Fulvestrant in advanced male breast cancer

case report

A 64-year-old man was diagnosed with breast cancer and underwent surgery in October 2000, when a radical mastectomy and axillary node dissection were carried out. Pathological examination revealed a $3 \times 2 \text{ cm}^2$ well-differentiated, invasive, ductal breast carcinoma (stage IIb), involving 1 of the 12 nodes that were tested. The tumour was found to be positive for both estrogen receptor (ER present in 40% of the tumoral cells) and progesterone receptor (in the 90% of the cells) and was HER-2/neu negative. The patient received six cycles of adjuvant chemotherapy (FEC75 regimen) followed by chest wall irradiation and tamoxifen 20 mg/day p.o. for 5 years.

In June 2005, the patient presented moderate/mild dyspnoea on exertion. Chest X-ray and thoracic computed tomography (CT) scan revealed pleuropulmonary metastatic disease. Four courses of 4-epirubicin chemotherapy (75 mg/m$^2$ i.v., every 3 weeks) were administered, followed by four courses of docetaxel (75 mg/m$^2$ i.v., every 3 weeks). In the evaluation after the fourth cycle, we found a pulmonary progression. Then, he received four cycles of capecitabine treatment (1250 mg/m$^2$ b.i.d. p.o. on days 1–14, every 3 weeks). At the next evaluation, there was an increase in the number and size of lung lesions (Figure 1). As he did not respond to chemotherapy, it was decided to initiate treatment with fulvestrant (loading-dose regimen: 500 mg i.m. on day 1, 250 mg i.m. on days 14 and 28, and followed by 250 mg i.m. monthly thereafter).

After 4 months of fulvestrant treatment, the patient reported an improvement in his dyspnoea and a new chest CT scan showed a partial response (partial reduction of the pulmonary lesions and pleural effusion), with a decrease in the size and number of the pulmonary nodules and pleural effusion (Figure 2).

discussion

Male breast cancer is rare in comparison to female breast cancer and represents ~1% of all diagnosed breast cancers [1]. The low incidence of male breast cancer precludes the development and completion of large clinical trials to assess the efficacy of breast cancer treatments in this population and, therefore, it is recommended that its management follows the same general principles as for female breast cancer [2]. Although male breast cancer shares many similarities with breast cancer in women,
there are also important differences, mainly in relation to its hormone dependency and responsiveness to endocrine therapy [3]. In females, 60%–70% of breast cancers are ER positive and/or PgR positive. In contrast, ~90% of male breast tumours express ER and >80% express PgR, showing a greater expression of ER-beta [4] and being probably produced by low estrogen levels in growing tumour microenvironment. The lower rate of HER-2/neu and p53 expression and a higher rate of Bcl-2 overexpression have been reported in male breast cancer [5]. Physiological mechanisms of hormonal production and conversion together with metabolic aberrations may also play an important role in the development of resistance to the hormonal manipulation. This should be considered during the design of a male breast cancer treatment plan. Consequently, it may be inappropriate to extrapolate the treatment principles established for female breast cancer to the management of male breast cancer.

In male breast cancer treatment, best responses have been observed with hormonal therapy. Among the different endocrine options available, tamoxifen is the best established [6]. However, additional hormonal treatment options are required. The use of aromatase inhibitors can be ineffective due to the high proportion of circulating estrogens in men that are independent of aromatase activity [6, 7]. Taking into account the experiences showed in the hormonal treatment of prostate cancer [8], different activity between steroid and nonsteroid aromatase inhibitors in male breast cancer should be considered.

Fulvestrant is an additional therapeutic option that has confirmed efficacy in women previously treated with tamoxifen. To date, there have only been limited data on the use of fulvestrant in male breast cancer. Its novel mechanism of action, along with the available in vitro data [9], indicates that fulvestrant may be a useful treatment option for these patients. The activity in this case report supports further evaluation of fulvestrant in the male breast cancer setting.

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