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Complete response after docetaxel+pertuzumab+trastuzumab chemotherapy for multimetastatic positive Her-2 breast cancer

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Summary

Human epidermal growth factor receptor 2 (Her-2)-positive breast cancer has been for a long time an aggressive with poor prognosis disease. However, thanks to targeted therapies, prolonged survival is possible, even in metastatic patients. Nevertheless, while the prognosis has improved, metastatic disease is still not curable. The authors report the original case of a 73-year-old Caucasian woman who presented with a T1a hormonal receptors and Her-2 positive multimetastatic (liver, bones, pleural, adrenal gland, and nodes). The patient began chemotherapy with docetaxel+pertuzumab+trastuzumab regimen with good tolerance, and no grade 3 or more adverse effect. Ca 15-3 level before treatment was high at 729 ng/ml and carcinoembryonic antigen (CEA) was at 1.2 ng/ml. After six cycles of chemotherapy, tomography positron emission scan showed metabolic complete response. Ca 15-3 level decreased to 35 ng/ml and CEA at 0.9 ng/ml. The patient is continuing pertuzumab+trastuzumab. Docetaxel associated to pertuzumab and trastuzumab in metastatic Her2-positive breast cancer is effective and can lead to complete response.

Key words: Breast cancer; Her-2 positive; Pertuzumab; Trastuzumab; Docetaxel; Metastases.

Introduction

Breast cancer is the most frequently diagnosed cancer in women. It is a heterogeneous disease, with many molecular subtypes identified. About 20 percent of breast cancer overexpress human epidermal growth factor receptor 2 (Her-2) which historically was associated with more aggressive phenotype and poorer prognosis. With the advent of trastuzumab therapy, however, the clinical outcome for patients with Her-2 positive tumors has markedly improved.

Case Report

The authors present the case of a 73-year-old Caucasian woman, gravida 3 and para 2. She had few comorbidities: hypertension, dyslipidemia, and hypothyroidism. Her mother was diagnosed with uterine cancer aged of 59 years.

One year before, she had a mammography that showed a 4-mm lesion in the right breast. A new mammography performed six months later showed a stable lump. Nine months later breast skin changes appeared with skin erythema and induration. Ultrasonography found a 4.8-mm right breast mass. Magnetic resonance imaging was performed, that concluded in a 8×5mm lump, with early enhancement. Ultrasound core biopsy was in favour of an invasive lobular estrogen receptors positive, progesterone negative, and Her-2 positive breast carcinoma.

The patient underwent breast conservation therapy and axillary lymph node dissection.

Immunohistological findings revealed a 35-mm right breast, invasive lobular cancer, without any angiolymphatic invasion. It was a high grade, SBR3, positive estrogen receptors 100%, negative progesterone receptors 5%, amplified Her-2, and Ki 67 at 20%; nine positive nodes were all massively infiltrated.

Tomography emission positron scan showed pathological hypermetabolism in nodes over and under the diaphragm, in liver, bones, in right adrenal gland, and in left pleura (Figure 1). The tumor was classified pT2N2a, Stage IV breast cancer. The patient was refered to the present oncology centre in order to begin chemotherapy.

On physical examination, the patient was Performans Status 0 and had no complaint. She had normal hepatic, renal, and hematologic functions. Pre-therapeutic Ca15-3 level was high at 729 ng/ml and CEA was at 1.2 ng/ml.

The patient received six cycles of chemotherapy regimen with docetaxel, associated with trastuzumab and pertuzumab. She reported no severe side-effects, only fatigue.

Tomography emission positron scan after chemotherapy showed complete metabolic response (Figure 2). Ca 15-3 and CEA levels dropped at respectively, 35 and 0.9 ng/ml. It was decided to continue the therapy with pertuzumab+ trastuzumab.

Discussion

Breast cancer is the most common cancer worldwide. In developed countries, between 6% and 10% of women will have metastatic disease when diagnosed with breast cancer [1].

The amplification of the human epidermal growth factor receptor 2 is observed in 25% to 30% of all breast cancers [2]. Patients with Her-2 positive breast cancer have more aggressive disease and significantly shortened disease-free survival and overall survival than do their counterparts without Her-2 overexpression. Trastuzumab has revolu-

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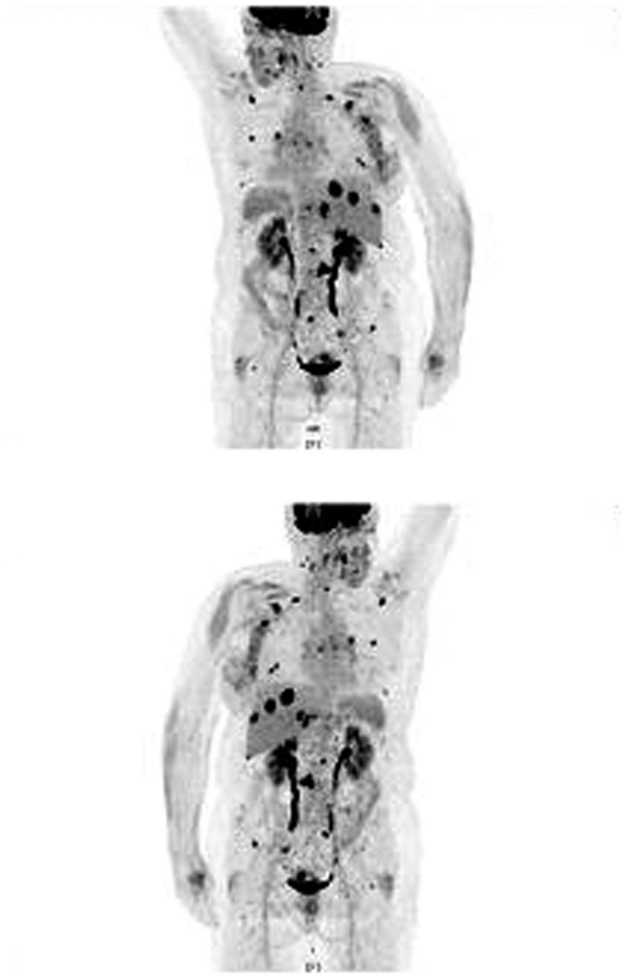

Figure 1. — Tomography emission positron scan before beginning chemotherapy.

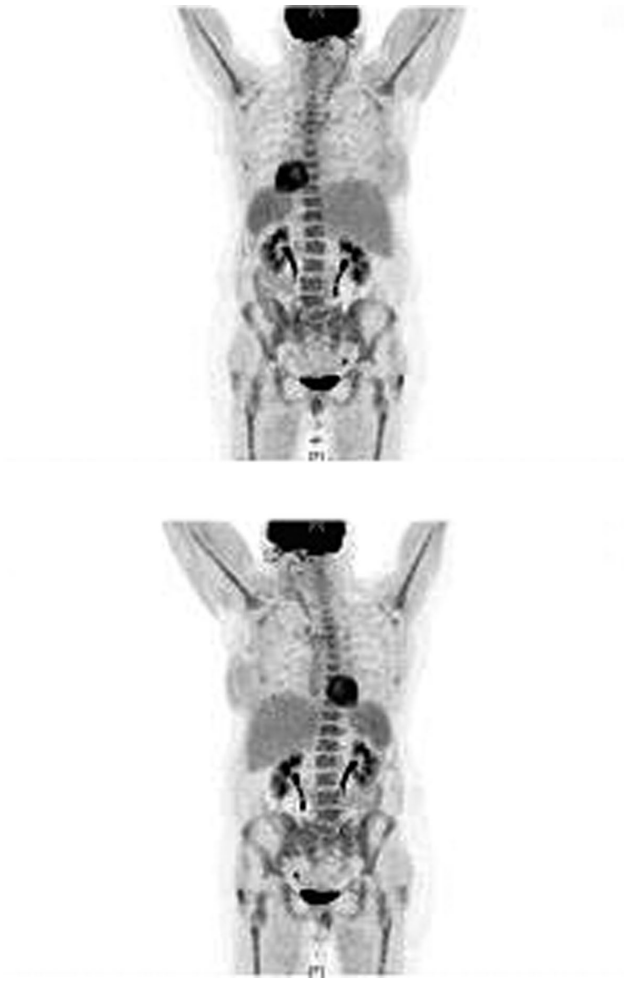

Figure 2. — Tomography emission positron scan after six cycles of chemotherapy.

tionized the treatment of Her-2 positive breast cancers [3]. Unfortunately, a large proportion of patients with Her-2 positive metastatic breast cancer treated with trastuzumab relapse after 12 to 24 months [4]. Nevertheless, a small proportion of Her-2 positive metastatic breast cancer patients remain in prolonged complete remission. The frequency of durable remission in this patient population is not known.

Pertuzumab is a Her-2 targeted humanized monoclonal antibody that inhibits dimerization and is more active than single inhibition with trastuzumab. Both trastuzumab and pertuzumab work against Her-2 positive breast cancers by blocking the cancer cell's ability to receive growth signals.

Based on the Clinical Evaluation Of Pertuzumab and Trastuzumab (CLEOPATRA) data, patients eligible to receive first-line treatment, for Her-2 positive metastatic breast cancer, should receive a triplet of chemotherapy in combination with trastuzumab and pertuzumab [5]. In the study, more than 80% of women who received the triplet had some response to the treatment compared to 69% of women who got only trastuzumab and docetaxel. The progression-free survival was six months longer in the group of women who received the three drugs.

The overall survival results showed that in the first arm, women lived about five years, whereas about only 3.5 years in the second arm.

In June 2012, the Food and Drug Administration approved using the targeted therapy pertuzumab in combination with trastuzumab and docetaxel to treat Her-2 positive metastatic breast cancer that has not yet been treated with either trastuzumab or chemotherapy.

Conclusion

The authors reported a case of complete response in a multimetastatic breast cancer elderly woman thanks to Her-

2 dual blockade and chemotherapy.

Once a poor prognosis, Her-2 advanced breast cancer has become the subtype of metastatic breast cancers with the longest medium survival, similar to luminal breast cancers. Her-2 targeted therapies have an undeniable favourable impact on the outcome of patients with Her-2 metastatic breast cancer.

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