

Case report

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Prolonged Disease Control with Lapatinib Monotherapy in HER2 Positive Metastatic Breast Cancer Patient: A Case Report

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A 50-year-old woman presented with locally advanced right breast cancer (cT2 cN3c M0) in September 2008. Diagnostic breast biopsy showed invasive carcinoma with the absence of hormonal receptor expression, Ki-67 35% HER2 2+ with presence of amplification by FISH. Fine needle aspiration of right supraclavicular lymph node showed presence of malignant cells of breast cancer.

From October 2008 to January 2009, she received neo-adjuvant anthracycline and paclitaxel combination followed by weekly paclitaxel and Trastuzumab. Right mastectomy and axillary lymph nodes dissection were carried out soon after. The pathological report showed invasive carcinoma and involvement of 9 of the 11 axillary lymph nodes removed [ypT2(m, is) (2.1 cm) ypN3c (11/17)]. The disease was still non endocrine

responsive (ER and PgR absent) HER2 was over-expressed and Ki-67 was 30%. Loco-regional irradiation was given to the breast area including the supraclavicular region. The patient received adjuvant chemotherapy with anthracycline and cyclophosphamide combination every three weeks for three cycles.

From July 2009 she was started on adjuvant trastuzumab and metronomic chemotherapy (cyclophosphamide and methotrexate). in December 2009, during trastuzumab therapy, an increase of tumor marker was reported, more than five times upper normal range.

A PET scan showed pathological increase uptake in right supraclavicular region and in mediastinal lymph nodes (Figure 1). Presence of tumor cells on supraclavicular nodes were confirmed by fine needle aspiration.

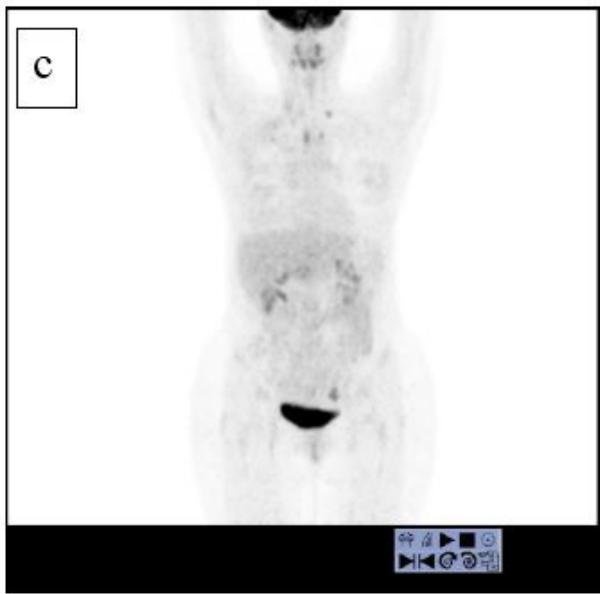
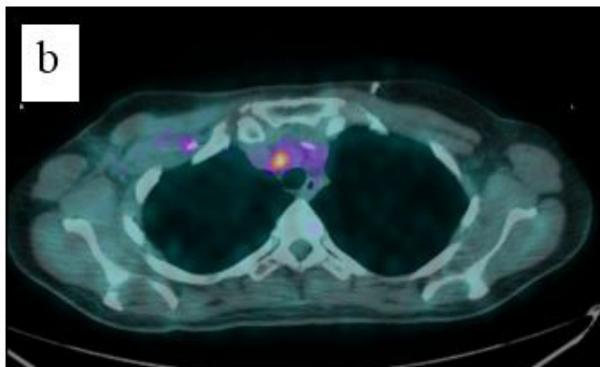
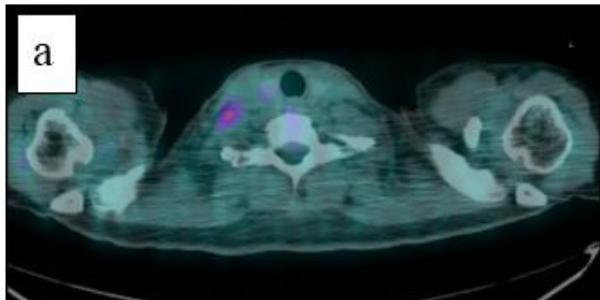


Figure 1: 18F-FDG PET/CT show in fused trans-axial images FDG-avid lymph nodes in right supraclavicular region (a) and in pre-vascular region of the mediastinum (b). MIP image (c) shows also non-specific uptake on the left supraclavicular region (site of central venous catheter) and the left ovary.

From April 2010 the patient started lapatinib and capecitabine combination with decrease of tumor markers in normal range and complete radiological response at the PET scan on September 2011 (Figure 2).

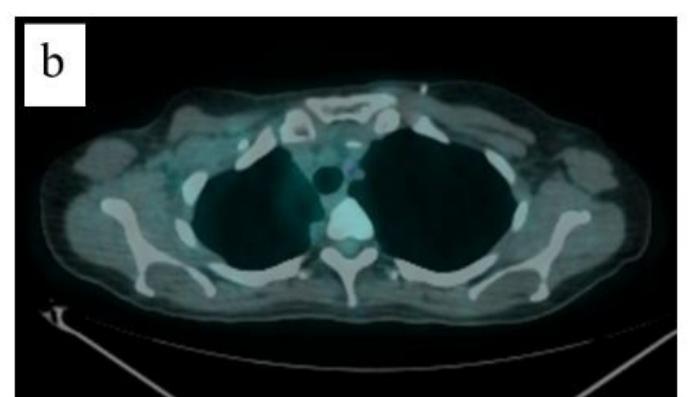
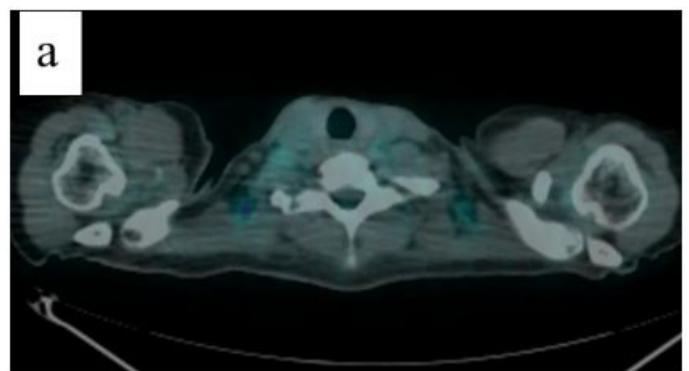


Figure 2: 18F-FDG PET/CT demonstrate in fused trans axial images the absence of uptake in right supraclavicular region (a) and in pre-vascular region of the mediastinum (b). MIP image (c) shows only non-specific uptake localized in the brown adipose tissue of the basis of the neck and bilateral supraclavicular regions.

From November 2011 the patient stopped capecitabine therapy and continued with lapatinib alone. A PET scan on September 2012 confirmed the complete response with persistence of tumoral markers in normal range. Regular echocardiograms

were done, no decrease of Left Ventricular Ejection Fraction (LVEF) was reported.

Our patient is still on treatment with lapatinib on December 2018. Lapatinib is an oral small molecule tyrosine kinase inhibitor and a dual EGFR and HER2 inhibitor. The combination of lapatinib and capecitabine represents a treatment option for metastatic HER2 positive breast cancer patients, previously treated with anthracycline, taxane and trastuzumab [1]. However, in the study of Blackwell et al. the use of lapatinib as single agent had modest clinical activity with response rates ranging from 5 to 8% in patients with heavily pre-treated HER2 positive metastatic breast cancer that progressed during prior treatment with trastuzumab [2]. By contrast, lapatinib monotherapy is a potentially effective treatment for relapsed or refractory HER2 positive inflammatory breast cancer achieving an objective response rate for combined clinically evaluable skin disease criteria and RECIST criteria (if applicable) of 39% [3].

Several data reported the safety and efficacy of prolonged use of trastuzumab and/or pertuzumab in metastatic breast cancer [4,5]. Data are also available with the prolonged use of antiangiogenic drug as bevacizumab [6].

In the study of Johnston et al. that evaluated the effect of adding lapatinib to the aromatase inhibitor, the median of treatment with letrozole-lapatinib was 40 weeks [4] while no data are reported with the use of lapatinib alone [7,8].

Generally, the metastatic breast cancer is an incurable disease. However, between 1% and 3% of patients who achieve a complete remission after chemotherapy doesn't experience a disease progression for prolonged period of time [6]. The patients who achieved long-term complete response compared with not responders are more frequently, premenopausal, with younger median age, lower tumor burden, and better performance status. The optimal duration of maintenance anti-HER2 therapy in patients achieving long-term complete remission is unknown. This needs to be balanced against toxicity, logistical burden and cost and may be considered in some patients, particularly if treatment re-challenge is available in case of progression [9]. On this topic the patient's preferences should be taken into account, too.

Our patient is on treatment with lapatinib from eight years, no grade 3-4 of toxicities or decrease of Left Ventricular Ejection Fraction (LVEF) were reported. Moreover, our patient achieved a complete response during lapatinib and capecitabine treatment and a persistent complete remission was observed during lapatinib monotherapy.

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