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LETTER TO THE EDITOR

A case of metastatic breast cancer successfully treated with lapatinib plus capecitabine therapy

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Introduction

Lapatinib is a dual tyrosine-kinase inhibitor which targets both human epidermal growth factor receptor 2 (HER2) and epidermal growth factor receptor (EGFR) tyrosine kinases [1]. It has the advantage of being administered orally. Lapatinib showed promising results both in trastuzumab-naive and in pretreated HER2-positive advanced breast cancer [2–5]. It has been shown that lapatinib plus capecitabine is superior to capecitabine alone in HER2-positive advanced breast cancer patients previously treated with anthracycline, taxane and trastuzumab [6]. Herein, we describe a case of metastatic breast cancer patient who had resistance to trastuzumab and showed a clinically complete response to lapatinib with capecitabine therapy.

Case report

A 53-year-old female was admitted to Department of General Surgery with nipple retraction of the right breast in December 2007. Excisional biopsy revealed infiltrative ductal carcinoma. Thereafter, radically modified mastectomy and axillary lymph nodes dissection were performed. Immunohistochemical staining of estrogen receptor (ER) and progesterone receptor (PR) were negative, but c-erb-B2 scored 3+. Computed tomography (CT) scans applied after surgery revealed milimetric nodules in the middle lobe of the right lung and mediastinal lymphadenopathies. She was classified as $T_2N_3M_1$ according to TNM classification. She received 6 cycles of docetaxel 75 mg/m^2 on day 1 every 3 weeks plus an initial dose of 8 mg/kg of trastuzumab followed by 6 mg/kg every 3 weeks as first-line treatment and continued with trastuzumab 6 mg/kg every 3 weeks. During trastuzumab therapy no adverse effects, including cardiotoxicity, were observed. While she was on trastuzumab, in January 2009 thorax CT scan showed progression in the number and size of lung nodules, mediastinal lymphadenopathies and a newly developed axillary lymphadenopathy 1.5 cm in size (Fig. 1). The patient was considered as resistant to trastuzumab and lapatinib 1,250 mg daily, and continuous treatment with capecitabine 2,000 mg/m^2/day (on days 1–14 in every 21 days) was initiated. She received 6 cycles of lapatinib and capecitabine until the end of August 2009. After the third and sixth cycles of treatment thorax CT scans were carried out on 17th April and 28th August 2009. They revealed clinical remission of all of the described lesions above (Fig. 2). The patient's performance status was improved as well with a PS of 0. She had no significant adverse symptoms and her treatment was continued for 12 months.

Discussion

De novo and acquired trastuzumab resistance are major clinical problems in breast cancer. Nearly all patients

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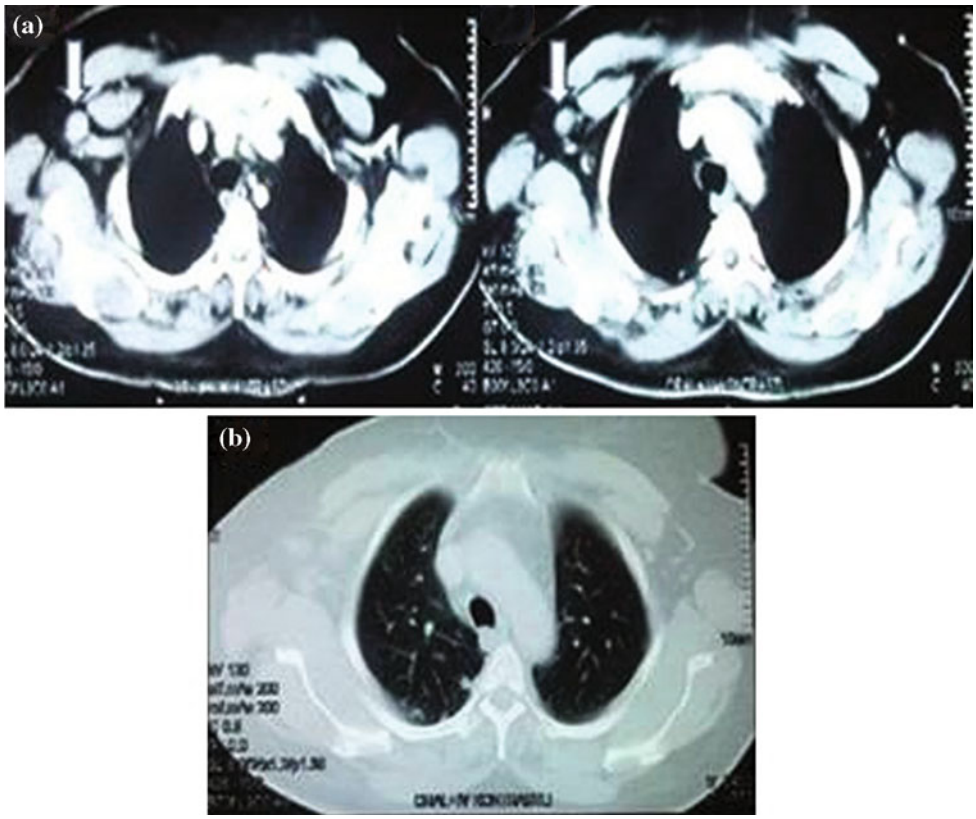

Fig. 1 Thorax CT scans applied before lapatinib plus capecitabine therapy; **a** 1.5 cm in size lymphadenopathy in the right axillary region and **b** metastatic nodules in the right lung

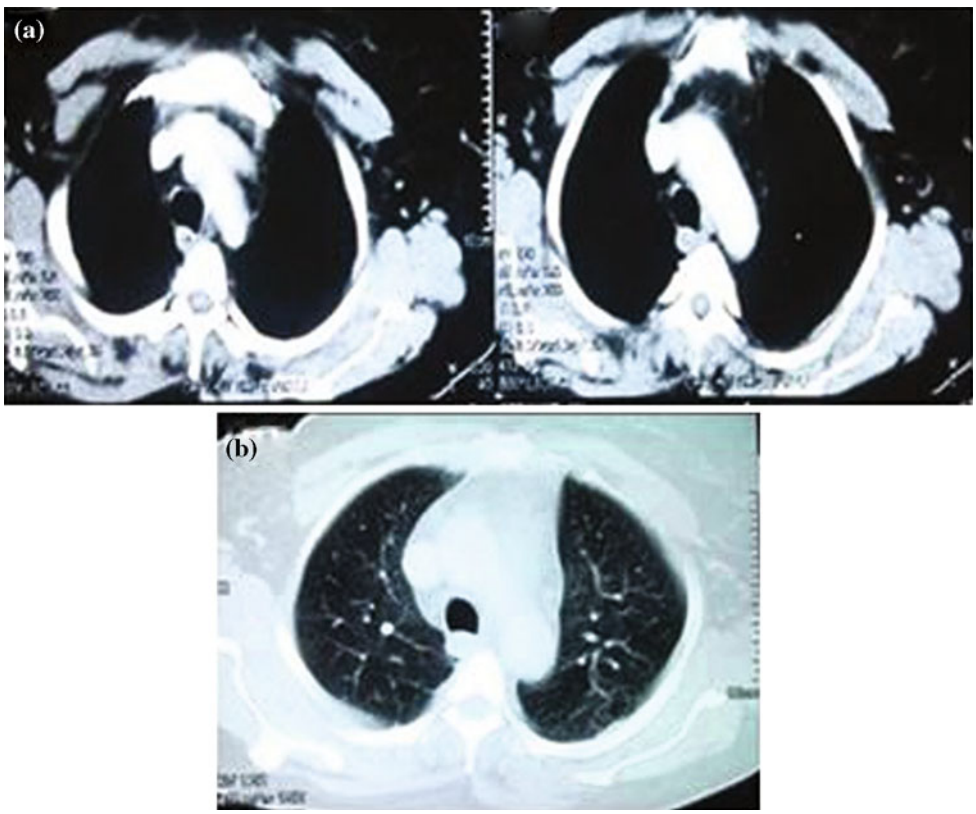

Fig. 2 Thorax CT scans applied after three courses of lapatinib plus capecitabine therapy; **a** no lymphadenopathy in the right axillary region and **b** no metastatic nodules in the right lung

receiving trastuzumab for metastatic disease will experience progression due to resistance to trastuzumab [1, 7, 8]. Hence, new agents are needed to block HER2 signaling for alternative treatments. The first of these new generation HER2 targeting agents, lapatinib, was approved for the treatment of HER2+ metastatic breast

cancer by the US Food and Drug Administration in 2007 [9].

Two large randomized phase III trials investigated the addition of lapatinib to chemotherapy regimens for advanced breast cancer. Geyer et al. [6] enrolled patients with HER2+ advanced breast cancer who previously received anthracycline, taxane and trastuzumab. Patients were randomly assigned to receive capacitabine monotherapy (2,500 mg/m^2 on days 1–14 of a 21 day cycle) or combination therapy with lapatinib 1,250 mg/day continuously plus capecitabine (2,000 mg/m^2 on days 1–14 of a 21 day cycle). The overall survival (OS) and overall response rate (ORR) were significantly higher in the combination group. In their study, complete response was obtained only in one patient (<1%) treated with lapatinib plus capecitabine combination therapy. Updated efficacy of this study was analyzed later with biomarker analyses [5]. The addition of lapatinib to capacitabine was found to be superior to capecitabine monotherapy alone and baseline extracellular domain (ECD) values as a biomarker failed to show the benefit of the addition of lapatinib to capecitabine. Di Leo et al. [10] composed a randomized, placebo-controlled study that investigated the results of adding lapatinib to paclitaxel as first-line therapy of advanced breast cancer in HER2 negative and HER2 uncharacterized patients. The paclitaxel dose was 175 mg/m^2 in every 3 weeks and patients were randomized to either lapatinib 1,500 mg or placebo daily. In this study, addition of lapatinib was associated with a longer median time to progression (TTP) and event free survival (EFS), ORR and clinical benefit rate were also significantly better in the HER2+ patients.

Hormonal status of our patient was ER (−), PR (−) and c-erb-B2 score was 3+. She was considered as trastuzumab-resistant and we considered lapatinib plus capecitabine for second-line chemotherapy regimen as a reasonable alternative for our patient. The pulmonary, mediastinal and axillary metastases showed a clinical complete response by the use of this combination treatment according to the RECIST criteria. She had no serious adverse effects except grade 1 nausea, dyspepsia, fatigue and hand–foot syndrome as in the study performed by Geyer et al. mentioned above. Therefore, no dose modification was needed.

There have been a few reports concerning the complete response to the lapatinib combination treatment in second-line setting. Complete response was seen only in one and partial response was seen in 21% of the patients in the most important published lapatinib and capecitabine combination treatment trial [6]. To our knowledge, this report contributes to the literature as a rare case of metastatic breast cancer with pulmonary and axillary metastases who achieved clinical remission after lapatinib plus capecitabine combination therapy. This combination should be an effective treatment option in metastatic breast cancer patients who have pulmonary and axillary metastases and resistance to trastuzumab.

Conflict of interest statement We declare that we have no conflict of interest.

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