large heterogenous left breast mass, with no palpable lymph nodes and was otherwise normal.

An ultrasound guided biopsy confirmed invasive ductal carcinoma. Immunohistochemistry showed the tumour was strongly positive for Estrogen (7/8) and progesterone receptors but negative forHER2. Staging with Computed Tomography (Thorax, abdomen, pelvis) and isotope bone scan was then performed. A 23cm fungating left breast mass with no metastatic disease was evident on CT scan staging. The case was discussed at the multi-disciplinary team meeting and the decision was to commence letrazole rather than proceed immediately to surgery. This was as a result

of the size of the tumour, and difficult reconstructive options. Six-monthly clinical reviews were arranged. There had been such a substantial improvement by December 2015 that it was felt that the tumour would now be amenable to surgery (Image 2). Repeat CT scan for staging was carried out at this time and was negative for any metastases. A decision was made to proceed to radical mastectomy with a rotated latissimus dorsiflap (+/- skin graft) in conjunction with plastic surgery. The patient had an excellent recovery and was discharged on day 8 post-operatively. She was followed up in clinic and was very happy with the result.(Image 2).

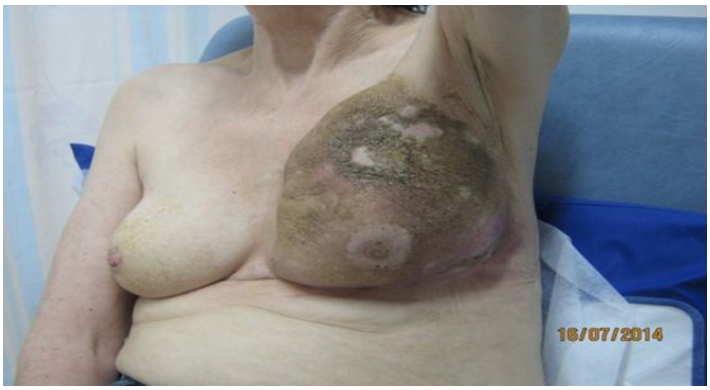

Figure 2: Computed Tomography of fungating left breast mass

Discussion

This case illustrates the role for hormone therapy to act as a bridging therapy in advanced cases of breast cancer which are not initially amenable to surgery.In this case, immediate surgery would have been more difficult and likely would have resulted in an inferior cosmetic outcome. Letrozole and Tamoxifen are two therapies used in the treatment of breast cancer.Letrozole has previously been demonstrated to be a safe and effective treatment in the neoadjuvant setting for patients who were unsuitable or unwilling to undergo immediate surgery. In addition, letrazole has been shown to be superior to tamoxifen when used preoperatively in terms of having an increased overall response rate and improving the likelihood of breast conserving surgery [3]. Breast cancer is dependent on Oestrogen, and inhibition of oestrogen can cause tumour regression. Tamoxifen is a Selective Estrogen Receptor Modulator (SERM) and works by preventing oestrogen binding to the oestrogen receptors.Aromatase inhibitors of which Letrozole is an example, prevent the production of oestrogen by blocking the conversion of androgens to oestrogen.

Studies have shown a correlation between high estrogen levels and a good response to neoadjuvant hormonal treatment in post-menopausal women [4]. In Pre-menopausal women oestrogen production is predominantly from the ovary, whereas in post-menopausal women oestrogen production is from conversion in peripheral tissues. Tamoxifen is used in cancers which are oestrogen receptor positive in premenopausal women.Aromatase inhibitors are contraindicated in pre-menopausal women due to the risk of ovarian cancer from ovarian stimulation. In post-menopausal women either tamoxifen or letrozole could be usedin oestrogen receptor positive tumours, however aromatase inhibitors such as letrozole are preferred as studies have shown that they are more beneficial than SERMS.

This was evident in our case whereby the tumour size decreased significantly from 23cm to 9cm over a 2 ½ year course of letrazole. A 2014 systematic review on the topic of neoadjuvant hormone therapy in breast cancer concluded that neoadjuvant hormonal therapy had similar response rates to neoadjuvant chem otherapyAdditionally,neoadjuvant hormone therapy could be use for longer periods of time compared with chemotherapy, while waiting for adequate downsizing to be suitable for surgical management [5]. However, one challenging aspect of using hormonal therapy is the development of blockade escape, and refractoriness to treatment. The insulin receptor/ insulin-like growth receptor has been identified as a mechanism of resistance to hormone therapy in ER + breast cancer [6].

In one study from the Netherlands, 35% of patients eventually experienced local progression of their disease despite hormone therapy, with a median time to progression of 20 months (+/- 17 months)after starting hormone therapy [7]. This case highlights the potential of using neoadjuvant hormonal therapy for specific subtypes of breast cancer that present with stage IV breast as an initial treatment approach and bridging to definitive surgical resection. Although surgery was carried out in this case, given the dramatic decrease in size attained with the use of Letrozole alone this could be an option in patients who were unsuitable for surgery due to comorbidities or patient refusal. Given the potential for resistance to hormone treatment to develop the timing of surgery if indeed it is being carried out is another decision to be made. In this case, we waited until the tumour had regressed to such a size as to be amenable to surgical resection rather than waiting for resistance to develop. Due to its side effects Letrozole remains confined to use in post-menopausal women or premenopausal women who have underwent ovarian removal or ablation therapies.

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